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Schneewind et al.

(54) METHODS AND COMPOSITIONS INVOLVING PROTECTIVE STAPHYLOCOCCAL ANTIGENS, SUCH AS EBH POLYPEPTIDES

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See application file for complete search history.

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(57) **ABSTRACT**

The present invention concerns methods and compositions for treating or preventing a bacterial infection, particularly infection by a *Staphylococcus* bacterium. The invention provides methods and compositions for stimulating an immune response against the bacteria. In certain embodiments, the methods and compositions involve an Ebh antigen.

21 Claims, 23 Drawing Sheets

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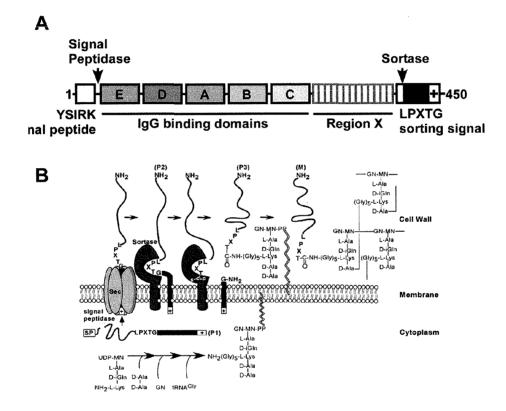
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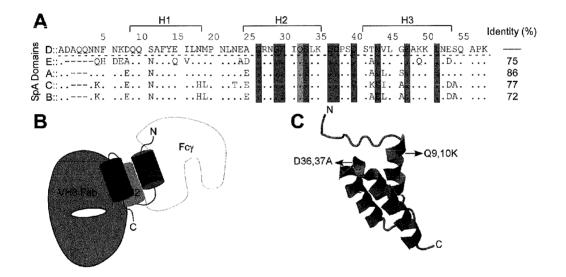
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FIGs. 1A-1B





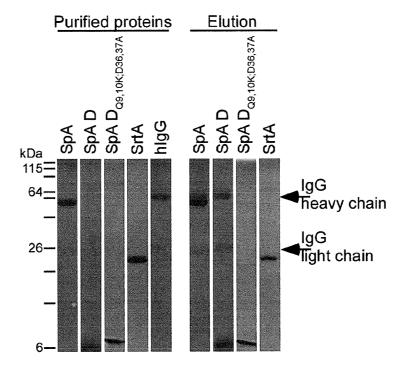


FIG. 3

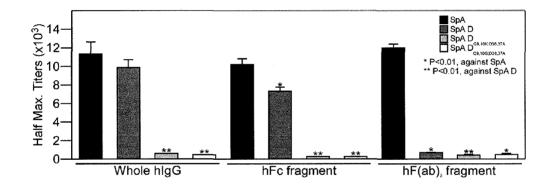


FIG. 4

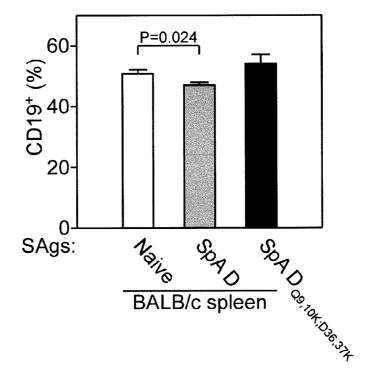


FIG. 5

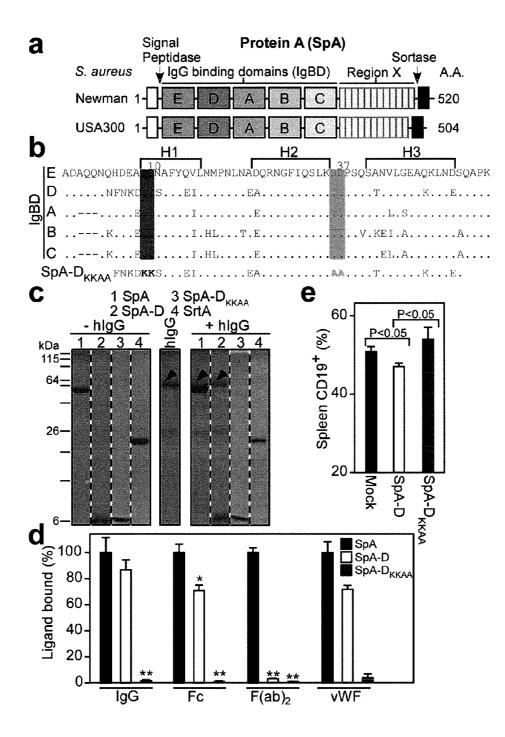


FIG. 6

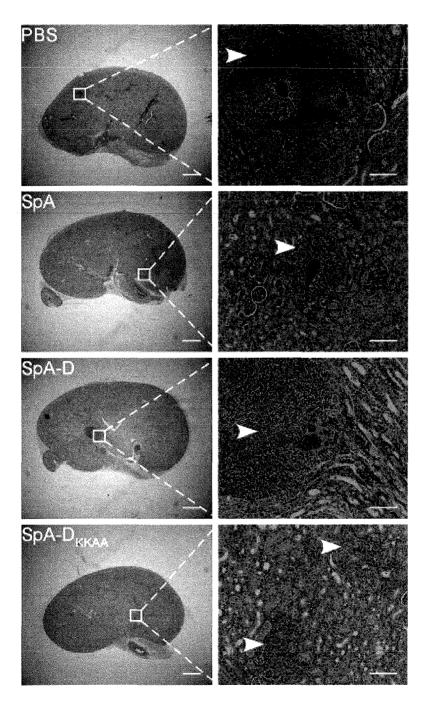


FIG. 7

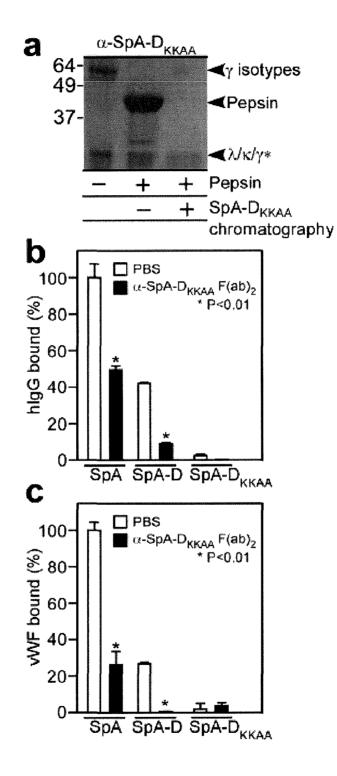


FIG. 8

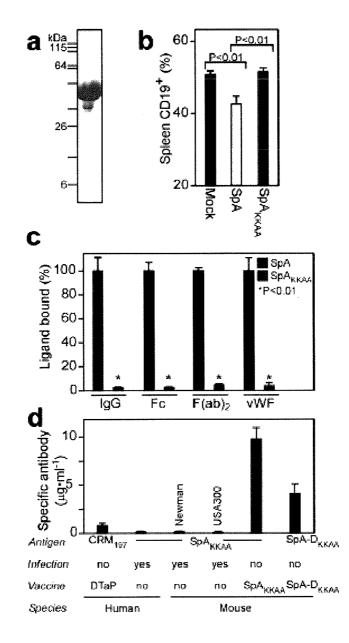


FIG. 9

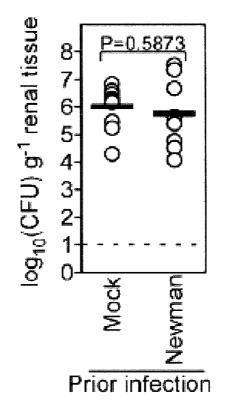


FIG. 10

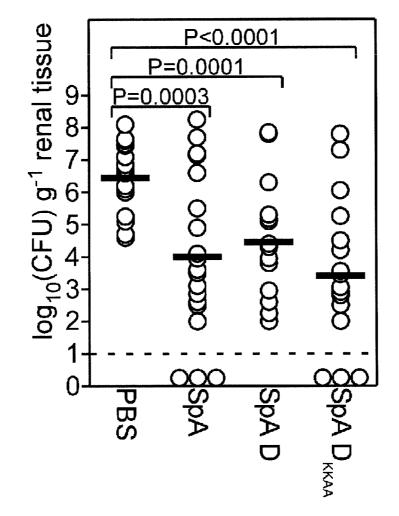


FIG. 11

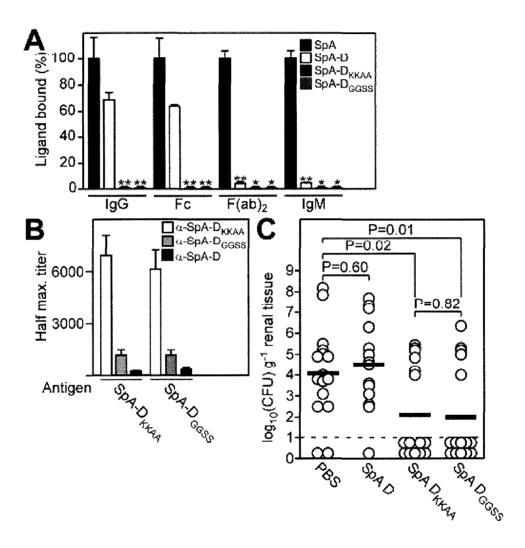
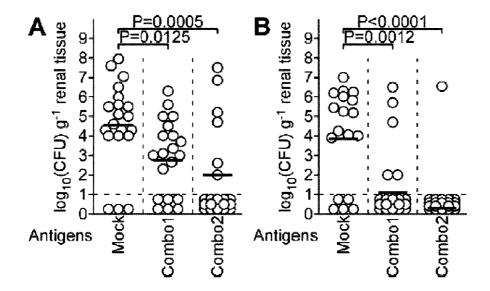
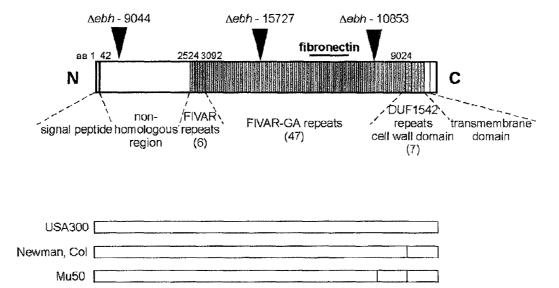


FIG. 12A-12C

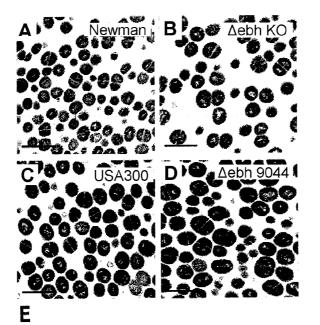


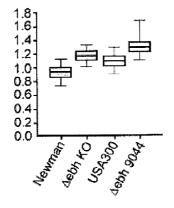
FIGs. 13A-13B



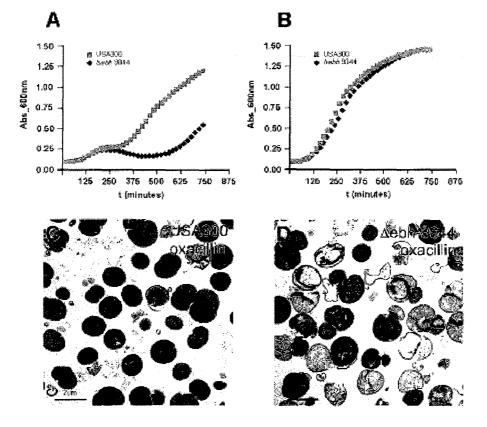
| = point mutation resulting in stop codon

FIG. 14





FIGs. 15A-15E



FIGs. 16A-16B

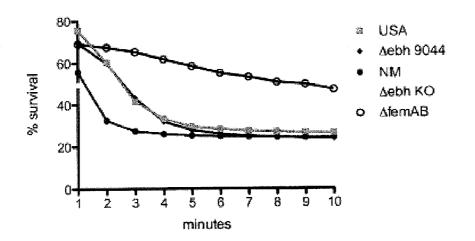
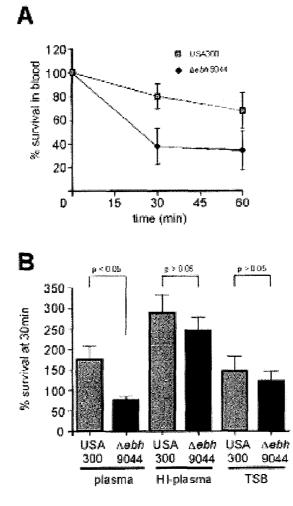


FIG. 17



FIGs. 18A-18B

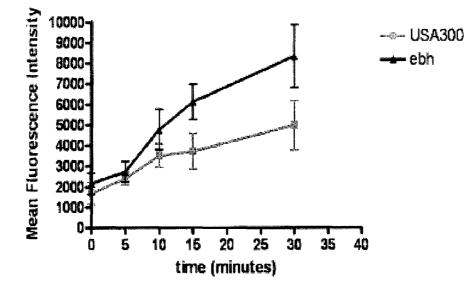
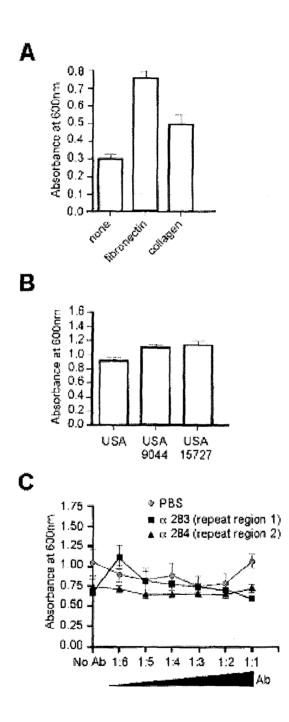
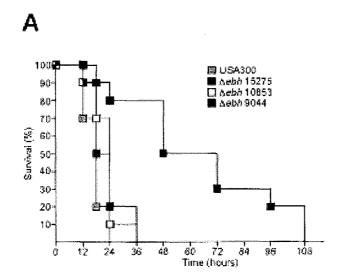


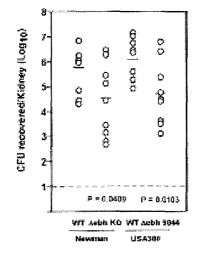
FIG. 19



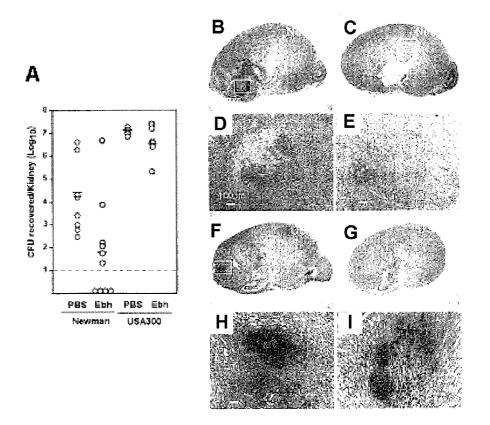
FIGs. 20A-20C



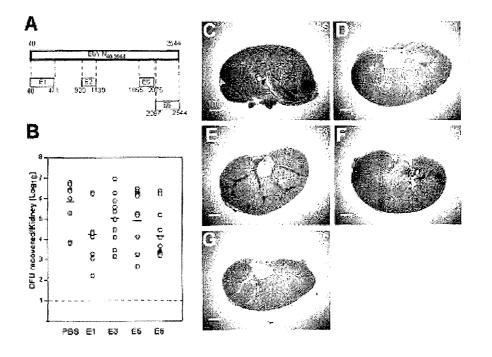




FIGs. 21A-21B



FIGs. 22A-22I



FIGs. 23A-23G

METHODS AND COMPOSITIONS INVOLVING PROTECTIVE STAPHYLOCOCCAL ANTIGENS, SUCH AS EBH POLYPEPTIDES

This application claims the benefit of U.S. Provisional Patent Application No. 61/483,396, filed May 6, 2011, each of which is incorporated herein by reference in its entirety.

This invention was made with government support under AI057153, AI042797, and GM007281 awarded by the ¹⁰ National Institutes of Health. The government has certain rights in the invention.

BACKGROUND OF THE INVENTION

I. Field of the Invention

The present invention relates generally to the fields of immunology, microbiology, and pathology. More particularly, it concerns methods and compositions involving bacterial Ebh polypeptides and segments thereof, which can be 20 used to invoke an immune response against the bacteria.

II. Background

The number of both community acquired and hospital acquired infections have increased over recent years with the increased use of intravascular devices. Hospital acquired 25 (nosocomial) infections are a major cause of morbidity and mortality, more particularly in the United States, where it affects more than 2 million patients annually. The most frequent infections are urinary tract infections (33% of the infections), followed by pneumonia (15.5%), surgical site infec- 30 tions (14.8%) and primary bloodstream infections (13%) (Emorl and Gaynes, 1993).

The major nosocomial pathogens include *Staphylococcus aureus*, coagulase-negative Staphylococci (mostly *Staphylococcus epidermidis*), *Enterococcus* spp., *Escherichia coli* and 35 *Pseudomonas aeruginosa*. Although these pathogens cause approximately the same number of infections, the severity of the disorders they can produce combined with the frequency of antibiotic resistant isolates balance this ranking towards S. *aureus* and *S. epidermidis* as being the most significant noso- 40 comial pathogens.

Staphylococci can cause a wide variety of diseases in humans and other animals through either toxin production or invasion. Staphylococcal toxins are a common cause of food poisoning, as the bacteria can grow in improperly-stored 45 food.

Staphylococcus epidermidis is a normal skin commensal which is also an important opportunistic pathogen responsible for infections of impaired medical devices and infections at sites of surgery. Medical devices infected by *S. epi-* 50 *dermidis* include cardiac pacemakers, cerebrospinal fluid shunts, continuous ambulatory peritoneal dialysis catheters, orthopedic devices and prosthetic heart valves.

Staphylococcus aureus is the most common cause of noso-comial infections with a significant morbidity and mortality. 55It is the cause of some cases of osteomyelitis, endocarditis,septic arthritis, pneumonia, abscesses, and toxic shock syn-drome. S. aureus can survive on dry surfaces, increasing thechance of transmission. Any S. aureus infection can cause thestaphylococcal scalded skin syndrome, a cutaneous reaction 60to exotoxin absorbed into the bloodstream. It can also cause atype of septicemia called pyaemia that can be life-threaten-ing. Methicillin-resistant Staphylococcus aureus (MRSA)has also become a major cause of hospital-acquired infections.65

S. aureus and *S. epidermidis* infections are typically treated with antibiotics, with penicillin being the drug of choice,

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whereas vancomycin is used for methicillin resistant isolates. The percentage of staphylococcal strains exhibiting widespectrum resistance to antibiotics has become increasingly prevalent, posing a threat for effective antimicrobial therapy. In addition, the recent emergence of vancomycin resistant *S. aureus* strain has aroused fear that MRSA strains are emerging and spreading for which no effective therapy is available.

An alternative to antibiotic treatment for staphylococcal infections is under investigation that uses antibodies directed against staphylococcal antigens. This therapy involves administration of polyclonal antisera (WO00/15238, WO00/12132) or treatment with monoclonal antibodies against lipoteichoic acid (WO98/57994).

An alternative approach to the use of antibiotics would be 15 the use of active vaccination to generate an immune response against staphylococci. The *S. aureus* genome has been sequenced and many of the coding sequences have been identified (WO02/094868, EP0786519), which could lead to the identification of potential antigens. The same is true for *S.* 20 *epidermidis* (WO01/34809). As a refinement of this approach, others have identified proteins that are recognized by hyperimmune sera from patients who have suffered staphylococcal infection (WO01/98499, WO02/059148).

S. aureus secretes a plethora of virulence factors into the extracellular milieu (Archer, 1998; Dinges et al., 2000; Foster, 2005; Shaw et al., 2004; Sibbald et al., 2006). Like most secreted proteins, these virulence factors are translocated by the Sec machinery across the plasma membrane. Proteins secreted by the Sec machinery bear an N-terminal leader peptide that is removed by leader peptidase once the preprotein is engaged in the Sec translocon (Dalbey and Wickner, 1985; van Wely et al., 2001). Recent genome analysis suggests that Actinobacteria and members of the Firmicutes encode an additional secretion system that recognizes a subset of proteins in a Sec-independent manner (Pallen, 2002). ESAT-6 (early secreted antigen target 6 kDa) and CFP-10 (culture filtrate antigen 10 kDa) of Mycobacterium tuberculosis represent the first substrates of this novel secretion system termed ESX-1 or 5 nm in M. tuberculosis (Andersen et al., 1995; Hsu et al, 2003; Pym et al., 2003; Stanley et al., 2003). In S. aureus, two ESAT-6 like factors designated EsxA and EsxB are secreted by the Ess pathway (ESAT-6 secretion system) (Burts et al., 2005).

The first generation of vaccines targeted against *S. aureus* or against the exoproteins it produces have met with limited success (Lee, 1996). There remains a need to develop effective vaccines against staphylococcal infections. Additional compositions for treating staphylococcal infections are also needed.

SUMMARY OF THE INVENTION

Ebh is a 1.1 MDa (10,422 amino acid residues) polypeptide, transcribed from a 30.1 kb gene single open reading frame. Although ebh is found in all *S. aureus* isolates, it displays variations in size, owing to the variable numbers of repeats in the mid—and 3' (C-terminal) sections of both the gene and its translational product. Gene variation in *S. aureus* is rare and variable genes are generally known to be contributors to virulence, including coagulase (coa), eap/map, sdrCDE, protein A (SpA), ESAT secretion genes (ess), and the accessory gene regulatory locus (agr) (Buckling et al, 2005; Watanabe et al., 2009).

In certain embodiments an Ebh polypeptide or antigen is a full length or polypeptide segment of Ebh polypeptide. In certain aspects, the Ebh polypeptide comprises or consists of the amino acid sequence that is 70, 75, 80, 85, 90, 95, 98, 99,

or 100% identical to the amino acid sequence of SEQ ID NO:24 or one or more segments of 10, 50, 100, 500, 1000, 2000, 3000, 4000, 5000 consecutive amino acids (including all values and ranges there between) of SEQ ID NO:24. In other embodiments the Ebh polypeptide or antigen comprises 5 a segment of the Ebh polypeptide. The Ebh polypeptide segment can comprise at least or at most 0, 1, 2, 3, 4, 5, 10, 20, 30, 40 or more (including all values and ranges there between) Ebh amino acid repeats (e.g., FIVAR, FIVAR-GA, and/or DUF1542 repeats). In certain aspects the Ebh segment or 10 antigen can comprise, consist of, or consist essentially of a polypeptide having an amino acid sequence that is 70, 75, 80, 85, 90, 95, 98, 99, or 100% identical to the amino acid sequence corresponding to amino acids 1, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 1000 to 100, 500, 600, 700, 800, 900, 15 1000, 2000, 3000, 10000 (including all values and ranges there between) of SEQ ID NO:24. In a further aspect, the Ebh polypeptide segment or antigen comprises an amino acid sequence corresponding to amino acids 40-2544 of SEQ ID NO:24 or a sequence 70, 75, 80, 85, 90, 95, 98, 99, or 100% 20 identical to the amino acid sequence of amino acids 40-2544 of SEQ ID NO:24. In a still further aspect the Ebh polypeptide segment or antigen comprises an amino acid sequence corresponding to amino acids 40-471 or 2087-2544 of SEQ ID NO:24 or a sequence 70, 75, 80, 85, 90, 95, 98, 99, or 100% 25 identical to the amino acid sequence of amino acids 40-471 or 2087-2544 of SEQ ID NO:24.

The Ebh polypeptide or antigen of the invention can be formulated in a pharmaceutically acceptable composition. The composition can further comprise one or more of, at least, 30 or at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 19 additional staphylococcal antigens, variants or immunogenic fragments thereof (e.g., Eap, SpA, SpA variants, SpA or a SpA variant (such as a SpA with amino acid substitutions as position(s) 9, 10, 36 and/or 37, e.g., 35 SpA_{KKAA}, SpA_{GGSS}, SpA_{KK}, SpA_{AA}), Emp, EsaB, EsaC, EsxA, EsxB (e.g., an EsxA-EsxB fusion protein), SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla (e.g., H35 mutants), IsdC, SasF, vWbp, or vWh). Thus, in some aspects a composition comprises an Ebh polypeptide and a Sta006, 40 Sta011, Hla (e.g., H35 mutants such as a H35L mutant) and/or an EsxA-EsxB fusion protein. In still further aspects, a composition comprises a Ebh polypeptide in combination with one of the antigens or antigen combinations disclosed in WO/2010/119343, incorporated herein by reference.

In certain aspects the bacterial antigens include one or more of sta001, sta002, sta003, sta004, sta005, sta006, sta007, sta008, sta009, sta010, sta011, sta012, sta013, sta014, sta015, sta016, sta017, sta018, sta019, sta020, sta021, sta022, $sta023, sta024, sta025, sta026, sta027, sta028, sta029, sta030, \ \ 50$ sta031, sta032, sta033, sta034, sta035, sta036, sta037, sta038, sta039, sta040, sta041, sta042, sta043, sta044, sta045, sta046, sta047, sta048, sta049, sta050, sta051, sta052, sta053, sta054, sta055, sta056, sta057, sta058, sta059, sta060, sta061, sta062, sta063, sta064, sta065, sta066, sta067, sta068, sta069, sta070, 55 sta071, sta072, sta073, sta074, sta075, sta076, sta077, sta078, sta079, sta080, sta081, sta082, sta083, sta084, sta085, sta086, sta087, sta088, sta089, sta090, sta091, sta092, sta093, sta094, sta095, sta096, sta097, sta098, sta099, sta100, sta101, sta102, sta103, sta104, sta105, sta106, sta107, sta108, sta109, sta110, 60 sta111, sta112, sta113, sta114, sta115, sta116, sta117, sta118, sta119, sta120, or EsxAB hybrid polypeptide or immunogenic fragment thereof (see PCT publication WO/2010/ 119343, which is incorporated herein by reference in its entirety).

Additional staphylococcal antigens that can be used in combination with an Ebh polypeptide include, but are not

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limited to 52 kDa vitronectin binding protein (WO 01/60852), Aaa (GenBank CAC80837), Aap (GenBank accession AJ249487), Ant (GenBank accession NP 372518), autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/ 0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg²⁺ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/ Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein (see PCT publications WO2007/113222, WO2006/032472, WO2006/032475, WO2007/113223, WO2006/032500, each of which is incorporated herein by reference in their entirety). The staphylococcal antigen or immunogenic fragment can be administered concurrently with the Ebh polypeptide or segment thereof. The staphylococcal antigen or immunogenic fragment and the Ebh polypeptide can be administered in the same composition. The Ebh polypeptide or segment thereof can also be a recombinant nucleic acid molecule encoding an Ebh polypeptide or segment thereof. A recombinant nucleic acid molecule can encode the Ebh polypeptide or segment thereof and at least one staphylococcal antigen or immunogenic fragment thereof.

In other aspects, the Ebh polypeptide or segment thereof may be used in combination with secreted factors or surface antigens including, but not limited to one or more of an isolated Eap, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, SpA, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, or vWh polypeptide, variant, or immunogenic segment thereof, sta001 antigen or immunogenic fragment thereof, sta002 antigen or immunogenic fragment thereof, sta003 antigen or immunogenic fragment thereof, sta004 antigen or immunogenic fragment thereof, sta005 antigen or immunogenic fragment thereof, sta006 antigen or immunogenic fragment thereof, sta007 antigen or immunogenic fragment thereof, sta008 antigen or immunogenic fragment 45 thereof, sta009 antigen or immunogenic fragment thereof, sta010 antigen or immunogenic fragment thereof, sta011 antigen or immunogenic fragment thereof, sta012 antigen or immunogenic fragment thereof, sta013 antigen or immunogenic fragment thereof, sta014 antigen or immunogenic fragment thereof, sta015 antigen or immunogenic fragment thereof, sta016 antigen or immunogenic fragment thereof, sta017 antigen or immunogenic fragment thereof, sta018 antigen or immunogenic fragment thereof, sta019 antigen or immunogenic fragment thereof, sta020 antigen or immunogenic fragment thereof, sta021 antigen or immunogenic fragment thereof, sta022 antigen or immunogenic fragment thereof, sta023 antigen or immunogenic fragment thereof, sta024 antigen or immunogenic fragment thereof, sta025 antigen or immunogenic fragment thereof, sta026 antigen or immunogenic fragment thereof, sta027 antigen or immunogenic fragment thereof, sta028 antigen or immunogenic fragment thereof, sta029 antigen or immunogenic fragment thereof, sta030 antigen or immunogenic fragment thereof, sta031 antigen or immunogenic fragment thereof, sta032 antigen or immunogenic fragment thereof, sta033 antigen or immunogenic fragment thereof, sta034 antigen or immunogenic fragment thereof, sta035 antigen or immunogenic frag-

thereof, sta037 antigen or immunogenic fragment thereof, sta038 antigen or immunogenic fragment thereof, sta039 antigen or immunogenic fragment thereof, sta040 antigen or immunogenic fragment thereof, sta041 antigen or immuno- 5 genic fragment thereof, sta042 antigen or immunogenic fragment thereof, sta043 antigen or immunogenic fragment thereof, sta044 antigen or immunogenic fragment thereof, sta045 antigen or immunogenic fragment thereof, sta046 antigen or immunogenic fragment thereof, sta047 antigen or 10 immunogenic fragment thereof, sta048 antigen or immunogenic fragment thereof, sta049 antigen or immunogenic fragment thereof, sta050 antigen or immunogenic fragment thereof, sta051 antigen or immunogenic fragment thereof, sta052 antigen or immunogenic fragment thereof, sta053 15 antigen or immunogenic fragment thereof, sta054 antigen or immunogenic fragment thereof, sta055 antigen or immunogenic fragment thereof, sta056 antigen or immunogenic fragment thereof, sta057 antigen or immunogenic fragment thereof, sta058 antigen or immunogenic fragment thereof, 20 sta059 antigen or immunogenic fragment thereof, sta060 antigen or immunogenic fragment thereof, sta061 antigen or immunogenic fragment thereof, sta062 antigen or immunogenic fragment thereof, sta063 antigen or immunogenic fragment thereof, sta064 antigen or immunogenic fragment 25 thereof, sta065 antigen or immunogenic fragment thereof, sta066 antigen or immunogenic fragment thereof, sta067 antigen or immunogenic fragment thereof, sta068 antigen or immunogenic fragment thereof, sta069 antigen or immunogenic fragment thereof, sta070 antigen or immunogenic frag- 30 ment thereof, sta071 antigen or immunogenic fragment thereof, sta072 antigen or immunogenic fragment thereof, sta073 antigen or immunogenic fragment thereof, sta074 antigen or immunogenic fragment thereof, sta075 antigen or immunogenic fragment thereof, sta076 antigen or immuno- 35 genic fragment thereof, sta077 antigen or immunogenic fragment thereof, sta078 antigen or immunogenic fragment thereof, sta079 antigen or immunogenic fragment thereof, sta080 antigen or immunogenic fragment thereof, sta081 antigen or immunogenic fragment thereof, sta082 antigen or 40 immunogenic fragment thereof, sta083 antigen or immunogenic fragment thereof, sta084 antigen or immunogenic fragment thereof, sta085 antigen or immunogenic fragment thereof, sta086 antigen or immunogenic fragment thereof, sta087 antigen or immunogenic fragment thereof, sta088 45 antigen or immunogenic fragment thereof, sta089 antigen or immunogenic fragment thereof, sta090 antigen or immunogenic fragment thereof, sta091 antigen or immunogenic fragment thereof, sta092 antigen or immunogenic fragment thereof, sta093 antigen or immunogenic fragment thereof, 50 sta094 antigen or immunogenic fragment thereof, sta095 antigen or immunogenic fragment thereof, sta096 antigen or immunogenic fragment thereof, sta097 antigen or immunogenic fragment thereof, sta098 antigen or immunogenic fragment thereof, sta099 antigen or immunogenic fragment 55 thereof, sta100 antigen or immunogenic fragment thereof, sta101 antigen or immunogenic fragment thereof, sta102 antigen or immunogenic fragment thereof, sta103 antigen or immunogenic fragment thereof, sta104 antigen or immunogenic fragment thereof, sta105 antigen or immunogenic frag- 60 ment thereof, sta106 antigen or immunogenic fragment thereof, sta107 antigen or immunogenic fragment thereof, sta108 antigen or immunogenic fragment thereof, sta109 antigen or immunogenic fragment thereof, sta110 antigen or immunogenic fragment thereof, sta111 antigen or immuno-65 genic fragment thereof, sta112 antigen or immunogenic fragment thereof, sta113 antigen or immunogenic fragment

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thereof, stal14 antigen or immunogenic fragment thereof, stal15 antigen or immunogenic fragment thereof, stal16 antigen or immunogenic fragment thereof, stal17 antigen or immunogenic fragment thereof, stal18 antigen or immunogenic fragment thereof, stal19 antigen or immunogenic fragment thereof, stal20 antigen or immunogenic fragment thereof, or EsxAB hybrid polypeptide or immunogenic fragment thereof.

Additional staphylococcal antigens that can be used in combination with an Ebh polypeptide or segment thereof include, but are not limited to 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5.648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein.

In certain embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of Eap, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, SpA, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh, 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288, 214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/ saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, Vitronectin binding protein, sta001, sta002, sta003, sta004, sta005, sta006, sta007, sta008, sta009, sta010, sta011, sta012, sta013, sta014, sta015, sta016, sta017, sta018, sta019, sta020, sta021, sta022, sta023, sta024, sta025, sta026, sta027, sta028, sta029, sta030, sta031, sta032, sta033, sta034, sta035, sta036, sta037, sta038, sta039, sta040, sta041, sta042, sta043, sta044, sta045, sta046, sta047, sta048, sta049, sta050, sta051, sta052, sta053, sta054, sta055, sta056, sta057, sta058, sta059, sta060, sta061, sta062, sta063, sta064, sta065, sta066, sta067, sta068, sta069, sta070, sta071, sta072, sta073, sta074, sta075, sta076, sta077, sta078, sta079, sta080, sta081, sta082, sta083, sta084, sta085, sta086, sta087, sta088, sta089, sta090, sta091, sta092, sta093, sta094, sta095, sta096, sta097, sta098, sta099, sta100, sta101, sta102, sta103, sta104, sta105, sta106, sta107, sta108, sta109, sta110, sta111, sta112, sta113, sta114, sta115, sta116, sta117, sta118, sta119, sta120, and/or EsxAB hybrid polypeptide or immunogenic fragment thereof can be specifically excluded from a formulation of the invention. In further embodiments the methods and compositions use or include or encode all or part of the SdrD, ClfA and/or FnbpB (FnbB) antigens.

Protein A (SpA) (SEQ ID NO:33), a cell wall anchored surface protein of *Staphylococcus aureus*, provides for bac-

terial evasion from innate and adaptive immune responses. Protein A binds immunoglobulins at their Fc portion, interacts with the VH3 domain of B cell receptors inappropriately stimulating B cell proliferation and apotosis, binds to von Willebrand factor A1 domains to activate intracellular clot- 5 ting, and also binds to the TNF Receptor-1 to contribute to the pathogenesis of Staphylococcal pneumonia. Due to the fact that Protein A captures immunoglobulin and displays toxic attributes, the possibility that this surface molecule may function as a vaccine in humans has not been rigorously pursued. 10 Here the inventors demonstrate that Protein A variants no longer able to bind to immunoglobulins, which are thereby removed of their toxigenic potential, i.e., are non-toxigenic, stimulate humoral immune responses that protect against staphylococcal disease.

In certain embodiments the SpA variant is a full length SpA variant comprising a variant A, B, C, D, and/or E domain. In certain aspects, the SpA variant comprises or consists of the amino acid sequence that is 80, 90, 95, 98, 99, or 100% identical to the amino acid sequence of SEQ ID NO:34 In 20 other embodiments the SpA variant comprises a segment of SpA. The SpA segment can comprise at least or at most 1, 2, 3, 4, 5 or more IgG binding domains. The IgG domains can be at least or at most 1, 2, 3, 4, 5 or more variant A, B, C, D, or E domains. In certain aspects the SpA variant comprises at least 25 or at most 1, 2, 3, 4, 5, or more variant A domains. In a further aspect the SpA variant comprises at least or at most 1, 2, 3, 4, 5, or more variant B domains. In still a further aspect the SpA variant comprises at least or at most 1, 2, 3, 4, 5, or more variant C domains. In yet a further aspect the SpA variant 30 comprises at least or at most 1, 2, 3, 4, 5, or more variant D domains. In certain aspects the SpA variant comprises at least or at most 1, 2, 3, 4, 5, or more variant E domains. In a further aspect the SpA variant comprises a combination of A, B, C, D, and E domains in various combinations and permutations. 35 The combinations can include all or part of a SpA signal peptide segment, a SpA region X segment, and/or a SpA sorting signal segment. In other aspects the SpA variant does not include a SpA signal peptide segment, a SpA region X segment, and/or a SpA sorting signal segment. In certain 40 aspects a variant A domain comprises a substitution at position(s) 7, 8, 34, and/or 35 of SEQ ID NO:4. In another aspect a variant B domain comprises a substitution at position(s) 7, 8, 34, and/or 35 of SEQ ID NO:6. In still another aspect a variant C domain comprises a substitution at position(s) 7, 8, 45 34, and/or 35 of SEQ ID NO:5. In certain aspects a variant D domain comprises a substitution at position(s) 9, 10, 36, and/or 37 of SEQ ID NO:2. In a further aspect a variant E domain comprises a substitution at position(s) 6, 7, 33, and/or 34 of SEQ ID NO:3.

In certain aspects, an SpA domain D variant or its equivalent can comprise a mutation at position 9 and 36; 9 and 37; 9 and 10; 36 and 37; 10 and 36; 10 and 37; 9, 36, and 37; 10, 36, and 37, 9, 10 and 36; or 9, 10 and 37 of SEQ ID NO:2. In a further aspect, analogous mutations can be included in one or 55 position 10 of SEQ ID NO:2 is replaced by a lysine. more of domains A, B, C, or E.

In further aspects, the amino acid glutamine (Q) at position 9 of SEQ ID NO:2 (or its analogous amino acid in other SpA domains) can be replaced with an alanine (A), an asparagine (N), an aspartic acid (D), a cysteine (C), a glutamic acid (E), 60 a phenylalanine (F), a glycine (G), a histidine (H), an isoleucine (I), a lysine (K), a leucine (L), a methionine (M), a proline (P), a serine (S), a threonine (T), a valine (V), a tryptophane (W), or a tyrosine (Y). In some aspects the glutamine at position 9 can be substituted with an arginine 65 (R). In a further aspect, the glutamine at position 9 of SEQ ID NO:2, or its equivalent, can be substituted with a lysine or a

glycine. Any 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the substitutions can be explicitly excluded.

In another aspect, the amino acid glutamine (Q) at position 10 of SEQ ID NO:2 (or its analogous amino acid in other SpA domains) can be replaced with an alanine (A), an asparagine (N), an aspartic acid (D), a cysteine (C), a glutamic acid (E), a phenylalanine (F), a glycine (G), a histidine (H), an isoleucine (I), a lysine (K), a leucine (L), a methionine (M), a proline (P), a serine (S), a threonine (T), a valine (V), a tryptophane (W), or a tyrosine (Y). In some aspects the glutamine at position 10 can be substituted with an arginine (R). In a further aspect, the glutamine at position 10 of SEQ ID NO:2, or its equivalent, can be substituted with a lysine or a glycine. Any 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the substitutions can be explicitly excluded.

In certain aspects, the aspartic acid (D) at position 36 of SEQ ID NO:2 (or its analogous amino acid in other SpA domains) can be replaced with an alanine (A), an asparagine (N), an arginine (R), a cysteine (C), a phenylalanine (F), a glycine (G), a histidine (H), an isoleucine (I), a lysine (K), a leucine (L), a methionine (M), a proline (P), a glutamine (Q), a serine (S), a threonine (T), a valine (V), a tryptophane (W), or a tyrosine (Y). In some aspects the aspartic acid at position 36 can be substituted with a glutamic acid (E). In certain aspects, an aspartic acid at position 36 of SEQ ID NO:2, or its equivalent, can be substituted with an alanine or a serine. Any 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the substitutions can be explicitly excluded.

In another aspect, the aspartic acid (D) at position 37 of SEQ ID NO:2 (or its analogous amino acid in other SpA domains) can be replaced with an alanine (A), a an asparagine (N), an arginine (R), a cysteine (C), a phenylalanine (F), a glycine (G), a histidine (H), an isoleucine (I), a lysine (K), a leucine (L), a methionine (M), a proline (P), a glutamine (Q), a serine (S), a threonine (T), a valine (V), a tryptophane (W), or a tyrosine (Y). In some aspects the aspartic acid at position 37 can be substituted with a glutamic acid (E). In certain aspects, an aspartic acid at position 37 of SEQ ID NO:2, or its equivalent, can be substituted with an alanine or a serine. Any 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the substitutions can be explicitly excluded.

In a particular embodiment the amino at position 9 of SEQ ID NO:2 (or an analogous amino acid in another SpA domain) is replaced by an alanine (A), a glycine (G), an isoleucine (I), a leucine (L), a proline (P), a serine (S), or a valine (V), In certain aspects the amino acid at position 9 of SEQ ID NO:2 is replaced by a glycine. In a further aspect the amino acid at position 9 of SEQ ID NO:2 is replaced by a lysine.

In a particular embodiment the amino at position 10 of SEQ ID NO:2 (or an analogous amino acid in another SpA domain) is replaced by an alanine (A), a glycine (G), an isoleucine (I), a leucine (L), a proline (P), a serine (S), or a valine (V), In certain aspects the amino acid at position 10 of SEQ ID NO:2 is replaced by a glycine. In a further aspect the amino acid at

In a particular embodiment the amino at position 36 of SEQ ID NO:2 (or an analogous amino acid in another SpA domain) is replaced by an alanine (A), a glycine (G), an isoleucine (I), a leucine (L), a proline (P), a serine (S), or a valine (V), In certain aspects the amino acid at position 36 of SEQ ID NO:2 is replaced by a serine. In a further aspect the amino acid at position 36 of SEQ ID NO:2 is replaced by an alanine.

In a particular embodiment the amino at position 37 of SEQ ID NO:2 (or an analogous amino acid in another SpA domain) is replaced by an alanine (A), a glycine (G), an isoleucine (I), a leucine (L), a proline (P), a serine (S), or a valine (V), In certain aspects the amino acid at position 37 of SEQ ID NO:2 is replaced by a serine. In a further aspect the amino acid at position 37 of SEQ ID NO:2 is replaced by an alanine.

In certain aspects the SpA variant includes (a) one or more amino acid substitution in an IgG Fc binding sub-domain of SpA domain A, B, C, D, and/or E that disrupts or decreases 5 binding to IgG Fc, and (b) one or more amino acid substitution in a VH3 binding sub-domain of SpA domain A, B, C, D, and/or E that disrupts or decreases binding to VH3. In still further aspects the amino acid sequence of a SpA variant comprises an amino acid sequence that is at least 50%, 60%, 10 70%, 80%, 90%, 95%, or 100% identical, including all values and ranges there between, to the amino acid sequence of SEQ ID NOs:2-6.

In a further aspect the SpA variant includes (a) one or more amino acid substitution in an IgG Fc binding sub-domain of 15 SpA domain D, or at a corresponding amino acid position in other IgG domains, that disrupts or decreases binding to IgG Fc, and (b) one or more amino acid substitution in a VH3 binding sub-domain of SpA domain D, or at a corresponding amino acid position in other IgG domains, that disrupts or 20 decreases binding to VH3. In certain aspects amino acid residue F5, Q9, Q10, S11, F13, Y14, L17, N28, I31, and/or K35 (SEQ ID NO:2, QQNNFNKDQQSAFYEILNMPNL-NEAQRNGFIQSLKDDPSQSTNVLGEAKKLNES) of the IgG Fc binding sub-domain of domain D are modified or 25 substituted. In certain aspects amino acid residue Q26, G29, F30, S33, D36, D37, Q40, N43, and/or E47 (SEQ ID NO:2) of the VH3 binding sub-domain of domain D are modified or substituted such that binding to Fc or VH3 is attenuated. In further aspects corresponding modifications or substitutions 30 can be engineered in corresponding positions of the domain A, B, C, and/or E. Corresponding positions are defined by alignment of the domain D amino acid sequence with one or more of the amino acid sequences from other IgG binding domains of SpA, for example see FIG. 2A. In certain aspects 35 the amino acid substitution can be any of the other 20 amino acids. In a further aspect conservative amino acid substitutions can be specifically excluded from possible amino acid substitutions. In other aspects only non-conservative substitutions are included. In any event, any substitution or combi- 40 nation of substitutions that reduces the binding of the domain such that SpA toxicity is significantly reduced is contemplated. The significance of the reduction in binding refers to a variant that produces minimal to no toxicity when introduced into a subject and can be assessed using in vitro methods 45 described herein.

In certain embodiments, a variant SpA comprises at least or at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more variant SpA domain D peptides. In certain aspects 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 19 or more amino acid residues of the 50 variant SpA are substituted or modified-including but not limited to amino acids F5, Q9, Q10, S11, F13, Y14, L17, N28, I31, and/or K35 (SEQ ID NO:2) of the IgG Fc binding subdomain of domain D and amino acid residue Q26, G29, F30, S33, D36, D37, Q40, N43, and/or E47 (SEQ ID NO:2) of the 55 VH3 binding sub-domain of domain D. In one aspect of the invention glutamine residues at position 9 and/or 10 of SEQ ID NO:2 (or corresponding positions in other domains) are mutated. In another aspect, aspartic acid residues 36 and/or 37 of SEQ ID NO:2 (or corresponding positions in other 60 domains) are mutated. In a further aspect, glutamine 9 and 10, and aspartic acid residues 36 and 37 are mutated. Purified non-toxigenic SpA or SpA-D mutants/variants described herein are no longer able to significantly bind (i.e., demonstrate attenuated or disrupted binding affinity) Fcy or F(ab)2 65 VH3 and also do not stimulate B cell apoptosis. These nontoxigenic Protein A variants can be used as subunit vaccines

and raise humoral immune responses and confer protective immunity against *S. aureus* challenge. Compared to wildtype full-length Protein A or the wild-type SpA-domain D, immunization with SpA-D variants resulted in an increase in Protein A specific antibody. Using a mouse model of staphylococcal challenge and abscess formation, it was observed that immunization with the non-toxigenic Protein A variants generated significant protection from staphylococcal infection and abscess formation. As virtually all *S. aureus* strains express Protein A, immunization of humans with the nontoxigenic Protein A variants can neutralize this virulence factor and thereby establish protective immunity. In certain aspects the protective immunity protects or ameliorates infection by drug resistant strains of *Staphylococcus*, such as USA300 and other MRSA strains.

Embodiments include the use of Protein A variants in methods and compositions for the treatment of bacterial and/ or staphylococcal infection. This application also provides an immunogenic composition comprising a Protein A variant or immunogenic fragment thereof. In certain aspects, the immunogenic fragment is a Protein A domain D segment. Furthermore, the present invention provides methods and compositions that can be used to treat (e.g., limiting staphylococcal abscess formation and/or persistence in a subject) or prevent bacterial infection. In some cases, methods for stimulating an immune response involve administering to the subject an effective amount of a composition including or encoding all or part of a Protein A variant polypeptide or antigen, and in certain aspects other bacterial proteins. Other bacterial proteins include, but are not limited to (i) a secreted virulence factor, and/or a cell surface protein or peptide, or (ii) a recombinant nucleic acid molecule encoding a secreted virulence factor, and/or a cell surface protein or peptide.

In other aspects, the subject can be administered all or part of a Protein A variant, such as a variant Protein A domain D segment. The polypeptide of the invention can be formulated in a pharmaceutically acceptable composition. The composition can further comprise one or more of at least or at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 19 additional staphylococcal antigens or immunogenic fragments thereof (e.g., Eap, Ebh, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla (e.g., H35 mutants), IsdC, SasF, vWbp, or vWh). Additional staphylococcal antigens that can be used in combination with a Protein A variant include, but are not limited to 52 kDa vitronectin binding protein (WO 01/60852), Aaa (GenBank CAC80837), Aap (GenBank accession AJ249487), Ant (Gen-Bank accession NP 372518), autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008, 341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/ saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein (see PCT publications WO2007/113222, WO2007/113223, WO2006/ 032472, WO2006/032475, WO2006/032500, each of which is incorporated herein by reference in their entirety). In certain aspects The SpA variant composition can further comprise SdrD, ClfA, and/or FnbpB (FnbB) staphylococcal anti25

gens or immunogenic fragments thereof. The staphylococcal antigen or immunogenic fragment can be administered concurrently with the Protein A variant. The staphylococcal antigen or immunogenic fragment and the Protein A variant can be administered in the same composition. The Protein A 5 variant can also be a recombinant nucleic acid molecule encoding a Protein A variant. A recombinant nucleic acid molecule can encode the Protein A variant and at least one staphylococcal antigen or immunogenic fragment thereof. As used herein, the term "modulate" or "modulation" encom- 10 passes the meanings of the words "enhance," or "inhibit." "Modulation" of activity may be either an increase or a decrease in activity. As used herein, the term "modulator" refers to compounds that effect the function of a moiety, including up-regulation, induction, stimulation, potentiation, 15 inhibition, down-regulation, or suppression of a protein, nucleic acid, gene, organism or the like.

In further aspects, an immunogenic composition comprises SdrD, ClfA, and/or FnbpB (FnbB) staphylococcal antigens or immunogenic fragments or variants thereof. In other 20 embodiments an immunogenic composition comprising SdrD, ClfA, and/or FnbpB (FnbB) staphylococcal antigens or immunogenic fragments thereof can be used in treating, ameliorating or inhibiting staphylococcal infection, as described herein.

In certain embodiments the methods and compositions use or include or encode all or part of the Protein A variant or antigen. In other aspects, the Protein A variant may be used in combination with secreted factors or surface antigens including, but not limited to one or more of an isolated Eap, Ebh, 30 Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, or vWh polypeptide or immunogenic segments or variants thereof. Additional staphylococcal antigens that can be used in combination with a Protein A variant include, but are not limited 35 to 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin bind- 40 ing protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648, 240), MRPII, Npase, RNA III activating protein (RAP), 45 SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vit- 50 ronectin binding protein. In certain embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of Eap, Ebh, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh, 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, 55 autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008, 341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immu- 60 nodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 65 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/

saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein can be specifically excluded from a formulation of the invention. In further embodiments the methods and compositions use or include or encode all or part of the SdrD, ClfA and/or FnbpB (FnbB) antigens.

In still further aspects, the isolated Protein A variant is multimerized, e.g., dimerized or a linear fusion of two or more polypeptides or peptide segments. In certain aspects of the invention, a composition comprises multimers or concatamers of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more isolated cell surface proteins or segments thereof. Concatamers are linear polypeptides having one or more repeating peptide units. SpA polypeptides or fragments can be consecutive or separated by a spacer or other peptide sequences, e.g., one or more additional bacterial peptide. In a further aspect, the other polypeptides or peptides contained in the multimer or concatamer can include, but are not limited to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 of Eap, Ebh, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh or immunogenic fragments or variants thereof. Additional staphylococcal antigens that can be used in combination with a Protein A variant include, but are not limited to 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/ 0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg²⁴ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/ Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein. In certain aspects the SpA variant is used in combination with SdrD, ClfA, and/or FnbpB (FnbB) antigens.

The term "Protein A variant" or "SpA variant" refers to polypeptides that include a SpA IgG domain having two or more amino acid substitutions that disrupt binding to Fc and VH3. In certain aspect, a SpA variant includes a variant domain D peptide, as well as variants of SpA polypeptides and segments thereof that are non-toxigenic and stimulate an immune response against staphylococcus bacteria Protein A and/or bacteria expressing such.

Embodiments of the present invention include methods for eliciting an immune response against a *staphylococcus* bacterium or staphylococci in a subject comprising providing to the subject an effective amount of a Protein A variant or a segment thereof. In certain aspects, the methods for eliciting an immune response against a staphylococcus bacterium or staphylococci in a subject comprising providing to the subject an effective amount of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or more secreted proteins and/or cell surface proteins or segments/fragments thereof. A secreted protein or cell surface protein includes, but is not limited to Eap, Ebh, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh, sta001, sta002, sta003, sta004, sta005, sta006, sta007, sta008, sta009, sta010, sta011, sta012, sta013, sta014, sta015, sta016, sta017, sta018, sta019, sta020, sta021, sta022, sta023, sta024, sta025, sta026, sta027, sta028, sta029, sta030, sta031, sta032, sta033, sta034, sta035, sta036, sta037, sta038, sta039, sta040, sta041, sta042, sta043, sta044, sta045, sta046, sta047, sta048, sta049, sta050, sta051, sta052, sta053, sta054, sta055, sta056, sta057, sta058, sta069, sta060, sta061, sta062, sta063, sta064, sta065, sta066, sta067, sta068, sta069, sta070, sta071, sta072, sta073, sta074, sta075, sta076, sta077, sta078, sta079, sta080, sta081, sta082, sta083, sta084, sta085, sta086, sta095, sta096, sta097, sta098, sta099, sta100, sta101, sta102, sta103, sta104, sta105, sta106, sta107, sta108, sta109, sta111, sta112, sta113, sta114, sta115, sta116, sta117, sta118, sta119, sta120, or EsxAB hybrid polypeptide or immunogenic fragment thereof.

Additional staphylococcal antigens that can be used in 15 combination with a Protein A variant include, but are not limited to 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, 20 FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue 25 (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/ saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein. In certain aspects an SpA variant is used in combination with SdrD, ClfA, and/or FnbpB (FnbB) antigens.

Embodiments of the invention include compositions that include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to Protein A, or a second protein or peptide that is a secreted bacterial protein or a bacterial cell surface $_{40}$ protein. In a further embodiment of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a Protein A domain D polypeptide (SEQ ID NO:2), domain E (SEQ ID NO:3), domain A (SEQ 45 ID NO:4), domain C (SEQ ID NO:5), domain B (SEQ ID NO:6), or a nucleic acid sequence encoding a Protein A domain D, domain E, domain A, domain C, or domain B polypeptide. In certain aspects a Protein A polypeptide segment will have an amino acid sequence of SEQ ID NO:8. 50 Similarity or identity, with identity being preferred, is known in the art and a number of different programs can be used to identify whether a protein (or nucleic acid) has sequence identity or similarity to a known sequence. Sequence identity and/or similarity is determined using standard techniques 55 known in the art, including, but not limited to, the local sequence identity algorithm of Smith & Waterman (1981), by the sequence identity alignment algorithm of Needleman & Wunsch (1970), by the search for similarity method of Pearson & Lipman (1988), by computerized implementations of 60 these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Drive, Madison, Wis.), the Best Fit sequence program described by Devereux et al. (1984), preferably using the default settings, or by inspection. Preferably, 65 percent identity is calculated by using alignment tools known to and readily ascertainable to those of skill in the art. Percent

identity is essentially the number of identical amino acids divided by the total number of amino acids compared times one hundred.

Still further embodiments include methods for stimulating in a subject a protective or therapeutic immune response against a *staphylococcus* bacterium comprising administering to the subject an effective amount of a composition including (i) a SpA variant, e.g., a variant SpA domain D polypeptide or peptide thereof; or, (ii) a nucleic acid molecule encoding such a SpA variant polypeptide or peptide thereof, or (iii) administering a SpA variant domain D polypeptide with any combination or permutation of bacterial proteins described herein. In a preferred embodiment the composition is not a *staphylococcus* bacterium. In certain aspects the subject is a human or a cow. In a further aspect the composition is formulated in a pharmaceutically acceptable formulation. The staphylococci may be *Staphylococcus aureus*.

Yet still further embodiments include vaccines comprising a pharmaceutically acceptable composition having an isolated SpA variant polypeptide, or any other combination or permutation of protein(s) or peptide(s) described herein, wherein the composition is capable of stimulating an immune response against a staphylococcus bacterium. The vaccine may comprise an isolated SpA variant polypeptide, or any other combination or permutation of protein(s) or peptide(s) described. In certain aspects of the invention the isolated SpA variant polypeptide, or any other combination or permutation of protein(s) or peptide(s) described are multimerized, e.g., dimerized or concatamerized. In a further aspect, the vaccine composition is contaminated by less than about 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, 0.5, 0.25, 0.05% (or any range derivable therein) of other Staphylococcal proteins. A composition may further comprise an isolated non-SpA polypeptide. Typically the vaccine comprises an adjuvant. In certain aspects a protein or 35 peptide of the invention is linked (covalently or non-covalently) to the adjuvant, preferably the adjuvant is chemically conjugated to the protein.

In still yet further embodiments, a vaccine composition is a pharmaceutically acceptable composition having a recombinant nucleic acid encoding all or part of a SpA variant polypeptide, or any other combination or permutation of protein(s) or peptide(s) described herein, wherein the composition is capable of stimulating an immune response against a staphylococcus bacteria. The vaccine composition may comprise a recombinant nucleic acid encoding all or part of a SpA variant polypeptide, or any other combination or permutation of protein(s) or peptide(s) described herein. In certain embodiments the recombinant nucleic acid contains a heterologous promoter. Preferably the recombinant nucleic acid is a vector. More preferably the vector is a plasmid or a viral vector. In some aspects the vaccine includes a recombinant, non-staphylococcus bacterium containing the nucleic acid. The recombinant non-staphylococci may be Salmonella or another gram-positive bacteria. The vaccine may comprise a pharmaceutically acceptable excipient, more preferably an adjuvant.

Still further embodiments include methods for stimulating in a subject a protective or therapeutic immune response against a *staphylococcus* bacterium comprising administering to the subject an effective amount of a composition of a SpA variant polypeptide or segment/fragment thereof and further comprising one or more of a Eap, Ebh, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, or vWh protein or peptide thereof. In a preferred embodiment the composition comprises a non-*staphylococcus* bacterium. In a further aspect the composition is formulated in a pharmaceutically acceptable formulation. The staphylococci for which a subject is being treated may be Staphylococcus aureus. Methods of the invention also include SpA variant compositions that contain 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or more secreted virulence factors and/or cell surface proteins, such as Eap, Ebh, Emp, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh, sta001, sta002, sta003, sta004, sta005, sta006, sta007, sta008, sta009, sta010, sta011, sta012, sta013, sta014, sta015, sta016, sta017, 10sta018, sta019, sta020, sta021, sta022, sta023, sta024, sta025, sta026, sta027, sta028, sta029, sta030, sta031, sta032, sta033, sta034, sta035, sta036, sta037, sta038, sta039, sta040, sta041, sta042, sta043, sta044, sta045, sta046, sta047, sta048, sta049, sta050, sta051, sta052, sta053, sta054, sta055, sta056, sta057, sta058, sta059, sta060, sta061, sta062, sta063, sta064, sta065, sta066, sta067, sta068, sta069, sta070, sta071, sta072, sta073, sta074, sta075, sta076, sta077, sta078, sta079, sta080, sta081, sta082, sta083, sta084, sta085, sta086, sta087, sta088, sta089, sta090, sta091, sta092, sta093, sta094, sta095, sta096, sta097, 20 sta098, sta099, sta100, sta101, sta102, sta103, sta104, sta105, sta106, sta107, sta108, sta109, sta110, sta111, sta112, sta113, sta114, sta115, sta116, sta117, sta118, sta119, sta120, or EsxAB hybrid polypeptide or immunogenic fragment thereof in various combinations. In certain aspects a vaccine formu- 25 lation includes Eap, Ebh, Emp, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, and vWh. In certain aspects an antigen combination can include (1) a SpA variant and IsdA; (2) SpA variant and ClfB; (3) SpA variant and SdrD; (4) SpA variant and Hla or 30 Hla variant; (5) SpA variant and ClfB, SdrD, and Hla or Hla variant; (6) SpA variant, IsdA, SdrD, and Hla or Hla variant; (7) SpA variant, IsdA, ClfB, and Hla or Hla variant; (8) SpA variant, IsdA, ClfB, and SdrD; (9) SpA variant, IsdA, ClfB, SdrD and Hla or Hla variant; (10) SpA variant, IsdA, ClfB, 35 EsaC proteins. and SdrD; (11) SpA variant, IsdA, SdrD, and Hla or Hla variant; (12) SpA variant, IsdA, and Hla or Hla variant; (13) SpA variant, IsdA, ClfB, and Hla or Hla variant; (14) SpA variant, ClfB, and SdrD; (15) SpA variant, ClfB, and Hla or Hla variant; (16) SpA variant, SdrD, and Hla or Hla variant; or 40 (17) SpA variant and Ebh, or a fragment thereof.

In certain aspects, a bacterium delivering a composition of the invention will be limited or attenuated with respect to prolonged or persistent growth or abscess formation. In yet a further aspect, SpA variant(s) can be overexpressed in an 45 attenuated bacterium to further enhance or supplement an immune response or vaccine formulation.

The term "EsxA protein" refers to a protein that includes isolated wild-type EsxA polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria EsxA proteins.

The term "EsxB protein" refers to a protein that includes isolated wild-type EsxB polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimu-155 late an immune response against *staphylococcus* bacteria EsxB proteins.

The term "SdrD protein" refers to a protein that includes isolated wild-type SdrD polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria SdrD proteins.

The term "SdrE protein" refers to a protein that includes isolated wild-type SdrE polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria SdrE proteins.

The term "IsdA protein" refers to a protein that includes isolated wild-type IsdA polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria IsdA proteins.

The term "IsdB protein" refers to a protein that includes isolated wild-type IsdB polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria IsdB proteins.

The term "Eap protein" refers to a protein that includes isolated wild-type Eap polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria Eap proteins.

The term "Ebh protein" refers to a protein that includes isolated wild-type Ebh polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria Ebh proteins.

The term "Emp protein" refers to a protein that includes isolated wild-type Emp polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria Emp proteins.

The term "EsaB protein" refers to a protein that includes isolated wild-type EsaB polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria EsaB proteins.

The term "EsaC protein" refers to a protein that includes isolated wild-type EsaC polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria EsaC proteins.

The term "SdrC protein" refers to a protein that includes isolated wild-type SdrC polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria SdrC proteins.

The term "ClfA protein" refers to a protein that includes isolated wild-type ClfA polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria ClfA proteins.

The term "ClfB protein" refers to a protein that includes isolated wild-type ClfB polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria ClfB proteins.

The term "Coa protein" refers to a protein that includes isolated wild-type Coa polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria Coa proteins.

The term "Hla protein" refers to a protein that includes isolated wild-type Hla polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria Hla proteins.

The term "IsdC protein" refers to a protein that includes isolated wild-type IsdC polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria IsdC proteins.

The term "SasF protein" refers to a protein that includes isolated wild-type SasF polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria SasF proteins.

The term "vWbp protein" refers to a protein that includes isolated wild-type vWbp (von Willebrand factor binding protein) polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria vWbp proteins.

The term "vWh protein" refers to a protein that includes isolated wild-type vWh (von Willebrand factor binding protein homolog) polypeptides from *staphylococcus* bacteria and segments thereof, as well as variants that stimulate an immune response against *staphylococcus* bacteria vWh proteins.

The 'sta001' antigen is annotated as '5'-nucleotidase fam- 15 ily protein. In the NCTC 8325 strain sta001 is SAOUHSC_ 00025 and has amino acid sequence SEQ ID NO:35 (GI: 88193846). In the Newman strain it is nwmn_0022 (GI: 151220234). It has also been referred to as AdsA and SasH and SA0024. 20

Useful sta001 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:35 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more 25 identity to SEQ ID No: 35; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No: 35, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta001 proteins include variants of SEQ ID No: 35. Preferred 30 fragments of (b) comprise an epitope from SEQ ID No: 35. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 35 ID No: 35 while retaining at least one epitope of SEQ ID No: 37. The final 34 C-terminal amino acids of SEQ ID No: 35 can usefully be omitted. The first 38 N-terminal amino acids of SEQ ID No: 35 can usefully be omitted. Other fragments omit one or more protein domains.

The sta002 antigen is annotated as 'lipoprotein'. In the NCTC• 8325 strain sta002 is SAOUHSC 00356 and has amino acid sequence SEQ ID NO:36 (GI:88194155). In the Newman strain it is nwmn_0364 (GI: 151220576).

Useful sta002 antigens can elicit an antibody (e.g. when 45 administered to a human) that recognizes SEQ ID NO:36 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:36; and/or (b) comprising a fragment 50 of at least 'n' consecutive amino acids of SEQ ID NO:36, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta002 proteins include variants of SEQ ID NO:36. Preferred 5 fragments of (b) comprise an epitope from SEQ ID NO:36. Other 55 preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:36 while retaining at least one epitope of SEQ ID NO:36. The 60 first 18 N-terminal amino acids of SEQ ID NO:36 can usefully be omitted. Other fragments omit one or more protein domains. $sta002_{19-187}$ and $sta002_{19-124}$ are two useful fragments of SEQ ID NO:36 which reduce the antigen's similarity with human proteins. 65

The 'sta003' antigen is annotated as 'surface protein'. In the NCTC 8325 strain sta003 is SAOUHSC_00400 and has

amino acid sequence SEQ ID NO:37 (GI:88194195). In the Newman strain it is nwmn_0401 (GI: 151220613).

Useful sta003 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:37 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:37; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:37, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta003 proteins include variants of SEQ ID NO:37. Preferred fragments of (b) comprise an epitope from SEQ ID NO:37. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:37 while retaining at least one epitope of SEQ ID 20 NO:37. The first 32N-terminal amino acids of SEQ ID NO:37 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta004' antigen is annotated as 'Siderophore binding protein FatB'. In the NCTC 8325 strain sta004 is SAOU-HSC_00749 and has amino acid sequence SEQ ID NO:38 (GI:88194514). In the Newman strain it is nwmn_0705 (GI: 151220917).

Useful sta004 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:38 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:38; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:38, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta004 proteins include variants of SEQ ID NO:38. Preferred fragments of (b) comprise an epitope from SEQ ID NO:38. Other preferred fragments lack one or more amino acids (e.g. 40 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:38 while retaining at least one epitope of SEQ ID NO:38. The first 18N-terminal amino acids of SEQ ID NO:38 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta005' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta005 is 10 SAOUHSC____01127 and has amino acid sequence SEQ ID NO:39 (GI: 88194870). In the Newman strain it is nwmn__1077 (GI: 151221289).

Useful sta005 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:39 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:39; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:39, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta005 proteins include variants of SEQ ID NO:39. Preferred fragments of (b) comprise an epitope from SEQ ID NO:39. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:39 while retaining at least one epitope of SEQ ID NO:39. The first 18N-terminal amino acids of SEQ ID NO:39 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta006' antigen is annotated as 'ferrichrome-binding protein', and has also been referred to as 25 'FhuD2' in the 5 literature. In the NCTC 8325 strain sta006 is SAOUHSC_02554 and has amino acid sequence SEQ ID NO:40 (GI: 88196199). In the Newman strain it is nwmn 2185 (GI: 151222397).

Useful sta006 antigens can elicit an antibody (e.g. when 10 administered to a human) that recognizes SEQ ID NO:40 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 30, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:40; and/or (b) comprising a 15 fragment of at least 'n' consecutive amino acids of SEQ ID NO:40, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta006 proteins include variants of SEQ ID NO:40. Preferred fragments of (b) comprise an epitope from SEO ID 20 NO:40. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:40 while retaining at least one epitope of SEQ ID 25 NO:40. The first 17 N-terminal amino acids of SEQ ID NO:40 can usefully be omitted. Other fragments omit one or more protein domains. A sta006 antigen may be lipidated e.g. with an acylated N-terminus cysteine. One useful sta006 sequence has a Met-Ala-Ser-sequence at the N-terminus.

The 'sta007' antigen is annotated as 'secretory antigen precursor'. In the NCTC 8325 strain sta007 is SAOUHSC_____02571 and has amino acid sequence SEQ ID NO:41 (GI: 88196215). In the Newman strain it is nwmn__2199 (GI: 151222411). Proteomic analysis has revealed that this protein 35 is secreted or surface-exposed.

Useful sta007 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:41 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 40 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:41; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:41, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 45 sta007 proteins include variants of SEQ ID NO:41. Preferred fragments of (b) comprise an epitope from SEQ ID NO:41. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 50 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:41 while retaining at least one epitope of SEQ ID NO:41. The first 27 N-terminal amino acids of SEQ ID NO:41 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta008' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta008 is SAOUHSC 02650 and has amino acid sequence SEQ ID NO:42 (GI:88196290). In the Newman strain it is nwm_2270 (GI: 151222482).

Useful sta008 antigens can elicit an antibody (e.g. when 60 administered to a human) that recognizes SEQ ID NO:42 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:42; and/or (b) comprising a fragment of 65 at least 'n' consecutive amino acids of SEQ ID NO:42, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30,

35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta008 proteins include variants of SEQ ID NO:42. Preferred fragments of (b) comprise an epitope from SEQ ID NO:42. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:42 while retaining at least one epitope of SEQ ID NO:42. The first 17N-terminal amino acids of SEQ ID NO:42 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta009' antigen is annotated as 'immunoglobulin G-binding protein Sbi'. In the NCTC 8325 strain sta009 is SAOUHSC 02706 and has amino acid sequence SEQ ID NO:43 (GI:88196346). In the Newman strain it is nwmn_ 2317 (GI: 151222529).

Useful sta009 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:43 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:43; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:43, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta009 proteins include variants of SEQ ID NO:43. Preferred fragments of (b) comprise an epitope from SEQ ID NO:43. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:43 while retaining at least one epitope of SEQ ID NO:43. The first 29 N-terminal amino acids of SEQ ID NO:43 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta010' antigen is annotated as 'immunodominant antigen A'. In the NCTC 8325 strain sta010 is SAOUHSC 02887 and has amino acid sequence SEQ ID NO:44 (GI: 88196515). In the Newman strain it is nwmn_2469 (GI: 151222681). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful sta010 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:44 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more) to SEO ID NO:44; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:44, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta010 proteins include variants of SEQ ID NO:44. Preferred fragments of (b) comprise an epitope from SEQ ID NO:44. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 55 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:44 while retaining at least one epitope of SEQ ID NO:44. The first 29N-terminal amino acids of SEQ ID NO:44 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta011' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta011 is SAOUHSC_00052 and has amino acid sequence SEQ ID NO:45 (GI:88193872).

Useful sta011 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:45 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:45; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:45, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 5 sta011 proteins include variants of SEQ ID NO:45. Preferred fragments of (b) comprise an epitope from SEQ ID NO:45. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 10 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:45 while retaining at least one epitope of SEQ ID NO:45. The first 23 N-terminal amino acids of SEQ ID NO:45 can usefully be omitted. Other fragments omit one or more protein domains. A sta011 antigen may be lipidated e.g. with 15 an acylated N-terminus cysteine.

The 'sta012' antigen is annotated as 'protein with leader'. In the NCTC 8325 strain sta012 is SAOUHSC_00106 and has amino acid sequence SEQ ID NO:46 (GI:88193919).

Useful sta012 antigens can elicit an antibody (e.g. when 20 administered to a human) that recognizes SEQ ID NO:46 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:46; and/or (b) comprising a fragment of 25 at least 'n' consecutive amino acids of SEQ ID NO:46, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta012 proteins include variants of SEQ ID NO:46. Preferred fragments of (b) comprise an epitope from SEQ ID NO:46. 30 Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:46 while retaining at least one epitope of SEQ ID 35 first 18 N-terminal amino acids of SEQ ID NO:49 can use-NO:46. The first 21 N-terminal amino acids of SEQ ID NO:46 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta013' antigen is annotated as 'poly-gammaglutamate capsule biosynthesis protein'. In the NCTC 8325 40 HSC_00171 and has amino acid sequence SEQ ID NO:50 strain staOB is SAOUHSC_00107 and has amino acid sequence SEQ ID NO:47 (GI:88193920).

Useful sta013 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:47 and/or may comprise an amino acid sequence: (a) having 50% 45 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:47; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:47, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 50 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta013 proteins include variants of SEQ ID NO:47. Preferred fragments of (b) comprise an epitope from SEQ ID NO:47. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 55 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:47 while retaining at least one epitope of SEQ ID NO:47. Other fragments omit one or more protein domains.

The 'sta014' antigen is annotated as 'lipoprotein'. In the 60 NCTC 8325 strain sta014 is SAOUHSC_00137 and has amino acid sequence SEQ ID NO:48 (GI:88193950).

Useful sta014 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:48 and/or may comprise an amino acid sequence: (a) having 50% 65 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or

more) to SEQ ID NO:48; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:48, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta014 proteins include variants of SEQ ID NO:48. Preferred fragments of (b) comprise an epitope from SEQ ID NO:48. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:48 while retaining at least one epitope of SEQ ID NO:48. The first 17 N-terminal amino acids of SEQ ID NO:48 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta015' antigen is annotated as 'extracellular solutebinding protein; ROD containing lipoprotein'. In the NCTC 8325 strain sta015 is SAOUHSC_00170 and has amino acid sequence SEQ ID NO:49 (GI:88193980).

Useful sta015 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEO ID NO:49 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:49; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO:49, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta015 proteins include variants of SEQ ID NO:49. Preferred fragments of (b) comprise an epitope from SEQ ID NO:49. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:49 while retaining at least one epitope of SEQ ID NO:49. The fully be omitted. Other fragments omit one or more protein domains.

The 'sta016' antigen is annotated as 'gamma-glutamyltranspeptidase'. In the NCTC 8325 strain sta016 is SAOU-(GI:88193981).

Useful sta016 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:50 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEO ID NO:50; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:50, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta016 proteins include variants of SEQ ID NO:50. Preferred fragments of (b) comprise an epitope from SEQ ID NO:50. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:50 while retaining at least one epitope of SEQ ID NO:50. Other fragments omit one or more protein domains. The 'sta017' antigen is annotated as 'lipoprotein'. In the

NCTC 8325 strain sta017 is SAOUHSC_00186 and has amino acid sequence SEQ ID NO:51 (GI:88193996).

Useful sta017 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:51 and/or may comprise an amino acid sequence: (a) having 50%) or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more) to SEQ ID NO:51; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:51, wherein In' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta017 proteins include variants of SEQ ID NO:51. Preferred fragments of (b) comprise an epitope from SEQ ID 5 NO:51. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:51 while retaining at least one epitope of SEQ ID 10 NO:51. The first 17N-terminal amino acids of SEQ ID NO:51 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta018' antigen is annotated as 'extracellular solutebinding protein'. In the NCTC 8325 strain sta018 is SAOU- 15 HSC_00201 and has amino acid sequence SEQ ID NO:52 (GI:881940U).

Useful sta018 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:52 and/or may comprise an amino acid sequence: (a) having 20 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more identity to SEQ ID NO:52; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:52, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 25 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta018 proteins include variants of SEQ ID NO:52. Preferred fragments of (b) comprise an epitope from SEQ ID NO:52. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 30 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:52 while retaining at least one epitope of SEQ ID NO:52. Other fragments omit one or more protein domains.

The 'sta019' antigen is annotated as 'peptidoglycan hydro- 35 lase'. In the NCTC 8325 strain sta019 is SAOUHSC_00248 and has amino acid sequence SEQ ID NO:53 (GI:88194055). In the Newman strain it is nwmn_0210 (GI: 151220422).

Useful sta019 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:53 40 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:53; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:53, 45 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta019 proteins include variants of SEQ ID NO:53. Preferred fragments of (b) comprise an epitope from SEQ ID NO:53. Other preferred fragments lack one or more amino acids (e.g. 50 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:53 while retaining at least one epitope of SEQ ID NO:53. The first 25 N-terminal amino acids of SEQ ID NO:53 55 can usefully be omitted. Other fragments omit one or more protein domains.

Sta019 does not adsorb well to aluminium hydroxide adjuvants, so Sta019 present in a composition may be unadsorbed or may be adsorbed to an alternative adjuvant e.g. to an 60 aluminium phosphate.

The 'sta020' antigen is annotated as 'exported protein'. In the NCTC 8325 strain sta020 is SAOUHSC_00253 and has amino acid sequence SEQ ID NO:54 (GI: δ 194059).

Useful sta020 antigens can elicit an antibody (e.g. when 65 administered to a human) that recognizes SEQ ID NO:54 and/or may comprise an amino acid sequence: (a) having

50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:54; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:54, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta020 proteins include variants of SEQ ID NO:54. Preferred fragments of (b) comprise an epitope from SEQ ID NO:54. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:54 while retaining at least one epitope of SEQ ID NO:54. The first 30N-terminal amino acids of SEQ ID NO:54 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta021' antigen is annotated as 'secretory antigen SsaA-like protein'. In the NCTC 8325 strain sta021 is SAOU-HSC_00256 and has amino acid sequence SEQ ID NO:55 (GI:88194062).

Useful sta021 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:55 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:55; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:55, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta021 proteins include variants of SEQ ID NO:55. Preferred fragments of (b) comprise an epitope from SEQ ID NO:55. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:55 while retaining at least one epitope of SEQ ID NO:55. The first 24 N-terminal amino acids of SEQ ID NO:55 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta022' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta022 is SAOUHSC_00279 and has amino acid sequence SEQ ID NO:56 (GI:88194083).

Useful sta022 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:56 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:56; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:56, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta022 proteins include variants of SEQ ID NO:56. Preferred fragments of (b) comprise an epitope from SEQ ID NO:56. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:56 while retaining at least one epitope of SEQ ID NO:56. The first 17Nterminal amino acids of SEQ ID NO:56 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta023' antigen is annotated as '5'-nucleotidase; lipoprotein e(P4) family'. In the NCTC 8325 strain sta023 is SAOUHSC_00284 and has amino acid sequence SEQ ID NO:57 (GI:88194087).

Useful sta023 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:57 and/or may comprise an amino acid sequence: (a) having 50%

or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:57; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:57, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 5 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta023 proteins include variants of SEQ ID NO:57. Preferred fragments of (b) comprise an epitope from SEQ ID NO:57. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 10 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:57 while retaining at least one epitope of SEQ ID NO:57. The first 31 N-terminal amino acids of SEQ ID NO:57 can usefully be omitted. Other fragments omit one or more 15 protein domains.

The 'sta024' antigen is annotated as 'lipase precursor'. In the NCTC 8325 strain sta024 is SAOUHSC_00300 and has amino acid sequence SEQ ID NO:58 (GI:88194101).

Useful sta024 antigens can elicit an antibody (e.g. when 20 administered to a human) that recognizes SEQ ID NO:58 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:58; and/or (b) comprising a fragment 25 of at least 'n' consecutive amino acids of SEQ ID NO:58, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta024 proteins include variants of SEQ ID NO:58. Preferred fragments of (b) comprise an epitope from SEQ ID NO:58. 30 Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:58 while retaining at least one epitope of SEQ ED 35 NO:58. The first 37N-terminal amino acids of SEQ ID NO:58 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta025' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta025 is SAOUHSC_00362 and has 40 HSC_00671 and has amino acid sequence SEQ ID NO:62 amino acid sequence SEQ ID NO:59 (GI:88194160).

Useful sta025 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:59 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 45 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEO ID NO:59; and/or (b) comprising a fragment of at least In' consecutive amino acids of SEQ ID NO:59, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These 50 sta025 proteins include variants of SEQ ID NO:59. Preferred fragments of (b) comprise an epitope from SEQ ID NO:59. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 55 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:59 while retaining at least one epitope of SEQ ID NO:59. The first 19N-terminal amino acids of SEQ ID NO:59 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta026' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta026 is SAOUHSC_00404 and has amino acid sequence SEQ ID NO:60 (GI:88194198).

Useful sta026 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:60 65 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:60; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:60, wherein In' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta026 proteins include variants of SEQ ID NO:60. Preferred fragments of (b) comprise an epitope from SEQ ID NO:60. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:60 while retaining at least one epitope of SEQ ID NO:60. The first 22N-terminal amino acids of SEQ ID NO:60 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta027' antigen is annotated as 'probable lipase'. In the NCTC 8325 strain sta027 is SAOUHSC_00661 and has amino acid sequence SEQ ID NO:61 (GI:88194426).

Useful sta027 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEO ID NO:61 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more identity to SEQ ID NO:61; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:61, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta027 proteins include variants of SEQ ID NO:61. Preferred fragments of (b) comprise an epitope from SEQ ID NO:61. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:61 while retaining at least one epitope of SEQ ID NO:61. The first 23N-terminal amino acids of SEQ ID NO:61 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta028' antigen is annotated as 'secretory antigen SsaA-like protein'. In the NCTC 8325 strain sta028 is SAOU-(GI:88194436). In the Newman strain it is nwmn_0634 (GI: 151220846).

Useful sta028 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:62 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more identity to SEQ ID NO:62; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:62, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta028 proteins include variants of SEQ ID NO:62. Preferred fragments of (b) comprise an epitope from SEQ ID NO:62. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:62 while retaining at least one epitope of SEQ ID NO:62. The first 25 N-terminal amino acids of SEQ ID NO:62 60 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta029' antigen is annotated as 'ferrichrome binding protein'. In the NCTC 8325 strain sta029 is SAOUHSC 00754 and has amino acid sequence SEQ ID NO:63 (GI: 88194518).

Useful sta029 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:63 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:63; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:63, 5 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta029 proteins include variants of SEQ ID NO:63. Preferred fragments of (b) comprise an epitope from SEQ ID NO:63. Other preferred fragments lack one or more amino acids (e.g. 10 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:63 while retaining at least one epitope of SEQ ID NO:63. The final 25 C-terminal amino acids of SEQ ID 15 NO:63 can usefully be omitted. The first 19 N-terminal amino acids of SEQ ID NO:63 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta030' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta030 is SAOUHSC 00808 and has 20 amino acid sequence according to SEQ ID NO:64 (NCBI accession no. GI:88194568).

Useful sta030 antigens can elicit an antibody (e.g. when administered to a human) that recognizes sta030 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 25 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:64; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:64, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 30 80, 90, 100, 150, 200 or more). These sta030 proteins include variants of SEQ ID NO:64. Preferred fragments of (b) comprise an epitope from an amino acid sequence of SEQ ED NO:64. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from 35 the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of an amino acid sequence of SEQ ID NO:64 while retaining at least one epitope of SEQ ID NO:64. The first 17 N-terminal amino acids of SEQ ID NO:64 can usefully be omitted. Other 40 dase precursor'. In the NCTC 8325 strain sta034 is SAOUfragments omit one or more protein domains.

The 'sta031' antigen is annotated as '5-nucleotidase family protein'. In the NCTC 8325 strain sta031 is SAOUHSC 00860 and has amino acid sequence SEQ ID NO:65 (GI: 88194617).

Useful sta031 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:65 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or 50 more) to SEQ ID NO:65; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:65, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta031 proteins include variants of SEQ ID NO:65. Preferred 55 fragments of (b) comprise an epitope from SEQ ID NO:65. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 60 ID NO:65 while retaining at least one epitope of SEQ ID NO:65. Other fragments omit one or more protein domains.

The 'sta032' antigen is annotated as 'serine protease HtrA'. In the NCTC 8325 strain sta032 is SAOUHSC 00958 and has amino acid sequence SEQ ID NO:66 (GI:88194715).

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Useful sta032 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:66

and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:66; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:66, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta032 proteins include variants of SEQ ID NO:66. Preferred fragments of (b) comprise an epitope from SEQ ID NO:66. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:66 while retaining at least one epitope of SEQ ID NO:66. Other fragments omit one or more protein domains.

The 'sta033' antigen is annotated as 'cysteine protease precursor'. In the NCTC 8325 strain sta033 is SAOUHSC 00987 and has amino acid sequence SEQ ID NO:67 (GI: 88194744).

Useful sta033 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:67 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:67; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:67, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta033 proteins include variants of SEQ ID NO:67. Preferred fragments of (b) comprise an epitope from SEQ ID NO:67. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:67 while retaining at least one epitope of SEQ ID NO:67. The first 29 N-terminal amino acids of SEQ ID NO:67 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta034' antigen is annotated as 'glutamyl endopepti-HSC_00988 and has amino acid sequence SEQ ID NO:68 (GI:88194745).

Useful sta034 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:68 45 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:68; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:68, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta034 proteins include variants of SEQ ID NO:68. Preferred fragments of (b) comprise an epitope from SEQ ID NO:68. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:68 while retaining at least one epitope of SEQ ID NO:68. The first 29 N-terminal amino acids of SEQ ID NO:68 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta035' antigen is annotated as 'fmt protein'. In the NCTC 8325 strain sta035 is SAOUHSC_00998 and has amino acid sequence SEQ ID NO:69 (GI:88194754).

Useful sta035 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:69 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:69; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:69, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 5 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta035 proteins include variants of SEQ ID NO:69. Preferred fragments of (b) comprise an epitope from SEQ ID NO:69. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 10 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:69 while retaining at least one epitope of SEQ ID NO:69. The first 25N-terminal amino acids of SEQ ID NO:69 can usefully be omitted. Other fragments omit one or more 15 protein domains.

The 'sta036' antigen is annotated as 'iron-regulated protein with leader'. In the NCTC 8325 strain sta036 is SAOUHSC_____01084 and has amino acid sequence SEQ ID NO:70 (GI: 88194831).

Useful sta036 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:70 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more 25 identity to SEQ ID NO:70; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:70, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta036 proteins include variants of SEQ ID NO:70. Preferred 30 fragments of (b) comprise an epitope from SEQ ID NO:70. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 35 ID NO:70 while retaining at least one epitope of SEQ ID NO:70. The first 27 C-terminal amino acids of SEQ ID NO:70 can usefully be omitted. The first 32 N-terminal amino acids of SEQ ID NO:70 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta037' antigen is annotated as 'iron ABC transporter; iron-binding protein IsdE'. In the NCTC 8325 strain sta037 is SAOUHSC 01085 and has amino acid sequence SEQ ID NO:71 (GI:88194832).

Useful sta037 antigens can elicit an antibody (e.g. when 45 administered to a human) that recognizes SEQ ID NO:71 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:71; and/or (b) comprising a fragment of 50 at least 'n' consecutive amino acids of SEQ ID NO:71, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta037 proteins include variants of SEQ ID NO:71. Preferred fragments of (b) comprise an epitope from SEQ ID NO:71. 55 Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:71 while retaining at least one epitope of SEQ ID 60 NO:71. The first 9 N-terminal amino acids of SEQ ID NO:71 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta038' antigen is annotated as 'NPQTN specific sortase B'. In the NCTC 8325 strain sta038 is SAOUHSC_ 01088 and has amino acid sequence SEQ ID NO:72 (GI: 88194835).

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Useful sta038 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:72 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEO ID NO:72; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEO ID NO:72, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta038 proteins include variants of SEQ ID NO:72. Preferred fragments of (b) comprise an epitope from SEQ ID NO:72. Other preferred fragments lack one or more amino acids)(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:72 while retaining at least one epitope of SEQ ID NO:72. The first 21N-terminal amino acids of SEQ ID NO:72 can usefully be omitted. Other fragments omit one or more 20 protein domains.

The 'sta039' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta039 is SAOUHSC_01124 and has amino acid sequence SEQ ID NO:73 (GI: 88194868).

Useful sta039 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:73 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:73; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:73, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta039 proteins include variants of SEQ ID NO:73. Preferred fragments of (b) comprise an epitope from SEQ ID NO:73. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 40 ID NO:73 while retaining at least one epitope of SEQ ID NO:73. The first 22 N-terminal amino acids of SEQ ID NO:73 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta040' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta040 is SAOUHSC_011125 and has amino acid sequence SEQ ID NO:74 (GI: 88194869). In the Newman strain it is nwmn_1076 (GI: 151221288).

Useful sta040 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:74 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:74; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:74, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta040 proteins include variants of SEQ ID NO:74. Preferred fragments of (b) comprise an epitope from SEQ ID NO:74. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:74 while retaining at least one epitope of SEQ ID NO:74. The first 21N-terminal amino acids of SEQ ID NO:74 can usefully be omitted. Other fragments omit one or more protein domains.

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The 'sta041' antigen is annotated as 'fibronectin-binding protein A-related'. In the NCTC 8325 strain sta041 is SAOU-HSC_01175 and has amino acid sequence SEQ ID NO:75 (GI:88194914).

Useful sta041 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEO ID NO:75 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:75; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:75, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta041 proteins include variants of SEQ ID NO:75. Preferred fragments of (b) comprise an epitope from SEQ ID NO:75. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 20 ID NO:75 while retaining at least one epitope of SEQ ID NO:75. Other fragments omit one or more protein domains.

The 'sta042, antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta042 is SAOUHSC_1180 and has amino acid sequence SEQ ID NO:76 (GI:88194919).

Useful sta042 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:76 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:76; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:76, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 35 sta042 proteins include variants of SEQ ID NO:76. Preferred fragments of (b) comprise an epitope from SEQ ID NO:76. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 40 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEO ID NO:76 while retaining at least one epitope of SEQ ID NO:76. The first 18 N-terminal amino acids of SEQ ID NO:76 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta043', antigen is annotated as 'cell wall hydrolase'. In the NCTC 8325 strain sta043 is SAOUHSC 01219 and has amino acid sequence SEQ ED NO:77 (GI:88194955).

Useful sta043 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:77 50 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:77; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:77, 55 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta043 proteins include variants of SEQ ED NO:77. Preferred fragments of (b) comprise an epitope from SEQ ID NO:77. Other preferred fragments lack one or more amino acids (e.g. 60 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:77 while retaining at least one epitope of SEQ ID NO:77. The first 38 N-terminal amino acids of SEQ ID NO:77 65 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta044' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta044 is SAOUHSC_01508 and has amino acid sequence SEQ ID NO:78 (GI:88195223).

Useful sta044 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:78 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:78; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:78, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta044 proteins include variants of SEQ ED NO:78. Preferred fragments of (b) comprise an epitope from SEQ ID NO:78. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:78 while retaining at least one epitope of SEQ ED NO:78. The first 17 N-terminal amino acids of SEQ ID NO:78 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta045' antigen is annotated as 'lipoprotein'. In the 25 NCTC 8325 strain sta045 is SAOUHSC 01627 and has amino acid sequence SEQ ID NO:79 (GI:88195337).

Useful sta045 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:79 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:79; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:79, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta045 proteins include variants of SEQ ID NO:79. Preferred fragments of (b) comprise an epitope from SEQ ID NO:79. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:79 while retaining at least one epitope of SEQ ID NO:79. The first 16N-terminal amino acids of SEQ ID NO:79 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta046' antigen is annotated as 'Excalibur protein'. In the NCTC 8325 strain sta046 is SAOUHSC 01918 and has amino acid sequence SEQ ID NO:80 (GI:88195613).

Useful sta046 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:80 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more) to SEQ ID NO:80; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:80, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta046 proteins include variants of SEQ ID NO:80. Preferred fragments of (b) comprise an epitope from SEQ ID NO:80. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:80 while retaining at least one epitope of SEQ ID NO:80. The first 53N-terminal amino acids of SEQ ID NO:80 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta047' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta047 is SAOUHSC_01920 and has amino acid sequence SEQ ID NO:81 (GI:88195615).

Useful sta047 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:81 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:81; and/or (b) comprising a fragment of 10at least V consecutive amino acids of SEQ ID NO:81, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta047 proteins include variants of SEQ ID NO:81. Preferred fragments of (b) comprise an epitope from SEQ ID NO:81. Other 15 preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:81 while retaining at least one epitope of SEQ ID NO:81. The 20 first 18N-terminal amino acids of SEQ ED NO:81 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta048' antigen is annotated as 'intracellular serine protease'. In the NCTC 8325 strain sta048 is SAOUHSC_ ²⁵ 01949 and has amino acid sequence SEQ ID NO:82 (GI: 88195642).

Useful sta048 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:82 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:82; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:82, 35 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta048 proteins include variants of SEQ ID NO:82. Preferred fragments of (b) comprise an epitope from SEO ID NO:82. Other preferred fragments lack one or more amino acids (e.g. 40 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:82 while retaining at least one epitope of SEQ ID NO:82. The first 27N-terminal amino acids of SEQ ID NO:82 45 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta049' antigen is annotated as 'protein export protein PrsA'. In the NCTC 8325 strain sta049 is SAOUHSC_01972 and has amino acid sequence SEQ ID NO:83 (GI:88195663). 50 In the Newman strain it is nwmn_1733 (GI:151221945).

Useful sta049 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:83 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 55 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:83; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:83, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 60 sta049 proteins include variants of SEQ ID NO:83. Preferred fragments of (b) comprise an epitope from SEQ ID NO:83. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 65 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:83 while retaining at least one epitope of SEQ ID

NO:83. The first 25 N-terminal amino acids of SEQID NO:83 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta050' antigen is annotated as 'staphopain thiol proteinase'. In the NCTC 8325 strain sta050 is SAOUHSC_ 02127 and has amino acid sequence SEQ ID NO:84 (GI: 88195808).

Useful sta050 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:84 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:84; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:84, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta050 proteins include variants of SEQ ID NO:84. Preferred fragments of (b) comprise an epitope from SEQ ID NO:84. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:84 while retaining at least one epitope of SEQ ID NO:84. The first 25N-terminal amino acids of SEQ ID NO:84 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta051' antigen is annotated as 'protein with leader'. In the NCTC 8325 strain sta051 is SAOUHSC_02147 and has amino acid sequence SEQ ID NO:85 (GI:88195827).

Useful sta051 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:85 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID NO:85; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:85, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta051 proteins include variants of SEQ ID NO:85. Preferred fragments of (b) comprise an epitope from SEQ ID NO:85. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:85 while retaining at least one epitope of SEQ ID NO:85. The first 24N-terminal amino acids of SEQ ID NO:85 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta052' antigen is annotated as 'ferric hydroxamate receptor I'. In the NCTC 8325 strain sta052 is SAOUHSC__02246 and has amino acid sequence SEQ ID NO:86 (GI: 88195918).

Useful sta052 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:86 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:86; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:86, wherein In' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta052 proteins include variants of SEQ ID NO:86. Preferred fragments of (b) comprise an epitope from SEQ ID NO:86. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ

ID NO:86 while retaining at least one epitope of SEQ ID NO:86. The first 17N-terminal amino acids of SEQ ID NO:86 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta053' antigen is annotated as 'srdH family protein'. 5 In the NCTC 8325 strain sta053 is SAOUHSC_02257 and has amino acid sequence SEQ ED NO:87 (GI:88195928).

Useful sta053 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:87 and/or may comprise an amino acid sequence: (a) having 50% 10 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:87; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:87, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 15 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta053 proteins include variants of SEQ ED NO:87. Preferred fragments of (b) comprise an epitope from SEQ ID NO:87. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 20 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:87 while retaining at least one epitope of SEQ ID NO:87. The first 26 N-terminal amino acids of SEQ ID NO:87 can usefully be omitted. Other fragments omit one or more 25 protein domains.

The 'sta054' antigen is annotated as 'Probable transglycosylase isaA precursor'. In the NCTC 8325 strain sta054 is SAOUHSC_02333 and has amino acid sequence SEQ ID NO:88 (GI:88195999).

Useful sta054 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:88 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or 35 more) to SEQ ID NO:88; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:88, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta054 proteins include variants of SEQ ID NO:88. Preferred 40 fragments of (b) comprise an epitope from SEQ ID NO:88. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 45 ID NO:88 while retaining at least one epitope of SEQ ID NO:88. The first 27N-terminal amino acids of SEO ID NO:88 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta055' antigen is annotated as 'surface hydrolase'. In 50 the NCTC 8325 strain sta055 is SAOUHSC_02448 and has amino acid sequence SEQ ID NO:89 (GI:88196100).

Useful sta055 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:89 and/or may comprise an amino acid sequence: (a) having 50% 55 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:89; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:89, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 60 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta055 proteins include variants of SEQ ID NO:89. Preferred fragments of (b) comprise an epitope from SEQ ID NO:89. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 65 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ

ID NO:89 while retaining at least one epitope of SEQ ID NO:89. The first 31 N-terminal amino acids of SEQ ID NO:89 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta056' antigen is annotated as 'hyaluronate lyase'. In the NCTC 8325 strain sta056 is SAOUHSC_02463 and has amino acid sequence SEQ ID NO:90 (GI:88196115).

Useful sta056 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:90 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more) to SEQ ID NO:90; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:90, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta056 proteins include variants of SEQ ID NO:90. Preferred fragments of (b) comprise an epitope from SEQ ID NO:90. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:90 while retaining at least one epitope of SEQ ID NO:90. The first 24N-terminal amino acids of SEQ ID NO:90 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta057' antigen is annotated as 'secretory antigen precursor SsaA'. In the NCTC 8325 strain sta057 is SAOU-HSC_02576 and has amino acid sequence SEQ ID NO:91 (GI:88 196220). In the Newman strain it is nwmn_2203 (GI:151222415).

Useful sta057 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:91 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:91; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:91, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta057 proteins include variants of SEQ ID NO:91. Preferred fragments of (b) comprise an epitope from SEQ ID NO:91. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:91 while retaining at least one epitope of SEO ID NO:91. The first 27N-terminal amino acids of SEQ ID NO:91 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta058' antigen is annotated as 'Zn-binding lipoprotein adcA-like'. In the NCTC 8325 strain sta058 is SAOU-HSC_02690 and has amino acid sequence SEQ ID NO:92 (GI:88196330).

Useful sta058 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:92 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:92; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:92, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta058 proteins include variants of SEQ ID NO:92. Preferred fragments of (b) comprise an epitope from SEQ ID NO:92. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the

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C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:92 while retaining at least one epitope of SEQ ID NO:92. The first 20 N-terminal amino acids of SEQ ID NO:92 can usefully be omitted. Other fragments omit one or more 5 protein domains.

The 'sta059' antigen is annotated as 'gamma-hemolysin h-gamma-ii subunit'. In the NCTC 8325 strain sta059 is SAOUHSC_02708 and has amino acid sequence SEQ ID NO:93 (GI:88196348).

Useful sta059 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:93 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or 15 more) to SEQ In NO:93; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ In NO:93, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta059 proteins include variants of SEO ED NO:93. Preferred 20 fragments of (b) comprise an epitope from SEQ ID NO:93. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 25 In NO:93 while retaining at least one epitope of SEQ ID NO:93. The first 20N-terminal amino acids of SEQ In NO:93 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta060' antigen is annotated as 'peptide ABC trans- 30 porter; peptide-binding protein'. In the NCTC 8325 strain sta060 IS SAOUHSC 02767 and has amino acid sequence SEQ ID NO:94 (GI:88196403).

Useful sta060 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:94 35 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more identity to SEQ In NO:94; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ In NO:94, 40 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta060 proteins include variants of SEQ ID NO:94. Preferred fragments of (b) comprise an epitope from SEQ In NO:94. Other preferred fragments lack one or more amino acids (e.g. 45 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:94 while retaining at least one epitope of SEQ In NO:94. The first 20N-terminal amino acids of SEQ In NO:94 50 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta061' antigen is annotated as 'protein with leader'. In the NCTC 8325 strain sta061 is SAOUHSC_02783 and has amino acid sequence SEQ ID NO:95 (GI:88196419).

Useful sta061 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:95 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more 60 identity to SEQ ID NO:95; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:95, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta061 proteins include variants of SEQ ID NO:95. Preferred 65 fragments of (b) comprise an epitope from SEQ ID NO:95. Other preferred fragments lack one or more amino acids (e.g.

1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:95 while retaining at least one epitope of SEQ ID NO:95. The first 21N-terminal amino acids of SEQ ID NO:95 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta062' antigen is annotated as 'protein with leader'. In the NCTC 8325 strain sta062 is SAOUHSC_02788 and has amino acid sequence SEQ ID NO:96 (GI: δ 196424).

Useful sta062 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:96 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%), 98%), 99%, 99.5%) or more) to SEQ ID NO:96; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:96, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta062 proteins include variants of SEO ID NO:96. Preferred fragments of (b) comprise an epitope from SEQ ID NO:96. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:96 while retaining at least one epitope of SEQ ID NO:96. The first 22N-terminal amino acids of SEQ ID NO:96 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta063, antigen is annotated as 'aureolysin'. In the NCTC 8325 strain sta063 is SAOUHSC_02971 and has amino acid sequence SEQ ID NO:97 (GI:88196592).

Useful sta063 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:97 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:97; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:97, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta063 proteins include variants of SEQ ID NO:97. Preferred fragments of (b) comprise an epitope from SEQ ID NO:97. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEO ID NO:97 while retaining at least one epitope of SEQ ID NO:97. The first 16N-terminal amino acids of SEQ ID NO:97 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta064' antigen is annotated as 'lipase'. In the NCTC 8325 strain sta064 is SAOUHSC_03006 and has amino acid sequence SEQ ID NO:98 (GI: 88 196625). In the Newman 55 strain it is nwmn 2569 (GI: 151222781).

Useful sta064 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:98 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:98; and/or (b) comprising a fragment of at least In' consecutive amino acids of SEQ ID NO:98, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta064 proteins include variants of SEQ ID NO:98. Preferred fragments of (b) comprise an epitope from SEQ ID NO:98. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:98 while retaining at least one epitope of SEQ ID NO:98. The first 34N-terminal amino acids of SEQ ID NO:98 scan usefully be omitted. Other fragments omit one or more protein domains.

The 'sta065' antigen is annotated as '1-phosphatidylinositol phosphodiesterase precursor'. In the NCTC 8325 strain sta065 is SAOUHSC 00051 and has amino acid sequence 10 SEQ ID NO:99 (GI:88193871).

Useful sta065 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:99 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 15 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:99; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:99, wherein In' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 20 sta065 proteins include variants of SEQ ID NO:99. Preferred fragments of (b) comprise an epitope from SEQ ID NO:99. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 25) 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:99 while retaining at least one epitope of SEQ ID NO:99. The first 26N-terminal amino acids of SEQ ID NO:99 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta066' antigen is annotated as 'protein'. In the NCTC 8325 strain sta066 is SAOUHSC_00172 and has amino acid sequence SEQ ID No:100 (GI:88193982).

Useful sta066 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:100 35 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:100; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:100, 40 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta066 proteins include variants of SEQ ID No:100. Preferred fragments of (b) comprise an epitope from SEQ ID No:100. Other preferred fragments lack one or more amino acids (e.g. 45 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:100 while retaining at least one epitope of SEQ ID No:100. The first 21 N-terminal amino acids of SEQ ID 50 No:100 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta067' antigen is annotated as 'bacterial extracellular solute-binding protein'. In the NCTC 8325 strain sta067 is SAOUHSC_00176 and has amino acid sequence SEQ ID 55 NO:101 (GI: δ 193986).

Useful sta067 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:101 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 60 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:101; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:101, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 65 sta067 proteins include variants of SEQ ID No:101. Preferred fragments of (b) comprise an epitope from SEQ ID No:101.

Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:101 while retaining at least one epitope of SEQ ID No:101. The first 20 N-terminal amino acids of SEQ ID No:101 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta068' antigen is annotated as 'iron permease FTRI'. In the NCTC 8325 strain sta068 is SAOUHSC_00327 and has amino acid sequence SEQ ID No:102 (GI:88194127).

Useful sta068 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:102 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:102; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:102, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta068 proteins include variants of SEQ ID No:102. Preferred fragments of (b) comprise an epitope from SEQ ID No:102. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED No:102 while retaining at least one epitope of SEQ ID No:102. The final 20 C-terminal amino acids of SEQ ID No:102 can usefully be omitted. The first 14 N-terminal amino acids of SEQ ID No: 102 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta069' antigen is annotated as 'autolysin precursor'. In the NCTC 8325 strain sta069 is SAOUHSC_00427 and has amino acid sequence SEQ ID No:103 (GI:88194219).

Useful sta069 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:103 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:103; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:103, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta069 proteins include variants of SEQ ID NO:103. Preferred fragments of (b) comprise an epitope from SEQ ID No:103. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:103 while retaining at least one epitope of SEQ ID NO:103. The first 25 N-terminal amino acids of SEQ ID NO:103 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta070' antigen is annotated as 'immunogenic secreted precursor-like protein (truncated)'. In the NCTC 8325 strain sta070 is SAOUHSC_00773 and has amino acid sequence SEQ ID No:104 (GI:88194535).

Useful sta070 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:104 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:104; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:104, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta070 proteins include variants of SEQ ID No:104. Preferred

fragments of (b) comprise an epitope from SEQ ID No:104. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:104 while retaining at least one epitope of SEQ ID No:104. The first 24 N-terminal amino acids of SEQ ID No:104 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta071' antigen is annotated as 'hemolysin'. In the 10 NCTC 8325 strain sta071 is SAOUHSC_00854 and has amino acid sequence SEQ ID NO:105 (GI:88194612).

Useful sta071 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:105 and/or may comprise an amino acid sequence: (a) having 50% 15 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:105; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:105, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 20 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta071 proteins include variants of SEQ ID No:105. Preferred fragments of (b) comprise an epitope from SEQ ID No:105. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 25 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:105 while retaining at least one epitope of SEQ ID No:105. The first 24 N-terminal amino acids of SEQ ID No:105 can usefully be omitted. Other fragments omit one or 30 more protein domains.

The 'sta072' antigen is annotated as 'extramembranal protein'. In the NCTC 8325 strain sta072 is SAOUHSC_00872 and has amino acid sequence SEQ ID No:106 (GI:88194629).

Useful sta072 antigens can elicit an antibody (e.g. when 35 administered to a human) that recognizes SEQ ID No:106 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:106; and/or (b) comprising a fragment of 40 HSC_01256 and has amino acid sequence SEQ ID NO:109 at least 'n' consecutive amino acids of SEQ ID No:106, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta072 proteins include variants of SEQ ID No:106. Preferred fragments of (b) comprise an epitope from SEQ ID No:106. 45 Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:106 while retaining at least one epitope of SEQ ID 50 No:106. The first 24 N-terminal amino acids of SEQ ID NO:106 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta073' antigen is annotated as 'bifunctional autolysin precursor'. In the NCTC 8325 strain sta073 is SAOUHSC_ 55 00994 and has amino acid sequence SEQ ID No:107 (GI: 88194750). In the Newman strain it is nwmn_0922 (GI: 151221134). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful sta073 antigens can elicit an antibody (e.g. when 60 administered to a human) that recognizes SEQ ID No:107 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:107; and/or (b) comprising a fragment of 65 at least 'n' consecutive amino acids of SEQ ID NO:107, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30,

35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta073 proteins include variants of SEQ ID No:107. Preferred fragments of (b) comprise an epitope from SEQ ID No:107. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:107 while retaining at least one epitope of SEQ ID NO:107. The first 24 N-terminal amino acids of SEQ ID NO:107 can usefully be omitted. Other fragments omit one or more protein domains.

A Sta073 antigen can usefully be included in a composition in combination with a Sta112. Sta073 does not adsorb well to aluminium hydroxide adjuvants, so Sta073 present in a composition may be unadsorbed or may be adsorbed to an alternative adjuvant e.g. to an aluminium phosphate.

The 'sta074' antigen is annotated as 'factor essential for methicillin resistance'. In the NCTC 8325 strain sta074 is SAOUHSC_01220 and has amino acid sequence SEQ ID No:108 (GI:88194956).

Useful sta074 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ED No:108 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:108; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:108, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta074 proteins include variants of SEQ ID No:108. Preferred fragments of (b) comprise an epitope from SEQ ID No:108. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:108 while retaining at least one epitope of SEQ ID No:108. Other fragments omit one or more protein domains.

The 'sta075' antigen is annotated as 'insulysin; peptidase family M16'. In the NCTC 8325 strain sta075 is SAOU-(GI:88194989).

Useful sta075 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:109 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEO ID No:109; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:109, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta075 proteins include variants of SEQ ID 10 No:109. Preferred fragments of (b) comprise an epitope from SEQ ID No:109. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:109 while retaining at least one epitope of SEQ ID No:109. Other fragments omit one or more protein domains.

The 'sta076' antigen is annotated as 'hydrolase'. In the NCTC 8325 strain sta076 is SAOUHSC_01263 and has amino acid sequence SEQ ID No:110 (GI:88194996).

Useful sta076 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:110 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:110; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:110, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta076 proteins include variants of SEQ ID No:110. Preferred 5 fragments of (b) comprise an epitope from SEQ ID No:110. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEO 10 ID No:110 while retaining at least one epitope of SEQ ID NO:110. The first 24 N-terminal amino acids of SEQ ID NO:110 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta077' antigen is annotated as 'protein'. In the NCTC 15 8325 strain sta077 is SAOUHSC_01317 and has amino acid sequence SEQ ID NO:111 (GI:88195047). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful sta077 antigens can elicit an antibody (e.g. when 20 administered to a human) that recognizes SEQ ID NO:111 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:111; and/or (b) comprising a fragment of 25 at least 'n' consecutive amino acids of SEQ ID NO:111, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta077 proteins include variants of SEQ ID No:111. Preferred fragments of (b) comprise an epitope from SEQ ID No:111. 30 Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:111 while retaining at least one epitope of SEQ ID 35 NO:114 can usefully be omitted. Other fragments omit one or NO:111. The first 20 N-terminal amino acids of SEQ ID NO:111 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta078' antigen is annotated as 'FtsK/SpoIIIE family protein'. In the NCTC 8325 strain sta078 is SAOUHSC_ 40 01857 and has amino acid sequence SEQ ID No:112 (GI: 88195555)

Useful sta078 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:112 and/or may comprise an amino acid sequence: (a) having 50% 45 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:112; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:112, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 50 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta078 proteins include variants of SEQ ID No:112. Preferred fragments of (b) comprise an epitope from SEQ ID No:112. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 55 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:112 while retaining at least one epitope of SEQ ID No:112. Other fragments omit one or more protein domains.

The 'sta079' antigen is annotated as 'serine protease SpIF'. 60 In the NCTC 8325 strain sta079 is SAOUHSC_01935 and has amino acid sequence SEQ ID NO:113 (GI:88195630).

Useful sta079 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:113 and/or may comprise an amino acid sequence: (a) having 50% 65 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 30 99.5%

or more) to SEQ ID NO:113; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:113, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta079 proteins include variants of SEQ ID NO:113. Preferred fragments of (b) comprise an epitope from SEQED NO:113. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 35 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:113 while retaining at least one epitope of SEQ ID NO:113. The first 36 N-terminal amino acids of SEQ ID NO:113 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta080' antigen is annotated as 'serine protease SpIE'. In the NCTC 8325 strain sta080 is SAOUHSC_01936 and has amino acid sequence SEQ ID No:114 (GI:88195631).

Useful sta080 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ED No:114 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:114; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:114, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta080 proteins include variants of SEQ ID NO:114. Preferred fragments of (b) comprise an epitope from SEQ ID NO:114. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED No:114 while retaining at least one epitope of SEQ ID NO:114. The first 36 N-terminal amino acids of SEQ ID more protein domains.

The 'sta081' antigen is annotated as 'serine protease SplD (EC:3.4.21.19)'. In the NCTC 8325 strain sta081 is SAOU-HSC_01938 and has amino acid sequence SEQ ID No:154 (GI:88195633).

Useful sta081 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:154 and/or may comprise an amino acid sequence: (a) having 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more identity to SEQ ID No:154; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEO ID NO:154, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta081 proteins include variants of SEQ ID No:154. Preferred fragments of (b) comprise an epitope from SEQ ID No:154. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from 30 the N-terminus of SEQ ID No:154 while retaining at least one epitope of SEQ ID No:154. The first 36 N-terminal amino acids of SEQ ID No:154 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta082' antigen is annotated as 'serine protease SplC' In the NCTC 8325 strain sta082 is SAOUHSC_01939 and has amino acid sequence SEQ ID NO:115 (GI:88195634).

Useful sta082 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:115 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%), 99.5% or more) to SEQ ID NO:115; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:115, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta082 proteins include variants of SEQ ID No:115. Preferred 5 fragments of (b) comprise an epitope from SEQ ID No:115. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 10 ID NO:115 while retaining at least one epitope of SEQ ID NO:115. The first 36 N-terminal amino acids of SEQ ID NO:115 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta083' antigen is annotated as 'serine protease SplB'. 15 In the NCTC 8325 strain sta083 is SAOUHSC_01941 and has amino acid sequence SEQ ID NO:116 (GI:88195635).

Useful sta083 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:116 and/or may comprise an amino acid sequence: (a) having 50% 20 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:116; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:116, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 25 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta083 proteins include variants of SEQ ID No:116. Preferred fragments of (b) comprise an epitope from SEQ ID No:116. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 30 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:116 while retaining at least one epitope of SEQ ID NO:116. The first 36 N-terminal amino acids of SEQ ID No:116 can usefully be omitted. Other fragments omit one or 35 more protein domains.

The 'sta084' antigen is annotated as 'serine protease SplA'. In the NCTC 8325 strain sta084 is SAOUHSC_01942 and has amino acid sequence SEQ ID No:117 (GI:88195636).

Useful sta084 antigens can elicit an antibody (e.g. when 40 administered to a human) that recognizes SEQ ID NO:117 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more) to SEQ ID NO:117; and/or (b) comprising a fragment 45 of at least 'n' consecutive amino acids of SEQ ID NO:117, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta084 proteins include variants of SEQ ID No:117. Preferred fragments of (b) comprise an epitope from SEQ ID No:117. 50 Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:117 while retaining at least one epitope of SEQ ID 55 6,7,8,9,10,15,20,25 or more) from the N-terminus of SEQ No:117. The first N-terminal amino acids of SEQ ID No:117 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta085' antigen is annotated as 'staphylokinase precursor'. In the NCTC 8325 strain sta085 is SAOUHSC_ 60 02171 and has amino acid sequence SEQ ID NO:118 (GI: 88195848)

Useful sta085 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:118 and/or may comprise an amino acid sequence: (a) having 50% 65 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or

more) to SEQ ID NO:118; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:118, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta085 proteins include variants of SEQ ID NO:118. Preferred fragments of (b) comprise an epitope from SEQ ID No:118. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEO ID NO:118 while retaining at least one epitope of SEQ ID NO:118. The first 27 N-terminal amino acids of SEQ ID NO:118 can usefully be omitted. Other fragments omit one or 20 more protein domains.

The 'sta086' antigen is annotated as 'OxaA-like protein'. In the NCTC 8325 strain sta086 is SAOUHSC_02327 and has amino acid sequence SEQ ID NO:119 (GI:88195993).

Useful sta086 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:119 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:119; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:119, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta086 proteins include variants of SEQ ID NO:119. Preferred fragments of (b) comprise an epitope from SEQ ID NO:119. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:119 while retaining at least one epitope of SEQ ID NO:119. The first 19 N-terminal amino acids of SEQ ID NO:119 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta087' antigen is annotated as 'teicoplanin resistance protein TcaA'. In the NCTC 8325 strain sta087 is SAOU-HSC_02635 and has amino acid sequence SEQ ID No:120 (GI:88196276).

Useful sta087 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:120 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:120; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEO ID No:120, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta087 proteins include variants of SEQ ID No:120. Preferred fragments of (b) comprise an epitope from SEQ ID No:120. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, ID No:120 while retaining at least one epitope of SEQ ID No:120. Other fragments omit one or more protein domains.

The 'sta088' antigen is annotated as 'esterase'. In the NCTC 8325 strain sta088 is SAOUHSC_02844 and has amino acid sequence SEQ ID No:121 (GI:88196477).

Useful sta088 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:121 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:121; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:121,

wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta088 proteins include variants of SEQ ID NO:121. Preferred fragments of (b) comprise an epitope from SEQ ID NO:121. Other preferred fragments lack one or more amino 5 acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the SEQ ID NO:121 while retaining at least one epitope of SEQ ID NO:121. The first 18 N-terminal amino acids of SEQ ID 10 NO:121 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta089' antigen is annotated as 'LysM domain protein'. In the NCTC 8325 strain sta089 is SAOUHSC_02855 and has amino acid sequence SEQ ID No:122 (GI:88196486). 15

Useful sta089 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:122 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or 20 more) to SEQID No:122; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:122, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta089 proteins include variants of SEQ ID No:122. Preferred fragments of 25 (b) comprise an epitope from SEQ ID No:122. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:122 30 while retaining at least one epitope of SEQ ID NO:122. The first 20 N-terminal amino acids of SEQ ID No:122 can usefully be omitted. Other fragments omit one or more protein domains

The 'sta090' antigen is annotated as 'LysM domain pro- 35 tein'. In the NCTC 8325 strain sta090 is SAOUHSC_02883 and has amino acid sequence SEQ ID No:123 (GI:88196512).

Useful sta090 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:123 and/or may comprise an amino acid sequence: (a) having 50% 40 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:123; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:123, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 45 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta090 proteins include variants of SEO ID No:123. Preferred fragments of (b) comprise an epitope from SEQ ID No:123. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 50 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:123 while retaining at least one epitope of SEQ ID No:123. The first 26 N-terminal amino acids of SEQ ID No:123 can usefully be omitted. Other fragments omit one or 55 more protein domains.

The 'sta091' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta091 is SAOUHSC_00685 and has amino acid sequence SEQ ID No:124 (GI:88194450).

Useful sta091 antigens can elicit an antibody (e.g. when 60 administered to a human) that recognizes SEQ ED No:124 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:124; and/or (b) comprising a fragment of 65 at least 'n' consecutive amino acids of SEQ ID NO:124, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30,

35, 40, 50, 60, 70, 80, 90, 100 or more). These sta091 proteins include variants of SEQ ID No:124. Preferred fragments of (b) comprise an epitope from SEQ ID No:124. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:124 while retaining at least one epitope of SEQ ID No:124. The first 15 N-terminal amino acids of SEQ ID No:124 can use-fully be omitted. Other fragments omit one or more protein domains.

The 'sta092' antigen is annotated as 'M23/M37 peptidase domain protein'. In the NCTC 8325 strain sta092 is SAOU-HSC_00174 and has amino acid sequence SEQ ID No:125 (GI:88193984).

Useful sta092 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:125 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:125; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:125, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta092 proteins include variants of SEQ ID NO:125. Preferred fragments of (b) comprise an epitope from SEQ ID NO:125. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:125 while retaining at least one epitope of SEQ ID NO:125. The first 25 N-terminal amino acids of SEQ ID No:125 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta093, antigen is annotated as 'protein'. In the NCTC 8325 strain sta093 is SAOUHSC_01854 and has amino acid sequence SEQ ID NO:126 (GI:88195552).

Useful sta093 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:126 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:126; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:126, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta093 proteins include variants of SEO ID NO:126. Preferred fragments of (b) comprise an epitope from SEQ ID NO:126. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:126 while retaining at least one epitope of SEQ ID No:126. Other fragments omit one or more protein domains

The 'sta094' antigen is annotated as 'protein'. In the NCTC 8325 strain sta094 is SAOUHSC_01512 and has amino acid sequence SEQ ID NO:127 (GI:88195226).

Useful sta094 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ED No:127 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:127; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:127, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta094 proteins include variants of SEQ ID No:127. Preferred fragments of (b) comprise an epitope from SEQ ID No:127. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 5 6, 7, 8, 9, 10, 15, 20, 25or more) from the N-terminus of SEQ ID No:127 while retaining at least one epitope of SEQ ID No:127. The first 17 N-terminal amino acids of SEQ ID NO:127 can usefully be omitted. Other fragments omit one or more protein domains. 10

The 'sta095' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta095 is SAOUHSC 00383 and has amino acid sequence SEQ ID No:128 (GI: 88194180). In the Newman strain it is nwmn_0388 (GI: 151220600)

Useful sta095 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:128 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or 20 more) to SEQ ID NO:128; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:128, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 20 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta095 proteins include variants of SEQ ID No:128. Preferred 25 fragments of (b) comprise an epitope from SEQ ID No:128. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ 30 ID No:128 while retaining at least one epitope of SEQ ID NO:128. The first 32 N-terminal amino acids of SEQ ID NO:128 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta096' antigen is annotated as 'superantigen-like 35 protein'. In the NCTC 8325 strain sta096 is SAOUHSC 00384 and has amino acid sequence SEQ ID No:129 (GI: 88194181). Useful sta096 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:129 and/or may comprise an amino acid sequence: (a) 40 having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%) or more) to SEQ ID No:129; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO:129, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 45 16, 18, 20, 25, 30, 35, 35 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta096 proteins include variants of SEQ ID No:129. Preferred fragments of (b) comprise an epitope from SEQ ID No:129. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) 50 from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:129 while retaining at least one epitope of SEQ ID NO:129. The first 30 N-terminal amino acids of SEQ ID NO:129 can usefully be omitted. Other fragments 55 6,7,8,9,10,15,20,25 or more) from the N-terminus of SEQ omit one or more protein domains.

The 'sta097' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta097 is SAOUHSC 00386 and has amino acid sequence SEQ ID No:130 (GI: 88194182)

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Useful sta097 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:130 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or 65 more) to SEQID No:130; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:130,

wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta097 proteins include variants of SEQ ID No:130. Preferred fragments of (b) comprise an epitope from SEQ ID No:130. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:130 while retaining at least one epitope of SEQ ID NO:130. The first 30 N-terminal amino acids of SEQ ID NO:130 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta098' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta098 is SAOUHSC 00389 and has amino acid sequence SEQ ID No:131 (GI:

88194184). In the Newman strain it is nwmn_0391 (GI: 151220603).

Useful sta098 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:131 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:131; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:131, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta098 proteins include variants of SEQ ID No:131. Preferred fragments of (b) comprise an epitope from SEQ ID No:131. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:131 while retaining at least one epitope of SEQ ID No:131. The first 30 N-terminal amino acids of SEQ ID No:131 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta099' antigen is annotated as 'superantigen-like protein 5'. In the NCTC 8325 strain sta099 is SAOUHSC 00390 and has amino acid sequence SEQ ID No:132 (GI: 88194185).

Useful sta099 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:132 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:132; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEO ID NO:132, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta099 proteins include variants of SEQ ID No:132. Preferred fragments of (b) comprise an epitope from SEQ ID No:132. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, ID No:132 while retaining at least one epitope of SEQ ID NO:132. The first 30 N-terminal amino acids of SEQ ID NO:132 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta100' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta100 is SAOUHSC 00391 and has amino acid sequence SEQ ID No:133 (GI: 88194186)

Useful sta100 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:133 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ED No:133; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:133, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These ⁵ sta100 proteins include variants of SEQ ID NO:133. Preferred fragments of (b) comprise an epitope from SEQ ID NO:133. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:133 while retaining at least one epitope of SEQ ID NO:133. The first 30 N-terminal amino acids of SEQ ID NO:133 can usefully be omitted. Other fragments omit one or 15 more protein domains.

The 'sta101' antigen is annotated as 'superantigen-like protein 7'. In the NCTC 8325 strain sta101 is SAOUHSC_00392 and has amino acid sequence SEQ ID No:134 (GI: 88194187). In the Newman strain it is nwrnn_0394 (GI: 20 151220606).

Useful sta101 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:134 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 25 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:134; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:134, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These 30 sta101 proteins include variants of SEQ ID No:134. Preferred fragments of (b) comprise an epitope from SEQ ID No:134. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 35 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED NO:134 while retaining at least one epitope of SEQ ID NO:134. The first 30 N-terminal amino acids of SEQ ID NO:134 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta102' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta102 is SAOUHSC_____00393 and has amino acid sequence SEQ ID No:135 (GI: 88194188).

Useful sta102 antigens can elicit an antibody (e.g. when 45 administered to a human) that recognizes SEQ ID NO:135 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO:135; and/or (b) comprising a fragment 50 of at least 'n' consecutive amino acids of SEQ ID NO:135, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta102 proteins include variants of SEQ ID NO:135. Preferred fragments of (b) comprise an epitope from SEQ ID 55 NO:135. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:135 while retaining at least one epitope of SEQ 60 ID NO:135. The first 17 N-terminal amino acids of SEQ ID NO:135 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta103' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta103 is SAOUHSC_____00394 and has amino acid sequence SEQ ID No:136 (GI: 88194189).

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Useful sta103 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:136 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:136; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:136, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta103 proteins include variants of SEQ ID No:136. Preferred fragments of (b) comprise an epitope from SEQ ID No:136. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:136 while retaining at least one epitope of SEQ ID No:136. The first 23 N-terminal amino acids of SEQ ID No:136 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta104' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta104 is SAOUHSC 00395 and has amino acid sequence SEQ ID No:137 (GI: 88194190).

Useful sta104 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:137 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:137; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:137, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta104 proteins include variants of SEQ ID No:137. Preferred fragments of (b) comprise an epitope from SEQ ID No:137. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:137 while retaining at least one epitope of SEQ ID NO: 40 137. Other fragments omit one or more protein domains.

The 'sta105' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain sta105 is 20 SAOUHSC_00399 and has amino acid sequence SEQ ID NO:138 (GI: 88194194). In the Newman strain it is nwmn_0400 (GI: 151220612).

Useful sta105 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEO ID No:138 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:138; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:138, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta105 proteins include variants of SEQ ID No:138. Preferred fragments of (b) comprise an epitope from SEQ ID NO:138. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:138 while retaining at least one epitope of SEQ ID NO:138. The first 30 N-terminal amino acids of SEQ ID NO:138 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta106' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain sta106 is SAOUHSC_01115 and has amino acid sequence SEQ ED NO:139 (GI:88194861).

Useful sta106 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:139 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or 5 more) to SEQID No:139; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:139, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta106 proteins include variants of SEO ID NO:139. Preferred fragments of 10 (b) comprise an epitope from SEQ ID No:139. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:139 15 while retaining at least one epitope of SEQ ID No:139. The first 16 N-terminal amino acids of SEQ ID No:139 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta107' antigen is annotated as 'hypothetical protein'. 20 In the NCTC 8325 strain sta107 is SAOUHSC_00354 and has amino acid sequence SEQ ID No:140 (GI:88194153).

Useful sta107 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:140 and/or may comprise an amino acid sequence: (a) having 50% 25 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:140; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:140, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 30 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta107 proteins include variants of SEQ ID No:140. Preferred fragments of (b) comprise an epitope from SEQ ID No:140. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 35 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED No:140 while retaining at least one epitope of SEQ ID NO:140. The first 35 N-terminal amino acids of SEQ ID NO:140 can usefully be omitted. Other fragments omit one or 40 more protein domains.

The 'sta108' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain sta108 is SAOUHSC_00717 and has amino acid sequence SEQ ID No:141 (GI:88194482).

Useful sta108 antigens can elicit an antibody (e.g. when 45 administered to a human) that recognizes SEQ ID No:141 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:141; and/or (b) comprising a fragment of 50 at least 'n' consecutive amino acids of SEQ ID No:141, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta108 proteins include variants of SEQ ID NO:141. Preferred fragments of (b) comprise an epitope from SEQ ID No:141. Other pre- 55 ferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:141 while retaining at least one epitope of SEQ ID No:141. The 60 first 20 N-terminal amino acids of SEQ ID No:141 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta109' antigen is annotated as 'N-acetylmuramoyl-L-alanine amidase'. In the NCTC 8325 strain sta109 is 65 SAOUHSC_02979 and has amino acid sequence SEQ ID No:142 (GI:88196599).

Useful sta109 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:142 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:142; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:142, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta109 proteins include variants of SEQ ID No:142. Preferred fragments of (b) comprise an epitope from SEQ ID No:142. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:142 while retaining at least one epitope of SEQ ID NO:142. The first 27 N-terminal amino acids of SEQ ID No:142 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stal10' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stal10 is SAOUHSC_01039 and has amino acid sequence SEQ ID NO:143 (GI:88194791).

Useful sta110 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:143 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:143; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:143, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta110 proteins include variants of SEQ ID No:143. Preferred fragments of (b) comprise an epitope from SEQ ID No:143. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:143 while retaining at least one epitope of SEQ ID NO:143. The first 19 N-terminal amino acids of SEQ ID No:143 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stal11' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stal11 is SAOUHSC_01005 and has amino acid sequence SEQ ED NO:144 (GI:88194760).

Useful sta111 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ED No:144 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ED No:144; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:144, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta111 proteins include variants of SEQ ID NO:144. Preferred fragments of (b) comprise an epitope from SEQ ED No:144. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED NO:144 while retaining at least one epitope of SEQ ID NO:144. The first 20 N-terminal amino acids of SEQ ID No:144 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta112' antigen is annotated as a putative 'ABC transporter, substrate-binding protein'. In the NCTC 8325 strain sta112 is SAOUHSC 00634 and has amino acid sequence SEQ ID No:145 (GI:88194402).

Useful sta112 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:145 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, or 5 more) to SEQ ED No:145; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:145, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta112 proteins include variants of SEQ ED NO:145. Pre- 10 ferred fragments of (b) comprise an epitope from SEQ ID NO:145. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of 15 SEQ ID No:145 while retaining at least one epitope of SEQ ID NO:145. The first 17 N-terminal amino acids of SEQ ID No:145 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stal13' antigen is annotated as 'hypothetical protein'. 20 In the NCTC 8325 strain stal13 is SAOUHSC_00728 and has amino acid sequence SEQ ID NO:146 (GI:88194493).

Useful sta113 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ED No:146 and/or may comprise an amino acid sequence: (a) having 50% 25 or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:146; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:146, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 30 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta113 proteins include variants of SEQ ID No:146. Preferred fragments of (b) comprise an epitope from SEQ ID No:146. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the 35 C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from 10 the N-terminus of SEQ ID No:146 while retaining at least one epitope of SEQ DD NO:146. The first 173 N-terminal amino acids of SEQ ID NO:146 can usefully be omitted. Other fragments omit one or 40 more protein domains.

The 'stal14' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stal14 is SAOUHSC_00810 and has amino acid sequence SEQ ID NO:147 (GI:88194570).

Useful sta114 antigens can elicit an antibody (e.g. when 45 administered to a human) that recognizes SEQ ED No:147 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:147; and/or (b) comprising a fragment of 50 at least 'n' consecutive amino acids of SEQ ID NO:147, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta114 proteins include variants of SEQ ID No:147. Preferred fragments of (b) comprise an epitope from SEQ ID No:147. Other 55 preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:147 while retaining at least one epitope of SEQ ID No:147. Other 60 fragments omit one or more protein domains.

The 'stal15' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stal15 is SAOUHSC_00817 and has amino acid sequence SEQ ID NO:148 (GI:88194576).

Useful sta115 antigens can elicit an antibody (e.g. when 65 administered to a human) that recognizes SEQ ID No:148 and/or may comprise an amino acid sequence: (a) having 50%

or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ED No:148; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:148, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 35 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta115 proteins include variants of SEQ ID No:148. Preferred fragments of (b) comprise an epitope from SEQ ID No:148. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:148 while retaining at least one epitope of SEQ ID No:148. The first 18 N-terminal amino acids of SEQ ID No:148 can usefully be omitted. Other fragments omit one or more protein domains

The 'stal16' antigen is annotated as 'formyl peptide receptor-like 1 inhibitory protein'. In the NCTC 8325 strain stal16 IS SAOUHSC 01112 and has amino acid sequence SEQ ID NO:149 (GI:88194858).

Useful sta116 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:149 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:149; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:149, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These stal16 proteins include variants of SEQ ID NO:149. Preferred fragments of (b) comprise an epitope from SEQ ID No:149. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO:149 while retaining at least one epitope of SEQ ID No:149. The first 20 N-terminal amino acids of SEQ ID No:149 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stal17' antigen is annotated as 'truncated betahemolysin'. In the NCTC 8325 strain stal17 is SAOUHSC_____02240 and has amino acid sequence SEQ ID NO:150 (GI: 88195913).

Useful sta117 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO:150 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID No:150; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO:150, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta117 proteins include variants of SEQ ID No:150. Preferred fragments of (b) comprise an epitope from SEQ ID No:150. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED No:150 while retaining at least one epitope of SEQ ID NO:150. Other fragments omit one or more protein domains.

The 'stal18' antigen is annotated as 'cell division protein FtsZ'. In the NCTC 8325 strain stal18 is SAOUHSC_01150 and has amino acid sequence SEQ ID NO:151 (GI: 88194892).

Useful stal18 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID No:151 and/or may comprise an amino acid sequence: (a) having 50%

or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%), 99%, 99.5%) or more) to SEQ ED No:151; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:151, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 5 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta118 proteins include variants of SEQ ID No:151. Preferred fragments of (b) comprise an epitope from SEQ ID No:151. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from 10 the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:151 while retaining at least one epitope of SEQ ID NO:151. Other fragments omit one or more protein domains. 15

The 'stal19' antigen is annotated as 'thioredoxin'. In the NCTC 8325 strain stal19 is SAOUHSC_01100 and has amino acid sequence SEQ ID NO:152 (GI:88194846).

Useful sta119 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEO ID No:152 20 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQID No:152; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID No:152, 25 wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta119 proteins include variants of SEQ ID NO:152. Preferred fragments of (b) comprise an epitope from SEQ ID No:152. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 30 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID No:152 while retaining at least one epitope of SEQ ID No:152. Other fragments omit one or more protein domains.

The 'sta120' antigen is annotated as 'alkyl hydroperoxide reductase subunit c'. In the NCTC 8325 strain sta120 is SAOUHSC_00365 and has amino acid sequence SEQ ID No:153 (GI:88194163).

Useful sta120 antigens can elicit an antibody (e.g. when 40 administered to a human) that recognizes SEQ ID No:153 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 35 99.5% or more) to SEQ ID No:153; and/or (b) comprising a fragment 45 of at least 'n' consecutive amino acids of SEQ ID No:153, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta120 proteins include variants of SEQ ID No:153. Preferred fragments of (b) comprise an epitope from SEQ ID No:153. Other 50 preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ED No:153 while retaining at least one epitope of SEQ ID No:153. Other 55 fragments omit one or more protein domains.

An immune response refers to a humoral response, a cellular response, or both a humoral and cellular response in an organism. An immune response can be measured by assays that include, but are not limited to, assays measuring the 60 presence or amount of antibodies that specifically recognize a protein or cell surface protein, assays measuring T-cell activation or proliferation, and/or assays that measure modulation in terms of activity or expression of one or more cytokines. 65

In still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%, identical or similar to an EsxA protein. In certain aspects the EsxA protein will have all or part of the amino acid sequence of SEQ ID No:11.

In still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%, identical or similar to an EsxB protein. In certain aspects the EsxB protein will have all or part of the amino acid sequence of SEQ ID No:12.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%, identical or similar to an SdrD protein. In certain aspects the SdrD protein will have all or part of the amino acid sequence of SEQ ID No:13.

In further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to an SdrE protein. In certain aspects the SdrE protein will have all or part of the amino acid sequence of SEQ ID No:14.

In still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%, identical or similar to an IsdA protein. In certain aspects the IsdA protein will have all or part of the amino acid sequence of SEQ ID NO:15.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%), or 99%) identical or similar to an IsdB protein. In certain aspects the IsdB protein will have all or part of the amino acid sequence of SEQ ID No:16.

Embodiments of the invention include compositions that include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%) identical or similar to a EsaB protein. In certain aspects the EsaB protein will have all or part of the amino acid sequence of SEQ ED No:17.

In a further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a ClfB protein. In certain aspects the ClfB protein will have all or part of the amino acid sequence of SEQ ID No:18.

In still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to an IsdC protein. In certain aspects the IsdC protein will have all or part of the amino acid sequence of SEQ ID No:19.

In yet further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a SasF protein. In certain aspects the SasF protein will have all or part of the amino acid sequence of SEQ ID NO:20.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a SdrC protein. In certain aspects the SdrC protein will have all or part of the amino acid sequence of SEQ ID NO:21.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%,

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or 99% identical or similar to a ClfA protein. In certain aspects the ClfA protein will have all or part of the amino acid sequence of SEQ ED NO:22.

In vet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or 5 is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to an Eap protein. In certain aspects the Eap protein will have all or part of the amino acid sequence of SEQ ID NO:23.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to an Ebh protein. In certain aspects the Ebh protein will have all or part of the amino acid 15 sequence of SEQ ID NO:24.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to an Emp protein. In certain 20 aspects the Emp protein will have all or part of the amino acid sequence of SEQ ID NO:25.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 25 or 99% identical or similar to an EsaC protein. In certain aspects the EsaC protein will have all or part of the amino acid sequence of SEQ ID NO:26. Sequence of EsaC polypeptides can be found in the protein databases and include, but are not limited to accession numbers ZP_02760162 (GI: 30 168727885), NP_645081.1 (GI:21281993), and NP_370813.1 (GI: 15923279), each of which is incorporated herein by reference as of the priority date of this application.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or 35 is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a Coa protein. In certain aspects the Coa protein will have all or part of the amino acid sequence of SEQ ID NO:27.

In yet still further embodiments of the invention a compo- 40 sition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a Hla protein. In certain aspects the Hla protein will have all or part of the amino acid sequence of SEQ ID NO:28.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a vWa protein. In certain aspects the vWa protein will have all or part of the amino acid 50 sequence of SEQ ID NO:29.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical or similar to a vWa protein. In certain aspects 55 the vWa protein will have all or part of the amino acid sequence of SEQ ID NO:32.

In yet still further embodiments of the invention a composition may include a polypeptide, peptide, or protein that is or is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 60 or 99% identical or similar to a FnbpB protein.

In certain aspects, a polypeptide or segment/fragment can have a sequence that is at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% or more identical to the amino acid sequence of the reference polypeptide. The term "simi-65 larity" refers to a polypeptide that has a sequence that has a certain percentage of amino acids that are either identical

with the reference polypeptide or constitute conservative substitutions with the reference polypeptides.

The polypeptides described herein may include 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or more variant amino acids within at least, or at most 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 300, 400, 500, 550, 1000or more contiguous amino acids, or any range derivable therein, of SEQ ID NO:2-30, or SEQ ID NO:32-155.

A polypeptide segment as described herein may include 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 300, 400, 500, 550, 1000 or more contiguous amino acids, or any range derivable therein, of SEQ ID NO:2-30, or SEO ID NO:33-155.

The compositions may be formulated in a pharmaceutically acceptable composition. In certain aspects of the invention the staphylococcus bacterium is an S. aureus bacterium.

In further aspects, a composition may be administered more than one time to the subject, and may be administered 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20 or more times. The administration of the compositions include, but is not limited to oral, parenteral, subcutaneous, intramuscular, intravenous, or various combinations thereof, including inhalation or aspiration.

In still further embodiments, a composition comprises a recombinant nucleic acid molecule encoding a polypeptide described herein or segments/fragments thereof. Typically a recombinant nucleic acid molecule encoding a polypeptide described herein contains a heterologous promoter. In certain aspects, a recombinant nucleic acid molecule of the invention is a vector, in still other aspects the vector is a plasmid. In certain embodiments the vector is a viral vector. In certain aspects a composition includes a recombinant, non-staphylococcus bacterium containing or expressing a polypeptide described herein. In particular aspects the recombinant non*staphylococcus* bacteria is *Salmonella* or another gram-positive bacteria. A composition is typically administered to mammals, such as human subjects, but administration to other animals that are capable of eliciting an immune response is contemplated. In further aspects the *staphylococ-* 5 *cus* bacterium containing or expressing the polypeptide is *Staphylococcus aureus*. In further embodiments the immune response is a protective immune response.

In further embodiments a composition comprises a recombinant nucleic acid molecule encoding all or part of one or 10 more of a Eap, Ebh, Emp, EsaB, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, SpA, vWbp, or vWh protein or peptide or variant thereof. Additional staphylococcal antigens that can be used in combination with the polypeptides described herein include, but 15 are not limited to 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), 20 Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating 25 protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/ saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP- 30 1, SSP-2, and/or Vitronectin binding protein. In particular aspects, a bacteria is a recombinant non-staphylococcus bacteria, such as a Salmonella or other gram-positive bacteria.

Compositions of the invention are typically administered to human subjects, but administration to other animals that 35 are capable of eliciting an immune response to a *staphylococcus* bacterium is contemplated, particularly cattle, horses, goats, sheep and other domestic animals, i.e., mammals.

In certain aspects the *staphylococcus* bacterium is a *Staphylococcus* aureus. In further embodiments the immune 40 response is a protective immune response. In still further aspects, the methods and compositions of the invention can be used to prevent, ameliorate, reduce, or treat infection of tissues or glands, e.g., mammary glands, particularly mastitis and other infections. Other methods include, but are not 45 limited to prophylactically reducing bacterial burden in a subject not exhibiting signs of infection, particularly those subjects suspected of or at risk of being colonized by a target bacteria, e.g., patients that are or will be at risk or susceptible to infection during a hospital stay, treatment, and/or recov- 50 erv.

Any embodiment discussed with respect to one aspect of the invention applies to other aspects of the invention as well. In particular, any embodiment discussed in the context of a SpA variant polypeptide or peptide or nucleic acid may be 55 implemented with respect to other antigens, such as Eap, Ebh, Emp, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh, 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen 60 binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/ 0169288), HarA, HBP, Immunodominant ABC transporter, 65 IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648,240),

MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/ Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein (or nucleic acids), and vice versa. It is also understood that any one or more of Eap, Ebh, Emp, EsaC, EsxA, EsxB, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, Coa, Hla, IsdC, SasF, vWbp, vWh, 52 kDa vitronectin binding protein (WO 01/60852), Aaa, Aap, Ant, autolysin glucosaminidase, autolysin amidase, Cna, collagen binding protein (U.S. Pat. No. 6,288,214), EFB (FIB), Elastin binding protein (EbpS), EPB, FbpA, fibrinogen binding protein (U.S. Pat. No. 6,008,341), Fibronectin binding protein (U.S. Pat. No. 5,840,846), FnbA, FnbB, GehD (US 2002/0169288), HarA, HBP, Immunodominant ABC transporter, IsaA/PisA, laminin receptor, Lipase GehD, MAP, Mg2+ transporter, MHC II analogue (U.S. Pat. No. 5,648,240), MRPII, Npase, RNA III activating protein (RAP), SasA, SasB, SasC, SasD, SasK, SBI, SdrF (WO 00/12689), SdrG/Fig (WO 00/12689), SdrH (WO 00/12689), SEA exotoxins (WO 00/02523), SEB exotoxins (WO 00/02523), SitC and Ni ABC transporter, SitC/MntC/saliva binding protein (U.S. Pat. No. 5,801,234), SsaA, SSP-1, SSP-2, and/or Vitronectin binding protein can be specifically excluded from a claimed composition.

Embodiments of the invention include compositions that contain or do not contain a bacterium. A composition may or may not include an attenuated or viable or intact staphylococcal bacterium. In certain aspects, the composition comprises a bacterium that is not a staphylococcal bacterium or does not contain staphylococcal bacteria. In certain embodiments a bacterial composition comprises an isolated or recombinantly expressed staphylococcal Protein A variant or a nucleotide encoding the same. The composition may be or include a recombinantly engineered *staphylococcus* bacterium that has been altered in a way that comprises specifically altering the bacterium with respect to a secreted virulence factor or cell surface protein. For example, the bacteria may be recombinantly modified to express more of the virulence factor or cell surface protein than it would express if unmodified.

The term "isolated" can refer to a nucleic acid or polypeptide that is substantially free of cellular material, bacterial material, viral material, or culture medium (when produced by recombinant DNA techniques) of their source of origin, or chemical precursors or other chemicals (when chemically synthesized). Moreover, an isolated compound refers to one that can be administered to a subject as an isolated compound; in other words, the compound may not simply be considered "isolated" if it is adhered to a column or embedded in an agarose gel. Moreover, an "isolated nucleic acid fragment" or "isolated peptide" is a nucleic acid or protein fragment that is not naturally occurring as a fragment and/or is not typically in the functional state.

Moieties of the invention, such as polypeptides, peptides, antigens, or immunogens, may be conjugated or linked covalently or noncovalently to other moieties such as adjuvants, proteins, peptides, supports, fluorescence moieties, or labels. The term "conjugate" or "immunoconjugate" is broadly used to define the operative association of one moiety with another agent and is not intended to refer solely to any type of operative association, and is particularly not limited to chemical "conjugation." Recombinant fusion proteins are particularly contemplated. Compositions of the invention may further comprise an adjuvant or a pharmaceutically acceptable excipient. An adjuvant may be covalently or noncovalently coupled to a polypeptide or peptide of the inven10

tion. In certain aspects, the adjuvant is chemically conjugated to a protein, polypeptide, or peptide.

The term "providing" is used according to its ordinary meaning to indicate "to supply or furnish for use." In some embodiments, the protein is provided directly by administering the protein, while in other embodiments, the protein is effectively provided by administering a nucleic acid that encodes the protein. In certain aspects the invention contemplates compositions comprising various combinations of nucleic acid, antigens, peptides, and/or epitopes.

The subject will have (e.g., are diagnosed with a staphylococcal infection), will be suspected of having, or will be at risk of developing a staphylococcal infection. Compositions of the present invention include immunogenic compositions wherein the antigen(s) or epitope(s) are contained in an 15 amount effective to achieve the intended purpose. More specifically, an effective amount means an amount of active ingredients necessary to stimulate or elicit an immune response, or provide resistance to, amelioration of, or mitigation of infection. In more specific aspects, an effective amount 20 prevents, alleviates or ameliorates symptoms of disease or infection, or prolongs the survival of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any preparation used 25 in the methods of the invention, an effective amount or dose can be estimated initially from in vitro studies, cell culture, and/or animal model assays. For example, a dose can be formulated in animal models to achieve a desired immune response or circulating antibody concentration or titer. Such 30 information can be used to more accurately determine useful doses in humans.

The embodiments in the Example section are understood to be embodiments of the invention that are applicable to all aspects of the invention.

The use of the term "or" in the claims is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and "and/or." It is also contemplated that anything listed using ⁴⁰ the term "or" may also be specifically excluded.

Throughout this application, the term "about" is used to indicate that a value includes the standard deviation of error for the device or method being employed to determine the value.

Following long-standing patent law, the words "a" and "an," when used in conjunction with the word "comprising" in the claims or specification, denotes one or more, unless specifically noted.

Other objects, features and advantages of the present ⁵⁰ invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific embodiments of the invention, are given by way of illustration only, since various changes and modifications ⁵⁵ within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

DESCRIPTION OF THE DRAWINGS

So that the matter in which the above-recited features, advantages and objects of the invention as well as others which will become clear are attained and can be understood in detail, more particular descriptions and certain embodiments of the invention briefly summarized above are illustrated in the appended drawings. These drawings form a part of the specification. It is to be noted, however, that the appended drawings illustrate certain embodiments of the invention and therefore are not to be considered limiting in their scope.

FIGS. 1A-1B. (FIG. 1A) Primary structure of the Protein A precursor with an N-terminal YSIRK motif signal peptide, five immunoglobulin binding domains as tandem repeats designated E, D, A, B, C, region X, and the LPXTG sorting signal. (FIG. 1B) Following synthesis of the Protein A precursor, staphylococci secrete this product via the Sec pathway, and sortase A cleaves the LPXTG sorting signal between the T and G residues. Nucleophilic attack of the amino group within lipid II at the sortase-Protein A thioester-linked intermediate forms the amide bond that links Protein A to the cell wall envelope and enables its display on the bacterial surface.

FIG. 2. Three dimensional model of the molecular interactions between the SpA-domain D of Protein A, the VH3 Fab domain of the B cell receptor, and of the Fc γ domain of immunoglobulin. The model is derived from two crystal structures (Graille et al., 2000 and Gouda et al., 1992) that revealed side chain residues involved in the formation of ionic bonds that enable these complexes. Gln-9 and Gln-10 of SpA-D promote binding to Fey, whereas Asp-36 and Asp-37 enable complex formation with VH3 Fab.

FIG. 3. Left panel—Coomassie Blue stained SDS-PAGE reveals the migrational position of purified His-tagged SpA, SpA-D, SpA-D_{Q9,10K;D36,37.4}, human IgG, and sortase A (SrtA), a control protein. Right panel—Coomassie Blue stained SDS-PAGE to reveal the elution of Protein A immunoglobulin complexes eluted following affinity chromatography of human IgG on Ni-NTA columns pre-charged with His-tagged SpA, SpA-D, SpA-D_{Q9,10K:D36,37.4} or SrtA.

FIG. 4. ELISA assays to quantify human immunoglobulin (hIgG), human F(ab)2 IgG fragments and human Fc fragments of immunoglobulin (hFc). Plates were coated with
³⁵ equal amounts of His-tagged SpA, SpA-D, SpA-D_{Q9,10K;D36,37,4} or SrtA. hIgG-HRP, F(ab)2—HRP and hFc-HRP were added onto the plates and incubated for an hour. Absorbance at 450 nm was recorded and plotted to determine the half maximal titers.

40 FIG. 5. Purified SpA-D, SpA-D_{Q9,10K;D36,37.4} or a PBS mock control were injected into the peritoneum of mice and analyzed for their ability to reduce the B cell population in the spleen of experimental BALB/c mice. Animals were killed 4 hours following injection, their spleen removed, tissue 45 homogenized and stained with CD 19 antibodies directed against B cells. The number of B cells was quantified by FACS sorting.

FIG. 6. Generation of a non-toxigenic protein A vaccine. a, Translational protein A (SpA) product of S. aureus Newman and USA300 LAC with an N-terminal signal peptide (white box), five immunoglobulin binding domains (IgBDs designated E, D, A, B and C), variable region X and C-terminal sorting signal (black box), b, Amino acid sequence of the five IgBDs as well as nontoxigenic SpA-D_{*KK44*}, with the positions of triple α -helical bundles (H1, H2 and H3) as well as glutamine (Q) 9, 10 and aspartate (D) 36, 37 indicated, c, Coomassie Blue-stained SDS-PAGE of SpA, SpA-D, SpA- D_{KK44} or SrtA purified on Ni-NTA sepharose in the presence or absence of human immunoglobulin (hIgG). d, ELISA 60 examining the association of immobilized SpA, SpA-D or SpA-D_{*KKAA*} with human IgG as well as its Fc or $F(ab)_2$ fragments and von Willebrand factor (vWF). e, CD19+ B lymphocytes in splenic tissue of BALB/c mice that had been mock immunized or treated with SpA-D or SpA-D_{KKAA} were quantified by FACS.

FIG. 7. Non-toxigenic protein A vaccine prevents abscess formation. Histopathology of renal tissue isolated during

necropsy of BALB/c mice that had been mock immunized (PBS) or vaccinated with SpA, SpA-D as well as SpA-D_{*KKAA*} and challenged with *S. aureus* Newman. Thin sectioned tissues were stained with hematoxylin-eosin. White arrows identify polymorphonuclear leukocyte (PMN) infiltrates. 5 Dark arrows identify staphylococcal abscess communities.

FIG. **8**. Antibodies raised by the non-toxigenic protein A vaccine block the B cell superantigen function of SpA. a, Rabbit antibodies raised against SpA-D_{*KKAA*} were purified on a matrix with immobilized antigen and analyzed by Coo- 10 massie Blue-stained SDS-PAGE. Antibodies were cleaved with pepsin and F(ab)₂ fragments were purified by a second round of affinity chromatography on SpA-D_{*KKAA*} matrix, b, SpA-D_{*KKAA*} specific F(ab)₂ interfere with the binding of SpA or SpA-D to human immunoglobulin (hIgG) or, c, to von 15 Willebrand Factor (vWF).

FIG. 9. Full-length non-toxigenic protein A generates improved immune responses, a, Full-length SpA_{KKAA} was purified on Ni-NTA sepharose and analyzed by Coomassie-Blue stained SDS-PAGE. b. CD19+ B lymphocytes in splenic 20 tissue of BALB/c mice that had been mock immunized or treated with SpA or SpA_{KK44} were quantified by FACS. c, ELISA examining the association of immobilized SpA or SpA_{KKAA} with human IgG as well as its Fc or $F(ab)_2$ fragments or von Willebrand factor (vWF). d, Human or mouse 25 serum antibody titers to diphtheria toxoid (CRM197) and non-toxigenic SpA $_{KKAA}$ or SpA-D $_{KKAA}$. Human volunteers with a history of DTaP immunization and staphylococcal infection (n=16) as well as mice (n=20) that had been infected with S. aureus Newman or USA 300 LAC or immunized with SpA_{KKAA} or SpA-D_{KKAA} were examined by quantitative dot blot.

FIG. **10**. Staphylococcal infection does not generate protective immunity. BALB/c mice (n=20) were infected with *S. aureus* Newman or mock challenged (PBS) for thirty days 35 and infection cleared with chloramphenicol treatment. Both cohorts of animals were then challenged with *S. aureus* Newman and bacterial load (CFU) in kidney tissue homogenate analyzed following necropsy on day 4.

FIG. 11. Comparison of abscess formation in mice treated 40 with PBS, SpA, SpA-D, and SpA- D_{KK44} .

FIGS. **12**A-**12**C. (A) ELISA examining the association of immobilized SpA, SpA-D, SpA-D_{*KKAA*} or SpA-D_{*GGSS*} with human IgG as well as its Fc or F(ab)₂ fragments and IgM. Statistical significance of SpA-D_{*KKAA*} and SpA-D_{*GGSS*} bind-45 ing to each ligand was compared against SpA-D; SpA-D binding was compared against SpA (n=3); * signifies P< 0.05; ** signifies P0.01. (B) ELISA examining the level of cross-reactive antibodies of hyper-immune sera samples collected from actively immunized mice (n=5) with SpA-D, 50 SpA-D_{*KKAA*} and SpA-D_{*GGSS*}. (C) Abscess formation in mice treated with PBS, SpA-D, SpA-D_{*KKAA*} and SpA-D_{*GGSS*}.

FIGS. **13A-13B**. BALB/c mice (n=18-20) were either mock immunized with PBS/adjuvant or injected with 25 µg of each antigen (Combo 1, ClfA+SdrD+FnBPB; Combo 2, 55 Combo 1+SpA_{KK44}. Immunized mice were challenged by intravenous inoculation with 1×10^7 CFU *S. aureus* Newman. Bacterial loads in kidney tissues were examined at A, day 4 and B, day 18 post challenge. Statistical significance was calculated with the unpaired two-tailed Students t-test and 60 P-values recorded; P-values <0.05 were deemed significant.

FIG. 14. Schematic of the protein domains of Ebh, location of insertions, and sites of variation between strains. Diagram of protein regions of Ebh, N terminal non-homologous region, FIYAR and GA domain repeats, DUF400 and transmembrane region arrows denote location of transposon insertions NMTN-9044, 15257, and 10853. Bars denote variation

in the amino acid level amongst different staphylococcal strains, lines denote amino acid insertions or changes resulting in a stop codon, gaps denote deletion of region. Protein diagram derived from EMBL.

FIGS. **15**A-**15**E. Transmission electron microscopic examination of Δ ebh. (A-D) mid-log cells were fixed, thin sectioned, and processed for transmission electron microscopy. (B, D) $\Delta\Delta$ ebh 9044 mutant cells appear enlarged compared to wild type cells. (E) The length of dividing cells was measured and the results plotted in a dot and whisker plot showing that Ebh mutant cells are significantly larger than wild type. Measurements are an average of 60-70 dividing cells counted in a total of 5 frames.

FIGS. **16**A-**16**D. Δ ebh growth in oxacillin. (A) Growth of staphylococcal cells in oxacillin. Overnight culture were normalized to OD₆₀₀ of 4.0 and inoculated 1:100 into TSB containing 2 ng/ml of oxacillin or (B) TSB alone and Abs_600 was measured for 15 hours. Δ ebh 9044 displayed a significant delay in growth. (C, D) mid-log cells grown in 2 µg/ml oxacillin were fixed, thin sectioned, and processed for transmission electron microscopy. Ebh mutant cells are more susceptible to oxacillin mediated lysis.

FIG. 17. Lysostaphin sensitivity of Δ ebh. Suspensions of wild-type and ebh mutant staphylococci were incubated with increasing concentrations of lysostaphin for 30 minutes and the absorbance at 600 nm determined as a measure for cell density and integrity of the cell wall envelope. The ebh mutants did not exhibit a significant difference in lysostaphin sensitivity as compared to the wild-type strain. Data shown are representative of two trials.

FIGS. **18**A-**18**B. Wild type and Ebh mutant survival in whole blood, plasma, and heat inactivated plasma. (A) midlog staphylococci were washed in PBS and incubated in lepirudin anticoagulated mouse blood for 30 minutes and bacterial survival assessed by colony formation on agar plates. Δ ebh 9044 displayed a significant defect in blood survival compared to wild type bacteria. (B) staphylococci were prepared as mentioned in A and incubated in plasma isolated from mouse blood by centrifugation, plasma was also heat inactivated by incubating at 60° C. for 30 minutes. The ebh mutant strain displayed a defect in plasma survival but no statistically significant difference in growth in heat inactivated plasma or TSB.

FIG. 19. Fluorescence assisted cell sorting of complement deposition on wild type and Δ ebh. Mid log USA300 staphylococci were washed and incubated with human plasma in PBS, after 30 minutes cells were washed and prepared for immunoblotting against C3b. The ebh mutant displayed significant increase in complement deposition. Data shown are an average of three trials.

FIGS. **20**A-**20**C. USA300 and Ebh mutant biofilm formation. (A) USA300 was grown in still culture overnight on fibronectin or collagen pre-coated 96 well plates. These plates were then washed three times with PBS and stained with safranin red. The amount of safranin staining is measured at Abs_450 nm and has been shown to correspond with the thickness of the cellular layer formed on the bottom of the well. (B) Mutations in ebh or icaA do not affect biofilm formation whereas a mutation in sortase A abrogates the biofilm. (C) antibodies against the repeat region of Ebh could perturb biofilm formation. Increasing amounts of normal rabbit sera and immunoreactive sera against 283 or 284 (fragments of repeat region of Ebh) were added to a still culture of USA300 in a fibronectin pre-coated plate.

FIGS. **21**A-**21**B. Virulence of ebh mutants in the mouse renal abscess and lethal challenge models. (A) Cohorts of 10 mice were injected into the retro-orbital plexus with 5×10^7

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CFU of S. aureus USA300 as well as Aebh mutants 9044, 15257, and 10853. Animal survival over time was recorded over 10 days. Only Aebh 9044 displayed a significant delay in time to death compared to wild type. (B) Mice were injected into the retro-orbital plexus with 5×10^6 CFU of staphylococ- ⁵ cal strains Newman and Δ ebh KO, USA300 and Δ ebh 9044. Following necropsy, animals were assessed for bacterial load in the renal tissue and histopathological features of abscess formation. A 1.2 log decrease in cfu was observed for Newman and a 1.4 log decrease for USA300 (Table 8). Both graphs are representative of two independent experiments.

FIGS. 22A-22I. Active immunization with Ebh N40-2544. Cohorts of 10 three-week old mice were vaccinated with purified His₆ Ebh $N_{40-2544}$ terminal protein, on day 0 (CFA 15 emulsified) and given a boost on day 11 (IFA emulsified). Four animals were then bled on day 20 and the entire cohort was challenged the following day with sublethal doses of Staphylococcus aureus strain Newman or USA300. Mice were sacrificed on the 5th day of infection and their kidneys 20 were harvested and assessed for bacteria load (A, Table 9) and abscess formation (B-I).

FIGS. 23A-23G. Active immunization with fragments of Ebh N40-2544-Cohorts of 10 three-week old mice were vaccinated with (A) purified recombinant His₆ tagged fragments ²⁵ of Ebh N_{40,2544} on day 0 (CFA emulsified) and given a boost on day 11 (IFA emulsified). Four animals were then bled on day 20 and the entire cohort was challenged the following day with a sublethal dose of Staphylococcus aureus strain Newman. Mice were sacrificed on the 5th day of infection and their kidneys were harvested and assessed for bacteria load (B, Table 10) and abscess formation (D-G).

DETAILED DESCRIPTION

Staphylococcus aureus is a commensal of the human skin and nares, and the leading cause of bloodstream, skin and soft tissue infections (Klevens et al., 2007). Recent dramatic increases in the mortality of staphylococcal diseases are $_{40}$ attributed to the spread of methicillin-resistant S. aureus (MRSA) strains often not susceptible to antibiotics (Kennedy et al., 2008). In a large retrospective study, the incidence of MRSA infections was 4.6% of all hospital admissions in the United States (Klevens et al., 2007). The annual health care 45 costs for 94,300 MRSA infected individuals in the United States exceed \$2.4 billion (Klevens et al., 2007). The current MRSA epidemic has precipitated a public health crisis that needs to be addressed by development of a preventive vaccine (Boucher and Corey, 2008). To date, an FDA licensed vaccine 50 that prevents S. aureus diseases is not available.

The inventors describe here the use of staphylococci polypeptides that can serve as subunit vaccines. The pathogenesis of staphylococcal infections is initiated as bacteria invade the skin or blood stream via trauma, surgical wounds, 55 or medical devices (Lowy, 1998). Although the invading pathogen may be phagocytosed and killed, staphylococci can also escape innate immune defenses and seed infections in organ tissues, inducing inflammatory responses that attract macrophages, neutrophils, and other phagocytes (Lowy, 60 1998). The responsive invasion of immune cells to the site of infection is accompanied by liquefaction necrosis as the host seeks to prevent staphylococcal spread and allow for removal of necrotic tissue debris (Lam et al., 1963). Such lesions can be observed by microscopy as hypercellular areas containing 65 necrotic tissue, leukocytes, and a central nidus of bacteria (Lam et al., 1963). Unless staphylococcal abscesses are sur-

gically drained and treated with antibiotics, disseminated infection and septicemia produce a lethal outcome (Sheagren, 1984).

I. STAPHYLOCOCCAL ANTIGENS

A. Ebh Protein

The methicillin-resistant Staphylococcus aureus isolate USA300 LAC expresses the Ebh protein (e.g., SEQ ID NO:24) on its surface. Mutations that disrupt the ebh reading frame increase the volume of staphylococcal cells and alter the dimensions of their crosswall septa. These ebh variants display increased susceptibility to methicillin as well as complement-mediated killing, which is associated with reduced survival of mutant staphylococci in blood and diminished virulence during animal infection. Immunization of mice with the N-terminal domain of Ebh (residues 1-2524) elicits humoral immune responses that confer protection against staphylococcal challenge. These data demonstrate that Ebh contributes to the characteristic cell growth and division patterns of S. aureus cells and may therefore be developed as a vaccine or immune therapy.

Envelope factors have been shown to contribute to the pathogenesis of S. aureus Newman infections in mice. Variants that indicated a requirement for certain envelope factors for abscess formation were subsequently tested for protective antigen attributes; the recombinant gene products were purified, used for immunization of animals, and the relative protective immunity in a mouse model was measured-with either active or passive immunization strategies. While these studies initially examined only sortase-anchored surface proteins, two cell wall associated factors (Emp and Eap) as well as envelope polysaccharides (CPS5 and PNAG/PIA) were also analyzed. Nevertheless, these studies did not consider the 35 staphylococcal protein designated Ebh. Ebh was first discovered in Staphylococcus epidermidis as a fibronectin binding protein. Ebh is found in both S. epidermidis and S. aureus isolates, but is absent from other staphylococcal species that are not known to play a major role in human disease.

Ebh is a 1.1 MDa (10,422 amino acid residues) polypeptide, transcribed from a 30.1 kb gene single open reading frame. Although ebh is found in all S. aureus isolates, it displays variations in size, owing to the variable numbers of repeats in the mid-and 3' (C-terminal) sections of both the gene and its translational product. Gene variation in S. aureus is rare and variable genes are generally known to be contributors to virulence, including coagulase (coa), eap/map, sdrCDE, protein A (spa), ESAT secretion genes (ess), and the accessory gene regulatory locus (agr) (Buckling et al., 2005; Watanabe et al., 2009).

In the MRSA strain USA300 LAC, the N-terminal domain of Ebh (residues 1-2524) displays no primary or secondary sequence homology to any other bacterial product and it does not harbor repeat structures. The middle domain is comprised of 6 tandem 54 residue FIVAR domain repeats, followed by 47 tandem repeats of 123 residue FIVAR-GA domains. FIVAR domains are known to bind polyssacharides and are found in many microbial envelope or secreted polypeptides that aid in cell wall stability or in the integrity of envelope structures. GA modules are known to bind to the host serum protein albumin. Seven tandem repeats of the 72 residue DUF1542 domain tether the FIVAR/FIVAR-GA repeats to the presumed transmembrane domain of Ebh, which is followed by a positively charged cytoplasmic domain. The genome sequences of geographically distinct but closely related USA300 isolates reveal variability even among clonal populations of the community-acquired methicillin-resistant 10

S. aureus strains (CA-MRSA). S. aureus Newman is a methicillin-sensitive strain, isolated from a human infection in 1952 and thereafter propagated in research laboratories. The genome sequence of S. aureus Newman was determined in 2006, which revealed a nucleotide substitution near the 3' end 5 of the ebh orf, causing premature termination of the Ebh polypeptide. Similar mutations in ebh can be found in other S. aureus laboratory strains, including COL and 8325-4. The protein displays 21% similarity to Mrp, a protein known to be involved in Na+ regulation and osmotic balance.

Williams et al. (2002) identified a fragment of S. epidermidis Ebh (Embp) that bound to fibronectin, but not to other extracellular matrix proteins such as collagen, fibrinogen, laminin, or vitronectin. Further, S. epidermidis Embp interacts with heparin, hyaluronate, and, to a lesser extent, plasminogen. Williams et al. noted that recombinant fragments of Embp interfere with S. epidermidis binding to fibronectin, in agreement with the conjecture that Embp/Ebh functions as an adhesin for extracellular matrix (Williams et al., 2002). Christner et al. (2010) reported that Embp contributes to S. 20 epidermidis biofilm formation in the absence of PNAG/PIA exopolysaccharide as well as Aap adhesin. This claim was derived from, a variant with a transposon insertion that provides constitutive promoter activity for the expression of a truncated Embp product, initiated within the FIYAR repeat 25 region. While the authors concluded that the FIYAR-GA repeats may be sufficient to mediate biofilm formation, it is not clear whether and how such truncated polypeptide can be secreted. Moreover, S. epidermidis growth in serum markedly increased Embp production, microbial aggregation with bio- 30 film formation, and increased staphylococcal resistance to macrophage phagocytosis (Christner et al., 2010).

Clarke et al. (2002) examined the MRSA strain COL, reporting Ebh expression during logarithmic growth and negative regulation by agr. Similar to Embp, the FIVAR/ 35 FIVAR-GA repeats of Ebh bind to fibronectin. A tandem repeat of FIVAR-GA was crystallized and its X-ray structure determined, which revealed double (FIVAR) and triple (GA module) alpha-helical bundles with elongated shape (Sakamoto et al., 2008; Tanaka et al., 2008). Assuming that the 40 entire polypeptide could be folded in a similar manner, the authors speculated that Ebh assumes a 320 nm long, rodshaped structure with a diameter of 20 A°. The same authors proposed that Ebh, due to entropic costs, would be more likely to lie across the bacterial surface than project itself 45 perpendicular to the staphylococcal cell wall envelope, and that such assembly may provide for envelope rigidity as well as resistance to staphylococcal lysis under hyperosmolar conditions. Kuroda et al. (2008) reported that S. aureus 8325-4 ebh variants are more susceptible to the glycopeptide teico- 50 planin, an antibiotic that inhibits peptidoglycan synthesis, and sensitive for Triton-X 100, a non-ionic detergent that otherwise does not affect the staphylococcal envelope. On the basis of these observations, the authors concluded that Ebh must be primarily a housekeeping factor that maintains cell 55 wall strength and rigidity in staphylococci.

All of the previous work on Ebh employed staphylococcal strains with truncated ebh genes and failed to explore the possibility that this protein contributes to disease pathogenesis or represent a target for vaccine and immune-therapeutic 60 development-as addressed in the present application.

B. Staphylcoccal Protein A (SpA)

All Staphylococcus aureus strains express the structural gene for Protein A (spa) (Jensen, 1958; Said-Salim et al., 2003), a well characterized virulence factor whose cell wall 65 anchored surface protein product (SpA) encompasses five highly homologous immunoglobulin binding domains desig-

nated E, D, A, B, and C (Sjodahl, 1977). These domains display 80% identity at the amino acid level, are 56 to 61 residues in length, and are organized as tandem repeats (Uhlen et al., 1984). SpA is synthesized as a precursor protein with an N-terminal YSIRK/GS signal peptide and a C-terminal LPXTG motif sorting signal (DeDent et al., 2008; Schneewind et al., 1992). Cell wall anchored Protein A is displayed in great abundance on the staphylococcal surface (DeDent et al., 2007; Sjoquist et al., 1972). Each of its immunoglobulin binding domains is composed of anti-parallel α -helices that assemble into a three helix bundle and bind the Fc domain of immunoglobulin G (IgG) (Deisenhofer, 1981; Deisenhofer et al., 1978), the VH3 heavy chain (Fab) of IgM (i.e., the B cell receptor) (Graille et al., 2000), the von Willebrand factor at its AI domain [vWF AI is a ligand for platelets] (O'Seaghdha et al., 2006) and the tumor necrosis factor α (TNF- α) receptor I (TNFRI) (Gomez et al., 2006), which is displayed on surfaces of airway epithelia (Gomez et al., 2004; Gomez et al., 2007).

SpA impedes neutrophil phagocytosis of staphylococci through its attribute of binding the Fc component of IgG (Jensen, 1958; Uhlen et al., 1984). Moreover, SpA is able to activate intravascular clotting via its binding to von Willebrand factor AI domains (Hartleib et al, 2000). Plasma proteins such as fibrinogen and fibronectin act as bridges between staphylococci (ClfA and ClfB) and the platelet integrin GPIIb/IIIa (O'Brien et al., 2002), an activity that is supplemented through Protein A association with vWF AI, which allows staphylococci to capture platelets via the GPIb- α platelet receptor (Foster, 2005; O'Seaghdha et al., 2006). SpA also binds TNFRI and this interaction contributes to the pathogenesis of staphylococcal pneumonia (Gomez et al., 2004). SpA activates proinflammatory signaling through TNFR1 mediated activation of TRAF2, the p38/c-Jun kinase, mitogen activate protein kinase (MAPK) and the Rel-transcription factor NF-KB. SpA binding further induces TNFR1 shedding, an activity that appears to require the TNF-converting enzyme (TACE)(Gomez et al., 2007). All of the aforementioned SpA activities are mediated through its five IgG binding domains and can be perturbed by the same amino acid substitutions, initially defined by their requirement for the interaction between Protein A and human IgG1 (Cedergren et al, 1993.

SpA also functions as a B cell superantigen by capturing the Fab region of VH3 bearing IgM, the B cell receptor (Gomez et al., 2007; Goodyear et al., 2003; Goodyear and Silverman, 2004; Roben et al., 1995). Following intravenous challenge, staphylococcal Protein A (SpA) mutations show a reduction in staphylococcal load in organ tissues and dramatically diminished ability to form abscesses (described herein). During infection with wildtype S. aureus, abscesses are formed within forty-eight hours and are detectable by light microscopy of hematoxylin-eosin stained, thin-sectioned kidney tissue, initially marked by an influx of polymorphonuclear leukocytes (PMNs). On day 5 of infection, abscesses increase in size and enclose a central population of staphylococci, surrounded by a layer of eosinophilic, amorphous material and a large cuff of PMNs. Histopathology revealed massive necrosis of PMNs in proximity to the staphylococcal nidus at the center of abscess lesions as well as a mantle of healthy phagocytes. The inventors also observed a rim of necrotic PMNs at the periphery of abscess lesions, bordering the eosinophilic pseudocapsule that separated healthy renal tissue from the infectious lesion. Staphylococcal variants lacking Protein A are unable to establish the histopathology features of abscesses and are cleared during infection.

In previous studies, Cedergren et al. (1993) engineered five individual substitutions in the Fc fragment binding sub-domain of the B domain of SpA, L17D, N28A, 131A and K35A. These authors created these proteins to test data gathered from a three dimensional structure of a complex between one 5 domain of SpA and Fc1. Cedergren et al. determined the effects of these mutations on stability and binding, but did not contemplate use of such substitutions for the production of a vaccine antigen.

Brown et al. (1998) describe studies designed to engineer 10 new proteins based on SpA that allow the use of more favorable elution conditions when used as affinity ligands. The mutations studied included single mutations of Q13A, Q14H, N15A, N15H, F17H, Y18F, L21H, N32H, or K39H. Brown et al. report that Q13A, N15A, N15H, and N32H substitutions 15 made little difference to the dissociation constant values and that the Y18F substitution resulted in a 2 fold decrease in binding affinity as compared to wild type SpA. Brown et al. also report that L21H and F17H substitutions decrease the binding affinity by five-fold and a hundred-fold respectively. 20 The authors also studied analogous substitutions in two tandem domains. Thus, the Brown et al. studies were directed to generating a SpA with a more favorable elution profile, hence the use of H is substitutions to provide a pH sensitive alteration in the binding affinity. Brown et al. is silent on the use of 25 SpA as a vaccine antigen.

Graille et al. (2000) describe a crystal structure of domain D of SpA and the Fab fragment of a human IgM antibody. Graille et al. define by analysis of a crystal structure the D domain amino acid residues that interact with the Fab frag- 30 ment as residues Q26, G29, F30, Q32, S33, D36, D37, Q40, N43, E47, or L51, as well as the amino acid residues that form the interface between the domain D sub-domains. Graille et al. define the molecular interactions of these two proteins, but is silent in regard to any use of substitutions in the interacting 35 residues in producing a vaccine antigen.

O'Seaghdha et al. (2006) describe studies directed at elucidating which sub-domain of domain D binds vWF. The authors generated single mutations in either the Fc or VH3 binding sub-domains, i.e., amino acid residues F5A, Q9A, 40 Q10A, F13A, Y14A, L17A, N28A, 131A, K35A, G29A, F30A, S33A, D36A, D37A, Q40A, E47A, or Q32A. The authors discovered that vWF binds the same sub-domain that binds Fc. O'Seaghda et al. define the sub-domain of domain D responsible for binding vWF, but is silent in regard to any 45 use of substitutions in the interacting residues in producing a vaccine antigen.

Gomez et al. (2006) describe the identification of residues responsible for activation of the TNFR1 by using single mutations of F5A, F13A, Y14A, L17A, N21A, 131A, Q32A, and 50 K35A. Gomez et al. is silent in regard to any use of substitutions in the interacting residues in producing a vaccine antigen.

Recombinant affinity tagged Protein A, a polypeptide encompassing the five IgG domains (EDCAB) (Sjodahl, 55 1977) but lacking the C-terminal Region X (Guss et al., 1984), was purified from recombinant *E. coli* and used as a vaccine antigen (Stranger-Jones et al., 2006). Because of the attributes of SpA in binding the Fc portion of IgG, a specific humoral immune response to Protein A could not be meaoured (Stranger-Jones et al., 2006). The inventors have overcome this obstacle through the generation of SpA- $D_{Q9,10K;D36,37.4}$. BALB/c mice immunized with recombinant Protein A (SpA) displayed significant protection against intravenous challenge with *S. aureus* strains: a 2.951 log 65 reduction in staphylococcal load as compared to the wildtype (P 0.005; Student's t-test) (Stranger-Jones et al., 2006). 72

SpA specific antibodies may cause phagocytic clearance prior to abscess formation and/or impact the formation of the aforementioned eosinophilic barrier in abscesses that separate staphylococcal communities from immune cells since these do not form during infection with Protein A mutant strains. Each of the five SpA domains (i.e., domains formed from three helix bundles designated E, D, A, B, and C) exerts similar binding properties (Jansson et al., 1998). The solution and crystal structure of the domain D has been solved both with and without the Fc and VH3 (Fab) ligands, which bind Protein A in a non-competitive manner at distinct sites (Graille et al., 2000). Mutations in residues known to be involved in IgG binding (FS, Q9, Q10, S11, F13, Y14, L17, N28, I31 and K35) are also required for vWF AI and TNFR1 binding (Cedergren et al., 1993; Gomez et al., 2006; O'Seaghdha et al., 2006), whereas residues important for the VH3 interaction (Q26, G29, F30, S33, D36, D37, Q40, N43, E47) appear to have no impact on the other binding activities (Graille et al., 2000; Jansson et al., 1998). SpA specifically targets a subset of B cells that express VH3 family related IgM on their surface, i.e., VH3 type B cell receptors (Roben et al., 1995). Upon interaction with SpA, these B cells proliferate and commit to apoptosis, leading to preferential and prolonged deletion of innate-like B lymphocytes (i.e., marginal zone B cells and follicular B2 cells)(Goodyear et al., 2003; Goodyear et al., 2004).

Molecular basis of Protein A surface display and function. Protein A is synthesized as a precursor in the bacterial cytoplasm and secreted via its YSIRK signal peptide at the cross wall, i.e. the cell division septum of staphylococci (FIG. 1) (DeDent et al., 2007; DeDent et al, 2008). Following cleavage of the C-terminal LPXTG sorting signal, Protein A is anchored to bacterial peptidoglycan crossbridges by sortase A (Mazmanian et al., 1999; Schneewind et al., 1995; Mazmanian et al., 2000). Protein A is the most abundant surface protein of staphylococci; the molecule is expressed by virtually all S. aureus strains (Cespedes et al., 2005; Kennedy et al., 2008; Said-Salim et al., 2003). Staphylococci turn over 15-20% of their cell wall per division cycle (Navarre and Schneewind, 1999). Murine hydrolases cleave the glycan strands and wall peptides of peptidoglycan, thereby releasing Protein A with its attached C-terminal cell wall disaccharide tetrapeptide into the extracellular medium (Ton-That et al., 1999). Thus, by physiological design, Protein A is both anchored to the cell wall and displayed on the bacterial surface but also released into surrounding tissues during host infection (Marraffini et al., 2006).

Protein A captures immunoglobulins on the bacterial surface and this biochemical activity enables staphylococcal escape from host innate and acquired immune responses (Jensen, 1958; Goodyear et al., 2004). Interestingly, region X of Protein A (Guss et al., 1984), a repeat domain that tethers the IgG binding domains to the LPXTG sorting signal/cell wall anchor, is perhaps the most variable portion of the staphylococcal genome (Said-Salim, 2003; Schneewind et al., 1992). Each of the five immunoglobulin binding domains of Protein A (SpA), formed from three helix bundles and designated E, D, A, B, and C, exerts similar structural and functional properties (Sjodahl, 1977; Jansson et al., 1998). The solution and crystal structure of the domain D has been solved both with and without the Fc and VH3 (Fab) ligands, which bind Protein A in a non-competitive manner at distinct sites (Graille 2000).

In the crystal structure complex, the Fab interacts with helix II and helix III of domain D via a surface composed of four VH region β -strands (Graille 2000). The major axis of helix II of domain D is approximately 50° to the orientation of

the strands, and the interhelical portion of domain D is most proximal to the CO strand. The site of interaction on Fab is remote from the Ig light chain and the heavy chain constant region. The interaction involves the following domain D residues: Asp-36 of helix II, Asp-37 and Gln-40 in the loop -5 between helix II and helix III and several other residues (Graille 2000). Both interacting surfaces are composed predominantly of polar side chains, with three negatively charged residues on domain D and two positively charged residues on the 2A2 Fab buried by the interaction, providing 10 an overall electrostatic attraction between the two molecules. Of the five polar interactions identified between Fab and domain D, three are between side chains. A salt bridge is formed between Arg-H19 and Asp-36 and two hydrogen bonds are made between Tyr-H59 and Asp-37 and between 15 Asn-H82a and Ser-33. Because of the conservation of Asp-36 and Asp-37 in all five IgG binding domains of Protein A, the inventors mutated these residues.

The SpA-D sites responsible for Fab binding are structurally separate from the domain surface that mediates Fcy bind-20 ing. The interaction of Fcy with domain D primarily involves residues in helix I with lesser involvement of helix II (Gouda et al., 1992; Deisenhofer, 1981). With the exception of the Gln-32, a minor contact in both complexes, none of the residues that mediate the Fcy interaction are involved in Fab 25 binding. To examine the spatial relationship between these different Ig-binding sites, the SpA domains in these complexes have been superimposed to construct a model of a complex between Fab, the SpA-domain D, and the Fcy molecule. In this ternary model, Fab and Fcy form a sandwich 30 about opposite faces of the helix II without evidence of steric hindrance of either interaction. These findings illustrate how, despite its small size (i.e., 56-61 aa), an SpA domain can simultaneously display both activities, explaining experimental evidence that the interactions of Fab with an indi- 35 vidual domain are noncompetitive. Residues for the interaction between SpA-D and Fcy are Gln-9 and Gln-10.

In contrast, occupancy of the Fc portion of IgG on the domain D blocks its interaction with vWF A1 and probably also TNFR1 (O'Seaghdha et al., 2006). Mutations in residues 40 essential for IgG Fc binding (F5, Q9, Q10, S11, F13, Y14, L17, N28, I31 and K35) are also required for vWF A1 and TNFR1 binding (O'Seaghdha et al., 2006; Cedergren et al., 1993; Gomez et al, 2006), whereas residues critical for the VH3 interaction (Q26, G29, F30, S33, D36, D37, Q40, N43, 45 E47) have no impact on the binding activities of IgG Fc, vWF A1 or TNFR1 (Jansson et al., 1998; Graille et al., 2000). The Protein A immunoglobulin Fab binding activity targets a subset of B cells that express VH3 family related IgM on their surface, i.e., these molecules function as VH3 type B cell 50 receptors (Roben et al., 1995). Upon interaction with SpA, these B cells rapidly proliferate and then commit to apoptosis, leading to preferential and prolonged deletion of innate-like B lymphocytes (i.e., marginal zone B cells and follicular B2 cells) (Goodyear and Silverman, 2004; Goodyear and Silver- 55 man, 2003). More than 40% of circulating B cells are targeted by the Protein A interaction and the VH3 family represents the largest family of human B cell receptors to impart protective humoral responses against pathogens (Goodyear and Silverman, 2004; Goodyear and Silverman, 2003). Thus, Protein A 60 functions analogously to staphylococcal superantigens (Roben et al., 1995), albeit that the latter class of molecules, for example SEB, TSST-1, TSST-2, form complexes with the T cell receptor to inappropriately stimulate host immune responses and thereby precipitating characteristic disease 65 features of staphylococcal infections (Roben et al., 1995; Tiedemann et al., 1995). Together these findings document

the contributions of Protein A in establishing staphylococcal infections and in modulating host immune responses.

In sum, Protein A domains can viewed as displaying two different interfaces for binding with host molecules and any development of Protein A based vaccines must consider the generation of variants that do not perturb host cell signaling, platelet aggregation, sequestration of immunoglobulins or the induction of B cell proliferation and apoptosis. Such Protein A variants should also be useful in analyzing vaccines for the ability of raising antibodies that block the aforementioned SpA activities and occupy the five repeat domains at their dual binding interfaces. This goal is articulated and pursued here for the first time and methods are described in detail for the generation of Protein A variants that can be used as a safe vaccine for humans. To perturb IgG Fey, vWF AI and TNFR1 binding, glutamine (Q) 9 and 10 [numbering derived from the SpA domain D as described in Uhlen et al., 1984] were mutated, and generated lysine substitutions for both glutamines with the expectation that these abolish the ligand attributes at the first binding interface. To perturb IgM Fab VH3 binding, aspartate (D) 36 and 37 were mutated, each of which is required for the association with the B cell receptor. D36 and D37 were both substituted with alanine. Q9,10K and D36,37A mutations are here combined in the recombinant molecule SpA-D $_{Q9,10K;D36,37A}$ and tested for the binding attributes of Protein A. Further, SpA-D and SpA-D_{Q9,10K;D36,37A} are subjected to immunization studies in mice and rabbits and analyzed for [1] the production of specific antibodies (SpA-D Ab); [2] the ability of SpA-D Ab to block the association between Protein A and its four different ligands; and, [3] the attributes of SpA-D Ab to generate protective immunity against staphylococcal infections. (See Examples section below).

C. Staphylococcal Coagulases

Coagulases are enzymes produced by Staphylococcus bacteria that convert fibrinogen to fibrin. Coa and vWh activate prothrombin without proteolysis (Friedrich et al., 2003). The coagulase•prothrombin complex recognizes fibrinogen as a specific substrate, converting it directly into fibrin. The crystal structure of the active complex revealed binding of the D1 and D2 domains to prothrombin and insertion of its Ile1-Val2 N-terminus into the Ile 16 pocket, inducing a functional active site in the zymogen through conformational change (Friedrich et al., 2003). Exosite I of α -thrombin, the fibrinogen recognition site, and proexosite I on prothrombin are blocked by the D2 of Coa (Friedrich et al., 2003). Nevertheless, association of the tetrameric (Coa•prothrombin)2 complex binds fibrinogen at a new site with high affinity (Panizzi et al., 2006). This model explains the coagulant properties and efficient fibrinogen conversion by coagulase (Panizzi et al., 2006).

Fibrinogen is a large glycoprotein (Mr ~340,000), formed by three pairs of A α -, B β -, and γ -chains covalently linked to form a "dimer of trimers," where A and B designate the fibrinopeptides released by thrombin cleavage (Panizzi et al., 2006). The elongated molecule folds into three separate domains, a central fragment E that contains the N-termini of all six chains and two flanking fragments D formed mainly by the C-termini of the B β - and γ -chains. These globular domains are connected by long triple-helical structures. Coagulase-prothrombin complexes, which convert human fibrinogen to the self-polymerizing fibrin, are not targeted by circulating thrombin inhibitors (Panizzi et al., 2006). Thus, staphylococcal coagulases bypass the physiological blood coagulation pathway.

All S. aureus strains secrete coagulase and vWbp (Bjerketorp et al., 2004; Field and Smith, 1945). Although early work reported important contributions of coagulase to the pathogenesis of staphylococcal infections (Ekstedt and Yotis, 1960; Smith et al., 1947), more recent investigations with molecular genetics tools challenged this view by observing no virulence phenotypes with endocarditis, skin abscess and mastitis mod-5 els in mice (Moreillon et al., 1995; Phonimdaeng et al., 1990). Generating isogenic variants of S. aureus Newman, a fully virulent clinical isolate (Duthie et al., 1952), it is described herein that coa mutants indeed display virulence defects in a lethal bacteremia and renal abscess model in mice. In the inventors experience, S. aureus 8325-4 is not fully virulent and it is presumed that mutational lesions in this strain may not be able to reveal virulence defects in vivo. Moreover, antibodies raised against Coa or vWbp perturb the pathogenesis of S. aureus Newman infections to a degree mirroring the 15 impact of gene deletions. Coa and vWbp contribute to staphylococcal abscess formation and lethal bacteremia and may also function as protective antigens in subunit vaccines.

Biochemical studies document the biological value of antibodies against Coa and vWbp. By binding to antigen and 20 blocking its association with clotting factors, the antibodies prevent the formation of Coa•prothrombin and vWbp•prothrombin complexes. Passive transfer studies revealed protection of experimental animals against staphylococcal abscess formation and lethal challenge by Coa and 25 vWbp antibodies. Thus, Coa and vWbp neutralizing antibodies generate immune protection against staphylococcal disease.

Earlier studies revealed a requirement of coagulase for resisting phagocytosis in blood (Smith et al., 1947) and the 30 inventors observed a similar phenotype for Δcoa mutants in lepirudin-treated mouse blood (see Example 3 below). As vWbp displays higher affinity for human prothrombin than the mouse counterpart, it is suspected the same may be true for Δv Wbp variants in human blood. Further, expression of 35 Coa and vWbp in abscess lesions as well as their striking distribution in the eosinophilic pseudocapsule surrounding (staphylococcal abscess communities (SACs) or the peripheral fibrin wall, suggest that secreted coagulases contribute to the establishment of these lesions. This hypothesis was tested 40 and, indeed, Δcoa mutants were defective in the establishment of abscesses. A corresponding test, blocking Coa function with specific antibodies, produced the same effect. Consequently, it is proposed that the clotting of fibrin is a critical event in the establishment of staphylococcal abscesses that 45 can be targeted for the development of protective vaccines. Due to their overlapping function on human prothrombin, both Coa and vWbp are considered excellent candidates for vaccine development.

D. Other Staphylococcal Antigens

Research over the past several decades identified S. aureus exotoxins, surface proteins and regulatory molecules as important virulence factors (Foster, 2005; Mazmanian et al, 2001; Novick, 2003). Much progress has been achieved regarding the regulation of these genes. For example, staphy-55 lococci perform a bacterial census via the secretion of autoinducing peptides that bind to a cognate receptor at threshold concentration, thereby activating phospho-relay reactions and transcriptional activation of many of the exotoxin genes (Novick, 2003). The pathogenesis of staphylococcal infec- 60 tions relies on these virulence factors (secreted exotoxins, exopolysaccharides, and surface adhesins). The development of staphylococcal vaccines is hindered by the multifaceted nature of staphylococcal invasion mechanisms. It is well established that live attenuated micro-organisms are highly 65 effective vaccines; immune responses elicited by such vaccines are often of greater magnitude and of longer duration

than those produced by non-replicating immunogens. One explanation for this may be that live attenuated strains establish limited infections in the host and mimic the early stages of natural infection. Embodiments of the invention are directed to compositions and methods including variant SpA polypeptides and peptides, as well as other immunogenic extracellular proteins, polypeptides, and peptides (including both secreted and cell surface proteins or peptides) of gram positive bacteria for the use in mitigating or immunizing against infection. In particular embodiments the bacteria is a *staphylococcus* bacteria. Extracellular proteins, polypeptides, or peptides include, but are not limited to secreted and cell surface proteins of the targeted bacteria.

The human pathogen S. aureus secretes EsxA and EsxB, two ESAT-6 like proteins, across the bacterial envelope (Burts et al., 2005, which is incorporated herein by reference). Staphylococcal esxA and esxB are clustered with six other genes in the order of transcription: esxA esaA essA esaB essB essC esaC esxB. The acronyms esa, ess, and esx stand for ESAT-6 secretion accessory, system, and extracellular, respectively, depending whether the encoded proteins play an accessory (esa) or direct (ess) role for secretion, or are secreted (esx) in the extracellular milieu. The entire cluster of eight genes is herein referred to as the Ess cluster. EsxA, esxB, essA, essB, and essC are all required for synthesis or secretion of EsxA and EsxB. Mutants that fail to produce EsxA, EsxB, and EssC display defects in the pathogenesis of S. aureus murine abscesses, suggesting that this specialized secretion system may be a general strategy of human bacterial pathogenesis. Secretion of non-WXG100 substrates by the ESX-1 pathway has been reported for several antigens including EspA, EspB, Rv3483c, and Rv3615c (Fortune et al., 2005; MacGurn et al., 2005; McLaughlin et al, 2007; Xu et al., 2007). The alternate ESX-5 pathway has also been shown to secrete both WXG100 and non-WXG100 proteins in pathogenic mycobacteria (Abdallah et al., 2007; Abdallah et al., 2006).

The Staphylococcus aureus Ess pathway can be viewed as a secretion module equipped with specialized transport components (Ess), accessory factors (Esa) and cognate secretion substrates (Esx). EssA, EssB and EssC are required for EsxA and EsxB secretion. Because EssA, EssB and EssC are predicted to be transmembrane proteins, it is contemplated that these proteins form a secretion apparatus. Some of the proteins in the ess gene cluster may actively transport secreted substrates (acting as motor) while others may regulate transport (regulator). Regulation may be achieved, but need not be limited to, transcriptional or post-translational mechanisms for secreted polypeptides, sorting of specific substrates to defined locations (e.g., extracellular medium or host cells), or 50 timing of secretion events during infection. At this point, it is unclear whether all secreted Esx proteins function as toxins or contribute indirectly to pathogenesis.

Staphylococci rely on surface protein mediated-adhesion to host cells or invasion of tissues as a strategy for escape from immune defenses. Furthermore, *S. aureus* utilize surface proteins to sequester iron from the host during infection. The majority of surface proteins involved in staphylococcal pathogenesis carry C-terminal sorting signals, i.e., they are covalently linked to the cell wall envelope by sortase. Further, staphylococcal strains lacking the genes required for surface protein anchoring, i.e., sortase A and B, display a dramatic defect in the virulence in several different mouse models of disease. Thus, surface protein antigens represent a validated vaccine target as the corresponding genes are essential for the development of staphylococcal disease and can be exploited in various embodiments of the invention. The sortase enzyme superfamily are Gram-positive transpeptidases responsible for anchoring surface protein virulence factors to the peptidoglycan cell wall layer. Two sortase isoforms have been identified in *Staphylococcus aureus*, SrtA and SrtB. These enzymes have been shown to recognize a LPXTG motif in substrate proteins. The SrtB isoform appears to be important 5 in heme iron acquisition and iron homeostasis, whereas the SrtA isoform plays a critical role in the pathogenesis of Grampositive bacteria by modulating the ability of the bacterium to adhere to host tissue via the covalent anchoring of adhesins and other proteins to the cell wall peptidoglycan. In certain 10 embodiments the SpA variants described herein can be used in combination with other staphylococcal proteins such as Coa, Eap, Ebh, Emp, EsaC, EsaB, EsxA, EsxB, Hla, SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, IsdC, SasF, vWbp, and/ or vWh proteins.

Certain aspects of the invention include methods and compositions concerning proteinaceous compositions including polypeptides, peptides, or nucleic acid encoding SpA variant(s) and other staphylococcal antigens such as other proteins transported by the Ess pathway, or sortase substrates. 20 These proteins may be modified by deletion, insertion, and/or substitution.

The Esx polypeptides include the amino acid sequence of Esx proteins from bacteria in the Staphylococcus genus. The Esx sequence may be from a particular staphylococcus spe- 25 cies, such as Staphylococcus aureus, and may be from a particular strain, such as Newman. In certain embodiments, the EsxA sequence is SAV0282 from strain Mu50 (which is the same amino acid sequence for Newman) and can be accessed using Genbank Accession Number Q99WU4 30 (gi|68565539), which is hereby incorporated by reference. In other embodiments, the EsxB sequence is SAV0290 from strain Mu50 (which is the same amino acid sequence for Newman) and can be accessed using Genbank Accession Number Q99WT7 (gil68565532), which is hereby incorpo- 35 rated by reference. In further embodiments, other polypeptides transported by the Ess pathway may be used, the sequences of which may be identified by one of skill in the art using databases and internet accessible resources.

The sortase substrate polypeptides include, but are not 40 limited to the amino acid sequence of SdrC, SdrD, SdrE, IsdA, IsdB, ClfA, ClfB, IsdC or SasF proteins from bacteria in the Staphylococcus genus. The sortase substrate polypeptide sequence may be from a particular staphylococcus species, such as Staphylococcus aureus, and may be from a 45 particular strain, such as Newman. In certain embodiments, the SdrD sequence is from strain N315 and can be accessed using Genbank Accession Number NP 373773.1 (gi|15926240), which is incorporated by reference. In other embodiments, the SdrE sequence is from strain N315 and can 50 be accessed using Genbank Accession Number NP 373774.1 (gil15926241), which is incorporated by reference. In other embodiments, the IsdA sequence is SAV1130 from strain Mu50 (which is the same amino acid sequence for Newman) and can be accessed using Genbank Accession Number 55 NP_371654.1 (gi|15924120), which is incorporated by reference. In other embodiments, the IsdB sequence is SAV1129 from strain Mu50 (which is the same amino acid sequence for Newman) and can be accessed using Genbank Accession Number NP 371653.1 (gi|15924119), which is incorporated 60 by reference. In further embodiments, other polypeptides transported by the Ess pathway or processed by sortase may be used, the sequences of which may be identified by one of skill in the art using databases and internet accessible resources. 65

In certain embodiments, fibronectin binding protein B sequence can include all or part of the precursor or mature

form of FnbpB. FnbpB sequence can be found in GenBank entries having accession numbers NC_009641.1, AAW37288. (GI:57285194), ZP_07362431 (GI: 304379700), EEV81932 (GI:257859074), NP_373026 (GI: 15925492) or other FnbpB amino acid sequences identified in GenBank.

Examples of various proteins that can be used in the context of the present invention can be identified by analysis of database submissions of bacterial genomes, including but not limited to accession numbers NC_002951 (GI:57650036 and GenBank CP000046), NC_002745 (GI:57634611 and GenBank BA000017), NC_002745 (GI:29165615 and Gen-Bank BA000018), NC_003923 (GI:21281729 and GenBank BA000033), NC_002952 (GI:49482253 and GenBank BX571856), NC_002953 (GI:49484912 and GenBank BX571857), NC_007793 (GI:87125858 and GenBank CP000255), NC_007795 (GI:87201381 and GenBank CP000253) each of which are incorporated by reference.

As used herein, a "protein" or "polypeptide" refers to a molecule comprising at least ten amino acid residues. In some embodiments, a wild-type version of a protein or polypeptide are employed, however, in many embodiments of the invention, a modified protein or polypeptide is employed to generate an immune response. The terms described above may be used interchangeably. A "modified protein" or "modified polypeptide" or a "variant" refers to a protein or polypeptide whose chemical structure, particularly its amino acid sequence, is altered with respect to the wild-type protein or polypeptide. In some embodiments, a modified/variant protein or polypeptide has at least one modified activity or function (recognizing that proteins or polypeptides may have multiple activities or functions). It is specifically contemplated that a modified/variant protein or polypeptide may be altered with respect to one activity or function yet retain a wild-type activity or function in other respects, such as immunogenicity.

In certain embodiments the size of a protein or polypeptide (wild-type or modified) may comprise, but is not limited to, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500, 525, 550, 575, 600, 625, 650, 675, 700, 725, 750, 775, 800, 825, 850, 875, 900, 925, 950, 975, 1000, 1100, 1200, 1300, 1400, 1500, 1750, 2000, 2250, 2500 amino molecules or greater, and any range derivable therein, or derivative of a corresponding amino sequence described or referenced herein. It is contemplated that polypeptides may be mutated by truncation, rendering them shorter than their corresponding wild-type form, but also they might be altered by fusing or conjugating a heterologous protein sequence with a particular function (e.g., for targeting or localization, for enhanced immunogenicity, for purification purposes, etc.).

As used herein, an "amino molecule" refers to any amino acid, amino acid derivative, or amino acid mimic known in the art. In certain embodiments, the residues of the proteinaceous molecule are sequential, without any non-amino molecule interrupting the sequence of amino molecule residues. In other embodiments, the sequence may comprise one or more non-amino molecule moieties. In particular embodiments, the sequence of residues of the proteinaceous molecule may be interrupted by one or more non-amino molecule moieties. Accordingly, the term "proteinaceous composition" encompasses amino molecule sequences comprising at least one of the 20 common amino acids in naturally synthesized proteins, or at least one modified or unusual amino acid.

Proteinaceous compositions may be made by any tech-5 nique known to those of skill in the art, including (i) the expression of proteins, polypeptides, or peptides through standard molecular biological techniques, (ii) the isolation of proteinaceous compounds from natural sources, or (iii) the chemical synthesis of proteinaceous materials. The nucle-10 otide as well as the protein, polypeptide, and peptide sequences for various genes have been previously disclosed, and may be found in the recognized computerized databases. One such database is the National Center for Biotechnology Information's Genbank and GenPept databases (on the World 15 Wide Web at ncbi.nlm.nih.gov/). The coding regions for these genes may be amplified and/or expressed using the techniques disclosed herein or as would be known to those of ordinary skill in the art.

Amino acid sequence variants of Ebh, SpA, coagulases and 20 other polypeptides of the invention can be substitutional, insertional, or deletion variants. A variation in a polypeptide of the invention may affect 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 25 47, 48, 49, 50, or more non-contiguous or contiguous amino acids of the polypeptide, as compared to wild-type. A variant can comprise an amino acid sequence that is at least 50%, 60%, 70%, 80%), or 90%, including all values and ranges there between, identical to any sequence provided or refer-

encoding nucleic acid sequence to generate a truncated protein. Insertional mutants typically involve the addition of material at a non-terminal point in the polypeptide. This may include the insertion of one or more residues. Terminal additions, called fusion proteins, may also be generated. These fusion proteins include multimers or concatamers of one or more peptide or polypeptide described or referenced herein.

Substitutional variants typically contain the exchange of one amino acid for another at one or more sites within the protein, and may be designed to modulate one or more properties of the polypeptide, with or without the loss of other functions or properties. Substitutions may be conservative, that is, one amino acid is replaced with one of similar shape and charge. Conservative substitutions are well known in the art and include, for example, the changes of: alanine to serine; arginine to lysine; asparagine to glutamine or histidine; aspartate to glutamate; cysteine to serine; glutamine to asparagine; glutamate to aspartate; glycine to proline; histidine to asparagine or glutamine; isoleucine to leucine or valine; leucine to valine or isoleucine; lysine to arginine; methionine to leucine or isoleucine; phenylalanine to tyrosine, leucine or methionine; serine to threonine; threonine to serine; tryptophan to tyrosine; tyrosine to tryptophan or phenylalanine; and valine to isoleucine or leucine. Alternatively, substitutions may be non-conservative such that a function or activity of the polypeptide is affected. Non-conservative changes typically involve substituting a residue with one that is chemically dissimilar, such as a polar or charged amino acid for a nonpolar or uncharged amino acid, and vice versa.

TABLE 1

		Exempla	ary surfa	ice prote	eins of S	5. aureus stra	ains.	
SAV#	SA#	Surface	MW2	Mu50	N315	Newman	MRSA252*	MSSA476*
SAV0111	SA0107	Spa	492	450	450	520	516	492
SAV2503	SA2291	FnBPA	1015	1038	1038	741		1015
SAV2502	SA2290	FnBPB	943	961	961	677	965	957
SAV0811	SA0742	ClfA	946	935	989	933	1029	928
SAV2630	SA2423	ClfB	907	877	877	913	873	905
Np	Np	Can	1183		_		1183	1183
SAV0561	SA0519	SdrC	955	953	953	947	906	957
SAV0562	SA0520	SdrD	1347	1385	1385	1315		1365
SAV0563	SA0521	SdrE	1141	1141	1141	1166	1137	1141
Np	Np	Pls						
SAV2654	SA2447	SasA	2275	2271	2271	2271	1351	2275
SAV2160	SA1964	SasB	686	2481	2481	2481	2222	685
	SA1577	SasC	2186	213	2186	2186	2189	2186
SAV0134	SA0129	SasD	241	241	241	241	221	241
SAV1130	SA0977	SasE/IsdA	350	350	350	350	354	350
SAV2646	SA2439	SasF	635	635	635	635	627	635
SAV2496		SasG	1371	525	927			1371
SAV0023	SA0022	SasH	772		772	772	786	786
SAV1731	SA1552	SasI	895	891	891	891	534	895
SAV1129	SA0976	SasJ/IsdB	645	645	645	645	652	645
	SA2381	SasK	198	211	211			197
	Np	SasL		232				
SAV1131	SA0978	IsdC	227	227	227	227	227	227

enced herein, e.g., SEQ ID NO:2-8 or SEQ ID No:11-30, A variant can include 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more substitute amino acids. A polypeptide processed or secreted by the Ess pathway or other surface ⁶⁰ proteins (see Table 1) or sortase substrates from any *staphy-lococcus* species and strain are contemplated for use in compositions and methods described herein.

Deletion variants typically lack one or more residues of the native or wild-type protein. Individual residues can be deleted 65 or a number of contiguous amino acids can be deleted. A stop codon may be introduced (by substitution or insertion) into an

Proteins of the invention may be recombinant, or synthesized in vitro. Alternatively, a non-recombinant or recombinant protein may be isolated from bacteria. It is also contemplated that a bacteria containing such a variant may be implemented in compositions and methods of the invention. Consequently, a protein need not be isolated.

The term "functionally equivalent codon" is used herein to refer to codons that encode the same amino acid, such as the six codons for arginine or serine, and also refers to codons that encode biologically equivalent amino acids

40

TABLE	2

		Code	on Table
Amino Acids			Codons
Alanine	Ala	A	GCA GCC GCG GCU
Cysteine	Суз	С	UGC UGU
Aspartic acid	Asp	D	GAC GAU
Glutamic acid	Glu	Е	GAA GAG
Phenyl- alanine	Phe	F	ບບດ ບບບ
Glycine	Gly	G	GGA GGC GGG GGU
Histidine	His	н	CAC CAU
Isoleucine	Ile	I	AUA AUC AUU
Lysine	Lys	к	AAA AAG
Leucine	Leu	L	UUA UUG CUA CUC CUG CUU
Methionine	Met	М	AUG
Asparagine	Asn	N	AAC AAU
Proline	Pro	Ρ	CCA CCC CCG CCU
Glutamine	Gln	Q	CAA CAG
Arginine	Arg	R	AGA AGG CGA CGC CGG CGU
Serine	Ser	S	AGC AGU UCA UCC UCG UCU
Threonine	Thr	т	ACA ACC ACG ACU
Valine	Val	v	GUA GUC GUG GUU
Tryptophan	Trp	W	UGG
Tyrosine	Tyr	Y	UAC UAU

It also will be understood that amino acid and nucleic acid sequences may include additional residues, such as additional N- or C-terminal amino acids, or 5' or 3' sequences, respectively, and yet still be essentially as set forth in one of the sequences disclosed herein, so long as the sequence meets the 45 criteria set forth above, including the maintenance of biological protein activity (e.g., immunogenicity) where protein expression is concerned. The addition of terminal sequences particularly applies to nucleic acid sequences that may, for example, include various non-coding sequences flanking 50 either of the 5' or 3' portions of the coding region.

The following is a discussion based upon changing of the amino acids of a protein to create a variant polypeptide or peptide. For example, certain amino acids may be substituted for other amino acids in a protein structure with or without 55 appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's functional activity, certain amino acid substitutions 60 can be made in a protein sequence, and in its underlying DNA coding sequence, and nevertheless produce a protein with a desirable property. It is thus contemplated by the inventors that various changes may be made in the DNA sequences of genes 65

It is contemplated that in compositions of the invention, there is between about 0.001 mg and about 10 mg of total

polypeptide, peptide, and/or protein per ml. The concentration of protein in a composition can be about, at least about or at most about 0.001, 0.010, 0.050, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, 9.5, 10.0 mg/ml or more (or any range derivable therein). Of this, about, at least about, or at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 10 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100% may be an SpA variant or a coagulase, and may be used in combination with other peptides or polypeptides, such as other 15 bacterial peptides and/or antigens.

The present invention contemplates the administration of variant SpA polypeptides or peptides to effect a preventative therapy or therapeutic effect against the development of a disease or condition associated with infection by a staphylo-20 coccus pathogen.

In certain aspects, combinations of staphylococcal antigens are used in the production of an immunogenic composition that is effective at treating or preventing staphylococcal infection. Staphylococcal infections progress through several 25 different stages. For example, the staphylococcal life cycle involves commensal colonization, initiation of infection by accessing adjoining tissues or the bloodstream, and/or anaerobic multiplication in the blood. The interplay between S. aureus virulence determinants and the host defense mecha-³⁰ nisms can induce complications such as endocarditis, metastatic abscess formation, and sepsis syndrome. Different molecules on the surface of the bacterium are involved in different steps of the infection cycle. Combinations of certain antigens can elicit an immune response which protects against mul-³⁵ tiple stages of staphylococcal infection. The effectiveness of the immune response can be measured either in animal model assays and/or using an opsonophagocytic assay.

II. POLYPEPTIDES AND POLYPEPTIDE PRODUCTION

The present invention describes polypeptides, peptides, and proteins and

immunogenic fragments thereof for use in various embodiments of the present invention. For example, specific polypeptides are assayed for or used to elicit an immune response. In specific embodiments, all or part of the proteins of the invention can also be synthesized in solution or on a solid support in accordance with conventional techniques. Various automatic synthesizers are commercially available and can be used in accordance with known protocols. See, for example, Stewart and Young, (1984); Tarn et al., (1983); Merrifield, (1986); and Barany and Merrifield (1979), each incorporated herein by reference.

Alternatively, recombinant DNA technology may be employed wherein a nucleotide sequence which encodes a peptide of the invention is inserted into an expression vector, transformed or transfected into an appropriate host cell and cultivated under conditions suitable for expression.

One embodiment of the invention includes the use of gene transfer to cells, including microorganisms, for the production and/or presentation of polypeptides or peptides. The gene for the polypeptide or peptide of interest may be transferred into appropriate host cells followed by culture of cells under the appropriate conditions. The generation of recombinant expression vectors, and the elements included therein, are well known in the art and briefly discussed herein. Alternatively, the protein to be produced may be an endogenous protein normally synthesized by the cell that is isolated and purified.

Another embodiment of the present invention uses autologous B lymphocyte cell lines, which are transfected with a 5 viral vector that expresses an immunogen product, and more specifically, a protein having immunogenic activity. Other examples of mammalian host cell lines include, but are not limited to Vero and HeLa cells, other B- and T-cell lines, such as CEM, 721.221, H9, Jurkat, Raji, as well as cell lines of 10 Chinese hamster ovary, W138, BHK, COS-7, 293, HepG2, 3T3, RIN and MDCK cells. In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or that modifies and processes the gene product in the manner desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the posttranslational processing and modification of proteins. Appropriate cell lines or host systems can be chosen to ensure the 20 correct modification and processing of the foreign protein expressed.

A number of selection systems may be used including, but not limited to HSV thymidine kinase, hypoxanthine-guanine phosphoribosyltransferase, and adenine phosphoribosyl- 25 transferase genes, in tk-, hgprt- or aprt-cells, respectively. Also, anti-metabolite resistance can be used as the basis of selection: for dhfr, which confers resistance to trimethoprim and methotrexate; gpt, which confers resistance to mycophenolic acid; neo, which confers resistance to the aminoglyco- 30 side G418; and hygro, which confers resistance to hygromycin.

Animal cells can be propagated in vitro in two modes: as non-anchorage-dependent cells growing in suspension throughout the bulk of the culture or as anchorage-dependent 35 cells requiring attachment to a solid substrate for their propagation (i.e., a monolayer type of cell growth).

Non-anchorage dependent or suspension cultures from continuous established cell lines are the most widely used means of large scale production of cells and cell products. 40 However, suspension cultured cells have limitations, such as tumorigenic potential and lower protein production than adherent cells.

Where a protein is specifically mentioned herein, it is preferably a reference to a native or recombinant protein or 45 optionally a protein in which any signal sequence has been removed. The protein may be isolated directly from the staphylococcal strain or produced by recombinant DNA techniques. Immunogenic fragments of the protein may be incorporated into the immunogenic composition of the invention. 50 These are fragments comprising at least 10 amino acids, 20 amino acids, 30 amino acids, 40 amino acids, 50 amino acids, or 100 amino acids, including all values and ranges there between, taken contiguously from the amino acid sequence of the protein. In addition, such immunogenic fragments are 55 immunologically reactive with antibodies generated against the Staphylococcal proteins or with antibodies generated by infection of a mammalian host with Staphylococci. Immunogenic fragments also include fragments that when administered at an effective dose, (either alone or as a hapten bound to 60 a carrier), elicit a protective or therapeutic immune response against Staphylococcal infection, in certain aspects it is protective against S. aureus and/or S. epidermidis infection. Such an immunogenic fragment may include, for example, the protein lacking an N-terminal leader sequence, and/or a trans-65 membrane domain and/or a C-terminal anchor domain. In a preferred aspect the immunogenic fragment according to the

invention comprises substantially all of the extracellular domain of a protein which has at least 80% identity, at least 85% identity, at least 95% identity, at least 95% identity, or at least 97-99%) identity, including all values and ranges there between, to a sequence selected segment of a polypeptide described or referenced herein.

Also included in immunogenic compositions of the invention are fusion proteins composed of one or more Staphylococcal proteins, or immunogenic fragments of staphylococcal proteins. Such fusion proteins may be made recombinantly and may comprise one portion of at least 1, 2, 3, 4, 5, or 6 staphylococcal proteins or segments. Alternatively, a fusion protein may comprise multiple portions of at least 1, 2, 3, 4 or 5 staphylococcal proteins. These may combine different Staphylococcal proteins and/or multiples of the same protein or proten fragment, or immunogenic fragments in the same protein (forming a multimer or a concatamer). Alternatively, the invention also includes individual fusion proteins of Staphylococcal proteins or immunogenic fragments thereof, as a fusion protein with heterologous sequences such as a provider of T-cell epitopes or purification tags, for example: β-galactosidase, glutathione-S-transferase, green fluorescent proteins (GFP), epitope tags such as FLAG, myc tag, poly histidine, or viral surface proteins such as influenza virus haemagglutinin, or bacterial proteins such as tetanus toxoid, diphtheria toxoid, or CRM197.

III. NUCLEIC ACIDS

In certain embodiments, the present invention concerns recombinant polynucleotides encoding the proteins, polypeptides, peptides of the invention. The nucleic acid sequences for SpA, coagulases and other bacterial proteins are included, all of which are incorporated by reference, and can be used to prepare peptides or polypeptides.

As used in this application, the term "polynucleotide" refers to a nucleic acid molecule that either is recombinant or has been isolated free of total genomic nucleic acid. Included within the term "polynucleotide" are oligonucleotides (nucleic acids of 100 residues or less in length), recombinant vectors, including, for example, plasmids, cosmids, phage, viruses, and the like. Polynucleotides include, in certain aspects, regulatory sequences, isolated substantially away from their naturally occurring genes or protein encoding sequences. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be RNA, DNA (genomic, cDNA or synthetic), analogs thereof, or a combination thereof. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide.

In this respect, the term "gene," "polynucleotide," or "nucleic acid" is used to refer to a nucleic acid that encodes a protein, polypeptide, or peptide (including any sequences required for proper transcription, post-translational modification, or localization). As will be understood by those in the art, this term encompasses genomic sequences, expression cassettes, cDNA sequences, and smaller engineered nucleic acid segments that express, or may be adapted to express, proteins, polypeptides, domains, peptides, fusion proteins, and mutants. A nucleic acid encoding all or part of a polypeptide may contain a contiguous nucleic acid sequence of: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 441, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 610, 620, 630, 640, 650, 660, 670, 680, 690, 700, 710, 720, 730, 740, 750, 760, 770, 780, 790, 800, 810, 820, 830, 840, 850, 860, 870, 880, 890, 900, 910, 920, 930, 940, 950, 960, 970, 980, 990, 1000, 1010, 1020, 1030, 1040, 1050, 1060, 1070, 1080, 1090, 1095, 1100, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 9000, 10000, or more nucleotides, nucleosides, or base pairs, including all 5 values and ranges therebetween, of a polynucleotide encoding one or more amino acid sequence described or referenced herein. It also is contemplated that a particular polypeptide may be encoded by nucleic acids containing variations having slightly different nucleic acid sequences but, nonetheless, 10 encode the same or substantially similar protein (see Table 3 above).

In particular embodiments, the invention concerns isolated nucleic acid segments and recombinant vectors incorporating nucleic acid sequences that encode a variant SpA or coagu- 15 lase. The term "recombinant" may be used in conjunction with a polynucleotide or polypeptide and generally refers to a polypeptide or polynucleotide produced and/or manipulated in vitro or that is a replication product of such a molecule.

In other embodiments, the invention concerns isolated 20 nucleic acid segments and recombinant vectors incorporating nucleic acid sequences that encode a variant SpA or coagulase polypeptide or peptide to generate an immune response in a subject. In various embodiments the nucleic acids of the invention may be used in genetic vaccines.

The nucleic acid segments used in the present invention can be combined with other nucleic acid sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary consid- 30 erably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant nucleic acid protocol. In some cases, a nucleic acid sequence may encode a polypep- 35 tide sequence with additional heterologous coding sequences, for example to allow for purification of the polypeptide, transport, secretion, post-translational modification, or for therapeutic benefits such as targeting or efficacy. As discussed above, a tag or other heterologous polypeptide 40 may be added to the modified polypeptide-encoding sequence, wherein "heterologous" refers to a polypeptide that is not the same as the modified polypeptide.

In certain other embodiments, the invention concerns isolated nucleic acid segments and recombinant vectors that 45 include within their sequence a contiguous nucleic acid sequence from SEQ ID NO:1 (SpA domain D) or SEQ ID NO:3 (SpA) or any other nucleic acid sequences encoding coagulases or other secreted virulence factors and/or surface proteins including proteins transported by the Ess pathway, 50 processed by sortase, or proteins incorporated herein by reference.

In certain embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein; those comprising at least 70%, 55 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher sequence identity, including all values and ranges there between, compared to a polynucleotide sequence of this invention using the methods described herein (e.g., BLAST analysis using standard parameters).

The invention also contemplates the use of polynucleotides which are complementary to all the above described polynucleotides.

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A. Vectors

Polypeptides of the invention may be encoded by a nucleic 65 acid molecule comprised in a vector. The term "vector" is used to refer to a carrier nucleic acid molecule into which a

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heterologous nucleic acid sequence can be inserted for introduction into a cell where it can be replicated and expressed. A nucleic acid sequence can be "heterologous," which means that it is in a context foreign to the cell in which the vector is being introduced or to the nucleic acid in which is incorporated, which includes a sequence homologous to a sequence in the cell or nucleic acid but in a position within the host cell or nucleic acid where it is ordinarily not found. Vectors include DNAs, RNAs, plasmids, cosmids, viruses (bacteriophage, animal viruses, and plant viruses), and artificial chromosomes (e.g., YACs). One of skill in the art would be well equipped to construct a vector through standard recombinant techniques (for example Sambrook et al., 2001; Ausubel et al., 1996, both incorporated herein by reference). In addition to encoding a variant SpA polypeptide the vector can encode other polypeptide sequences such as a one or more other bacterial peptide, a tag, or an immunogenicity enhancing peptide. Useful vectors encoding such fusion proteins include pIN vectors (Inouye et al., 1985), vectors encoding a stretch of histidines, and pGEX vectors, for use in generating glutathione S-transferase (GST) soluble fusion proteins for later purification and separation or cleavage.

The term "expression vector" refers to a vector containing a nucleic acid sequence coding for at least part of a gene 25 product capable of being transcribed. In some cases, RNA molecules are then translated into a protein, polypeptide, or peptide. Expression vectors can contain a variety of "control sequences," which refer to nucleic acid sequences necessary for the transcription and possibly translation of an operably linked coding sequence in a particular host organism. In addition to control sequences that govern transcription and translation, vectors and expression vectors may contain nucleic acid sequences that serve other functions as well and are described herein.

B. Promoters and Enhancers

A "promoter" is a control sequence. The promoter is typically a region of a nucleic acid sequence at which initiation and rate of transcription are controlled. It may contain genetic elements at which regulatory proteins and molecules may bind such as RNA polymerase and other transcription factors. The phrases "operatively positioned," "operatively linked," "under control," and "under transcriptional control" mean that a promoter is in a correct functional location and/or orientation in relation to a nucleic acid sequence to control transcriptional initiation and expression of that sequence. A promoter may or may not be used in conjunction with an "enhancer," which refers to a cis-acting regulatory sequence involved in the transcriptional activation of a nucleic acid sequence.

Naturally, it may be important to employ a promoter and/or enhancer that effectively directs the expression of the DNA segment in the cell type or organism chosen for expression. Those of skill in the art of molecular biology generally know the use of promoters, enhancers, and cell type combinations for protein expression (see Sambrook et al., 2001, incorporated herein by reference). The promoters employed may be constitutive, tissue-specific, or inducible and in certain embodiments may direct high level expression of the introduced DNA segment under specified conditions, such as large-scale production of recombinant proteins or peptides.

Various elements/promoters may be employed in the context of the present invention to regulate the expression of a gene. Examples of such inducible elements, which are regions of a nucleic acid sequence that can be activated in response to a specific stimulus, include but are not limited to Immunoglobulin Heavy Chain (Banerji et al., 1983; Gilles et al., 1983; Grosschedl et al., 1985; Atchinson et al., 1986,

1987; Imler et al., 1987; Weinberger et al., 1984; Kiledjian et al, 1988; Porton et al; 1990), Immunoglobulin Light Chain (Queen et al., 1983; Picard et al., 1984), T Cell Receptor (Luria et al., 1987; Winoto et al., 1989; Redondo et al; 1990), HLA DQ α and/or DQ β Sullivan et al., 1987), β Interferon 5 (Goodbourn et al., 1986; Fujita et al., 1987; Goodboum et al, 1988), Interleukin-2 (Greene et al., 1989), Interleukin-2 Receptor (Greene et al., 1989; Lin et al, 1990), MHC Class II 5 (Koch et al., 1989), MHC Class II HLA-DRaSherman et al., 1989), β-Actin (Kawamoto et al., 1988; Ng et al; 1989), 10 Muscle Creatine Kinase (MCK) (Jaynes et al., 1988; Horlick et al., 1989; Johnson et al., 1989), Prealbumin (Transthyretin) (Costa et al., 1988), Elastase I (Ornitz et al., 1987), Metallothionein (MTII) (Karin et al., 1987; Culotta et al., 1989), Collagenase (Pinkert et al., 1987; Angel et al., 1987), Albu- 15 min (Pinkert et al., 1987; Tronche et al., 1989, 1990), α-Fetoprotein (Godbout et al., 1988; Campere et al., 1989), γ-Globin (Bodine et al., 1987; Perez-Stable et al., 1990), β-Globin (Trudel et al., 1987), c-fos (Cohen et al., 1987), c-Ha-Ras (Triesman, 1986; Deschamps et al., 1985), Insulin 20 (Edlund et al., 1985), Neural Cell Adhesion Molecule (NCAM) (Hirsh et al., 1990), α1-Antitrypain (Latimer et al., 1990), H2B (TH2B) Histone (Hwang et al, 1990), Mouse and/or Type I Collagen (Ripe et al., 1989), Glucose-Regulated Proteins (GRP94 and GRP78) (Chang et al., 1989), Rat 25 Growth Hormone (Larsen et al., 1986), Human Serum Amyloid A (SAA) (Edbrooke et al., 1989), Troponin I (TN I) (Yutzey et al., 1989), Platelet-Derived Growth Factor (PDGF) (Pech et al., 1989), Duchenne Muscular Dystrophy (Klamut et al., 1990), SV40 (Banerji et al., 1981; Moreau et al., 1981; 30 Sleigh et al., 1985; Firak et al., 1986; Herr et al., 1986; Imbra et al., 1986; Kadesch et al., 1986; Wang et al., 1986; Ondek et al., 1987; Kuhl et al., 1987; Schaffner et al., 1988), Polyoma (Swartzendruber et al., 1975; Vasseur et al., 1980; Katinka et al, 1980, 1981; Tyndell et al., 1981; Dandolo et al., 1983; de 35 Villiers et al., 1984; Hen et al., 1986; Satake et al., 1988; Campbell et al., 1988), Retroviruses (Kriegler et al., 1982, 1983; Levinson et al, 1982; Kriegler et al., 1983, 1984a, b, 1988; Bosze et al., 1986; Miksicek et al., 1986; Celander et al, 1987; Thiesen et al., 1988; Celander et al., 1988; Choi et al., 40 1988; Reisman et al., 1989), Papilloma Virus (Campo et al., 1983; Lusky et al., 1983; Spandidos and Wilkie, 1983; Spalholz et al., 1985; Lusky et al., 1986; Cripe et al., 1987; Gloss et al., 1987; Hirochika et al., 1987; Stephens et al, 1987), Hepatitis B Virus (Bulla et al., 1986; Jameel et al., 1986; 45 Shaul et al., 1987; Spandau et al, 1988; Vannice et al., 1988), Human Immunodeficiency Virus (Muesing et al., 1987; Hauber et al, 1988; Jakobovits et al., 1988; Feng et al., 1988; Takebe et al., 1988; Rosen et al., 1988; Berkhout et al, 1989; Laspia et al., 1989; Sharp et al., 1989; Braddock et al., 1989), 50 Cytomegalovirus (CMV) IE (Weber et al., 1984; Boshart et al., 1985; Foecking et al., 1986), Gibbon Ape Leukemia Virus (Holbrook et al., 1987; Quinn et al., 1989).

Inducible elements include, but are not limited to MT II-Phorbol Ester (TFAVHeavy metals (Palmiter et al., 1982; 55 Haslinger et al., 1985; Searle et al., 1985; Stuart et al, 1985; Imagawa et al., 1987, Karin et al., 1987; Angel et al., 1987b; McNeall et al., 1989); MMTV (mouse mammary tumor virus)-Glucocorticoids (Huang et al., 1981; Lee et al., 1981; Majors et al, 1983; Chandler et al., 1983; Lee et al., 1984; 60 Ponta et al., 1985; Sakai et al., 1988); P-Interferon-poly(rI) x/poly(rc) (Tavernier et al., 1983); Adenovirus 5 E2-E1A (Imperiale et al., 1984); Collagenase-Phorbol Ester (TPA) (Angel et al., 1987a); Stromelysin-Phorbol Ester (TPA) (Angel et al, 1987b); SV40-Phorbol Ester (TPA) (Angel et al., 65 1987b); Murine MX Gene-Interferon, Newcastle Disease Virus (Hug et al., 1988); GRP78 Gene-A23187 (Resendez et

al., 1988); α -2-Macroglobulin-IL-6 (Kunz et al., 1989); Vimentin-Serum (Rittling et al., 1989); MHC Class I Gene H-2 κ b-Interferon (Blanar et al., 1989); HSP70-E1A/SV40 Large T Antigen (Taylor et al., 1989); HSP70-E1A/SV40 Large T Antigen (Taylor et al., 1989); 1990a, 1990b); Proliferin-Phorbol Ester/TPA (Mordacq et al., 1989); Tumor Necrosis Factor-PMA (Hensel et al., 1989); and Thyroid Stimulating Hormone α Gene-Thyroid Hormone (Chatterjee et al., 1989).

The particular promoter that is employed to control the expression of peptide or protein encoding polynucleotide of the invention is not believed to be critical, so long as it is capable of expressing the polynucleotide in a targeted cell, preferably a bacterial cell. Where a human cell is targeted, it is preferable to position the polynucleotide coding region adjacent to and under the control of a promoter that is capable of being expressed in a human cell. Generally speaking, such a promoter might include either a bacterial, human or viral promoter.

In embodiments in which a vector is administered to a subject for expression of the protein, it is contemplated that a desirable promoter for use with the vector is one that is not down-regulated by cytokines or one that is strong enough that even if down-regulated, it produces an effective amount of a variant SpA for eliciting an immune response. Non-limiting examples of these are CMV IE and RSV LTR. Tissue specific promoters can be used, particularly if expression is in cells in which expression of an antigen is desirable, such as dendritic cells or macrophages. The mammalian MHC I and MHC II promoters are examples of such tissue-specific promoters.

C. Initiation Signals and Internal Ribosome Binding Sites (IRES)

A specific initiation signal also may be required for efficient translation of coding sequences. These signals include the ATG initiation codon or adjacent sequences. Exogenous translational control signals, including the ATG initiation codon, may need to be provided. One of ordinary skill in the art would readily be capable of determining this and providing the necessary signals.

In certain embodiments of the invention, the use of internal ribosome entry sites (IRES) elements are used to create multigene, or polycistronic, messages. IRES elements are able to bypass the ribosome scanning model of 5' methylated Cap dependent translation and begin translation at internal sites (Pelletier and Sonenberg, 1988; Macejak and Sarnow, 1991). IRES elements can be linked to heterologous open reading frames. Multiple open reading frames can be transcribed together, each separated by an IRES, creating polycistronic messages. Multiple genes can be efficiently expressed using a single promoter/enhancer to transcribe a single message (see U.S. Pat. Nos. 5,925,565 and 5,935,819, herein incorporated by reference).

D. Selectable and Screenable Markers

In certain embodiments of the invention, cells containing a nucleic acid construct of the present invention may be identified in vitro or in vivo by encoding a screenable or selectable marker in the expression vector. When transcribed and translated, a marker confers an identifiable change to the cell permitting easy identification of cells containing the expression vector. Generally, a selectable marker is one that confers a property that allows for selection. A positive selectable marker is one in which the presence of the marker allows for its selection, while a negative selectable marker is one in which its presence prevents its selection. An example of a positive selectable marker is a drug resistance marker.

E. Host Cells

As used herein, the terms "cell," "cell line," and "cell culture" may be used interchangeably. All of these terms also

include their progeny, which is any and all subsequent generations. It is understood that all progeny may not be identical due to deliberate or inadvertent mutations. In the context of expressing a heterologous nucleic acid sequence, "host cell" refers to a prokaryotic or eukaryotic cell, and it includes any ⁵ transformable organism that is capable of replicating a vector or expressing a heterologous gene encoded by a vector. A host cell can, and has been, used as a recipient for vectors or viruses. A host cell may be "transfected" or "transformed," which refers to a process by which exogenous nucleic acid, ¹⁰ such as a recombinant protein-encoding sequence, is transferred or introduced into the host cell. A transformed cell includes the primary subject cell and its progeny.

Host cells may be derived from prokaryotes or eukaryotes, including bacteria, yeast cells, insect cells, and mammalian cells for replication of the vector or expression of part or all of the nucleic acid sequence(s). Numerous cell lines and cultures are available for use as a host cell, and they can be obtained through the American Type Culture Collection (ATCC), which is an organization that serves as an archive for living cultures and genetic materials (www.atcc.org).

F. Expression Systems

Numerous expression systems exist that comprise at least a part or all of the compositions discussed above. Prokaryoteand/or eukaryote-based systems can be employed for use ²⁵ with the present invention to produce nucleic acid sequences, or their cognate polypeptides, proteins and peptides. Many such systems are commercially and widely available.

The insect cell/baculovirus system can produce a high level of protein expression of a heterologous nucleic acid segment, ³⁰ such as described in U.S. Pat. Nos. 5,871,986, 4,879,236, both herein incorporated by reference, and which can be bought, for example, under the name MAXBAC® 2.0 from INVITROGEN® and BACPACK[™] BACULOVIRUS EXPRESSION SYSTEM FROM CLONTECH®. ³⁵

In addition to the disclosed expression systems of the invention, other examples of/expression systems include STRATAGENE®'s COMPLETE CONTROL™ Inducible Mammalian Expression System, which involves a synthetic ecdysone-inducible receptor, or its pET Expression System, 40 an E. coli expression system. Another example of an inducible expression system is available from INVITROGEN®, which carries the T-REXTM (tetracycline-regulated expression) System, an inducible mammalian expression system that uses the full-length CMV promoter. INVITROGEN® 45 also provides a yeast expression system called the Pichia methanolica Expression System, which is designed for highlevel production of recombinant proteins in the methylotrophic yeast Pichia methanolica. One of skill in the art would know how to express a vector, such as an expression 50 construct, to produce a nucleic acid sequence or its cognate polypeptide, protein, or peptide.

IV. POLYSACCHARIDES

The immunogenic compositions of the invention may further comprise capsular polysaccharides including one or more of PIA (also known as PNAG) and/or *S. aureus* Type V and/or type VIII capsular polysaccharide and/or *S. epidermidis* Type I, and/or Type II and/or Type III capsular polysac- 60 charide.

A. PIA (PNAG)

It is now clear that the various forms of staphylococcal surface polysaccharides identified as PS/A, PIA and SAA are the same chemical entity—PNAG (Maira-Litran et al., 2004). 65 Therefore the term PIA or PNAG encompasses all these polysaccharides or oligosaccharides derived from them. 90

PIA is a polysaccharide intercellular adhesin and is composed of a polymer of β -(1 \rightarrow 6)-linked glucosamine substituted with N-acetyl and O-succinyl constituents. This polysaccharide is present in both S. aureus and S. epidermidis and can be isolated from either source (Joyce et al., 2003; Maira-Litran et al., 2002). For example, PNAG may be isolated from S. aureus strain MN8m (WO04/43407). PIA isolated from S. epidermidis is a integral constituent of biofilm. It is responsible for mediating cell-cell adhesion and probably also functions to shield the growing colony from the host's immune response. The polysaccharide previously known as poly-N-succinyl- β -(1 \rightarrow 6)-glucosamine (PNSG) was recently shown not to have the expected structure since the identification of N-succinylation was incorrect (Maira-Litran et al., 2002). Therefore the polysaccharide formally known as PNSG and now found to be PNAG is also encompassed by the term PIA.

PIA (or PNAG) may be of different sizes varying from over 400 kDa to between 75 and 400 kDa to between 10 and 75 kDa to oligosaccharides composed of up to 30 repeat units (of β -(1 \rightarrow 6)-linked glucosamine substituted with N-acetyl and O-succinyl constituents). Any size of PIA polysaccharide or oligosaccharide may be use in an immunogenic composition of the invention, in one aspect the polysaccharide is over 40 kDa. Sizing may be achieved by any method known in the art, for instance by microfluidization, ultrasonic irradiation or by chemical cleavage (WO 03/53462, EP497524, EP497525). In certain aspects PIA (PNAG) is at least or at most 40-400 kDa, 40-300 kDa, 50-350 kDa, 60-300 kDa, 50-250 kDa and 60-200 kDa.

PIA (PNAG) can have different degree of acetylation due to substitution on the amino groups by acetate. PIA produced
³⁵ in vitro is almost fully substituted on amino groups (95-100%). Alternatively, a deacetylated PIA (PNAG) can be used having less than 60%, 50%, 40%, 30%, 20%, 10% acetylation. Use of a deacetylated PIA (PNAG) is preferred since non-acetylated epitopes of PNAG are efficient at mediating opsonic killing of Gram positive bacteria, preferably *S. aureus* and/or *S. epidermidis*. In certain aspects, the PIA (PNAG) has a size between 40 kDa and 300 kDa and is deacetylated so that less than 60%, 50%, 40%, 30% or 20% of amino groups are acetylated.

The term deacetylated PNAG (dPNAG) refers to a PNAG polysaccharide or oligosaccharide in which less than 60%, 50%, 40%, 30%, 20% or 10% of the amino agroups are acetylated. In certain aspects, PNAG is deaceylated to form dPNAG by chemically treating the native polysaccharide. For example, the native PNAG is treated with a basic solution such that the pH rises to above 10. For instance the PNAG is treated with 0.1-5 M, 0.2-4 M, 0.3-3 M, 0.5-2 M, 0.75-1.5 M or 1 M NaOH, KOH or NH4OH. Treatment is for at least 10 to 30 minutes, or 1, 2, 3, 4, 5, 10, 15 or 20 hours at a temperature of 20-100, 25-80, 30-60 or 30-50 or 35-45° C. dPNAG may be prepared as described in WO 04/43405.

The polysaccharide(s) can be conjugated or unconjugated to a carrier protein.

B. Type 5 and Type 8 Polysaccharides from S. aureus

Most strains of *S. aureus* that cause infection in man contain either Type 5 or Type 8 polysaccharides. Approximately 60% of human strains are Type 8 and approximately 30% are Type 5. The structures of Type 5 and Type 8 capsular polysaccharide antigens are described in Moreau et al., (1990) and Fournier et al., (1984). Both have FucNAcp in their repeat

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unit as well as ManNAcA which can be used to introduce a sulfhydryl group. The structures are:

Type 5

 \rightarrow 4)- β -D-ManNAcA(3OAc)-(1 \rightarrow 4)- α -L-FucNAc (1 \rightarrow 3)- β -D-FucNAc-(1 \rightarrow

Type 8

 \rightarrow 3)- β -D-ManNAcA(4OAc)-(1 \rightarrow 3)- α -L-FucNAc

 $(1 \rightarrow 3)$ - β -D-FucNAc- $(1 \rightarrow 2)$

Recently (Jones, 2005) NMR spectroscopy revised the structures to:

Type 5

 \rightarrow 4)- β -D-ManNAcA-(1 \rightarrow 4)- α -L-FucNAc(3OAc)-

 $(1\rightarrow 3)$ - β -D-FucNAc- $(1\rightarrow$

Type 8

 \rightarrow 3)- β -D-ManNAcA(4OAc)-(1 \rightarrow 3)- α -L-FucNAc (1 \rightarrow 3)- α -D-FucNAc(1 \rightarrow

Polysaccharides may be extracted from the appropriate strain of *S. aureus* using method well known to of skill in the art, See U.S. Pat. No. 6,294,177. For example, ATCC 12902 is a Type 5 *S. aureus* strain and ATCC 12605 is a Type 8 *S.* 20 *aureus* strain.

Polysaccharides are of native size or alternatively may be sized, for instance by microfluidisation, ultrasonic irradiation, or by chemical treatment. The invention also covers oligosaccharides derived from the type 5 and 8 polysaccha-25 rides from *S. aureus*. The type 5 and 8 polysaccharides included in the immunogenic composition of the invention are preferably conjugated to a carrier protein as described below or are alternatively unconjugated. The immunogenic compositions of the invention alternatively contains either 30 type 5 or type 8 polysaccharide.

C. S. aureus 336 Antigen

In an embodiment, the immunogenic composition of the invention comprises the *S. aureus* 336 antigen described in U.S. Pat. No. 6,294,177. The 336 antigen comprises β -linked 35 hexosamine, contains no O-acetyl groups, and specifically binds to antibodies to *S. aureus* Type 336 deposited under ATCC 55804. In an embodiment, the 336 antigen is a polysaccharide which is of native size or alternatively may be sized, for instance by microfluidisation, ultrasonic irradiation, or by 40 chemical treatment. The invention also covers oligosaccharides derived from the 336 antigen. The 336 antigen can be unconjugated or conjugated to a carrier protein.

D. Type I, II and III Polysaccharides from S. epidermidis

Amongst the problems associated with the use of polysac- 45 charides in vaccination, is the fact that polysaccharides per se are poor immunogens. It is preferred that the polysaccharides utilized in the invention are linked to a protein carrier which provide bystander T-cell help to improve immunogenicity. Examples of such carriers which may be conjugated to 50 polysaccharide immunogens include the Diphtheria and Tetanus toxoids (DT, DT CRM197 and TT respectively), Keyhole Limpet Haemocyanin (KLH), and the purified protein derivative of Tuberculin (PPD), Pseudomonas aeruginosa exoprotein A (rEPA), protein D from Haemophilus influenzae, pneu- 55 molysin or fragments of any of the above. Fragments suitable for use include fragments encompassing T-helper epitopes. In particular the protein D fragment from H. influenza will preferably contain the N-terminal 1/3 of the protein. Protein D is an IgD-binding protein from Haemophilus influenzae (EP 0 594 60 610 B1) and is a potential immunogen. In addition, staphylococcal proteins may be used as a carrier protein in the polysaccharide conjugates of the invention.

A carrier protein that would be particularly advantageous to use in the context of a staphylococcal vaccine is staphylococcal alpha toxoid. The native form may be conjugated to a polysaccharide since the process of conjugation reduces tox-

icity. Preferably genetically detoxified alpha toxins such as the His35Leu or His35Arg variants are used as carriers since residual toxicity is lower. Alternatively the alpha toxin is chemically detoxified by treatment with a cross-linking reagent, formaldehyde or glutaraldehyde. A genetically detoxified alpha toxin is optionally chemically detoxified, preferably by treatment with a cross-linking reagent, formaldehyde or glutaraldehyde to further reduce toxicity.

The polysaccharides may be linked to the carrier protein(s) by any known method (for example those methods described in U.S. Pat. Nos. 4,372,945, 4,474,757, and 4,356,170). Preferably, CDAP conjugation chemistry is carried out (see WO95/08348). In CDAP, the cyanylating reagent 1-cyano-dimethylaminopyridinium tetrafluoroborate (CDAP) is preferably used for the synthesis of polysaccharide-protein conjugates. The cyanilation reaction can be performed under relatively mild conditions, which avoids hydrolysis of the alkaline sensitive polysaccharides. This synthesis allows direct coupling to a carrier protein.

Conjugation preferably involves producing a direct linkage between the carrier protein and polysaccharide. Optionally a spacer (such as adipic dihydride (ADH)) may be introduced between the carrier protein and the polysaccharide.

V. IMMUNE RESPONSE AND ASSAYS

As discussed above, the invention concerns evoking or inducing an immune response in a subject against a variant SpA or coagulase peptide. In one embodiment, the immune response can protect against or treat a subject having, suspected of having, or at risk of developing an infection or related disease, particularly those related to staphylococci. One use of the immunogenic compositions of the invention is to prevent nosocomial infections by inoculating a subject prior to undergoing procedures in a hospital or other environment having an increased risk of infection.

A. Immunoassays

The present invention includes the implementation of serological assays to evaluate whether and to what extent an immune response is induced or evoked by compositions of the invention. There are many types of immunoassays that can be implemented. Immunoassays encompassed by the present invention include, but are not limited to, those described in U.S. Pat. No. 4,367,110 (double monoclonal antibody sandwich assay) and U.S. Pat. No. 4,452,901 (western blot). Other assays include immunoprecipitation of labeled ligands and immunocytochemistry, both in vitro and in vivo.

Immunoassays generally are binding assays. Certain preferred immunoassays are the various types of enzyme linked immunosorbent assays (ELISAs) and radioimmunoassays (RIA) known in the art. Immunohistochemical detection using tissue sections is also particularly useful. In one example, antibodies or antigens are immobilized on a selected surface, such as a well in a polystyrene microtiter plate, dipstick, or column support. Then, a test composition suspected of containing the desired antigen or antibody, such as a clinical sample, is added to the wells. After binding and washing to remove non specifically bound immune complexes, the bound antigen or antibody may be detected. Detection is generally achieved by the addition of another antibody, specific for the desired antigen or antibody, that is linked to a detectable label. This type of ELISA is known as a "sandwich ELISA." Detection also may be achieved by the addition of a second antibody specific for the desired antigen, followed by the addition of a third antibody that has binding affinity for the second antibody, with the third antibody being linked to a detectable label.

Competition ELISAs are also possible implementations in which test samples compete for binding with known amounts of labeled antigens or antibodies. The amount of reactive species in the unknown sample is determined by mixing the sample with the known labeled species before or during incubation with coated wells. The presence of reactive species in the sample acts to reduce the amount of labeled species available for binding to the well and thus reduces the ultimate signal. Irrespective of the format employed, ELISAs have certain features in common, such as coating, incubating or binding, washing to remove non specifically bound species, and detecting the bound immune complexes.

Antigen or antibodies may also be linked to a solid support, such as in the form of plate, beads, dipstick, membrane, or column matrix, and the sample to be analyzed is applied to the immobilized antigen or antibody. In coating a plate with either antigen or antibody, one will generally incubate the 20 wells of the plate with a solution of the antigen or antibody, either overnight or for a specified period. The wells of the plate will then be washed to remove incompletely-adsorbed material. Any remaining available surfaces of the wells are then "coated" with a nonspecific protein that is antigenically 25 neutral with regard to the test antisera. These include bovine serum albumin (BSA), casein, and solutions of milk powder. The coating allows for blocking of nonspecific adsorption sites on the immobilizing surface and thus reduces the background caused by nonspecific binding of antisera onto the 30 surface.

B. Diagnosis of Bacterial Infection

In addition to the use of proteins, polypeptides, and/or peptides, as well as antibodies binding these polypeptides, proteins, and/or peptides, to treat or prevent infection as 35 described above, the present invention contemplates the use of these polypeptides, proteins, peptides, and/or antibodies in a variety of ways, including the detection of the presence of Staphylococci to diagnose an infection, whether in a patient or on medical equipment which may also become infected. In 40 accordance with the invention, a preferred method of detecting the presence of infections involves the steps of obtaining a sample suspected of being infected by one or more staphylococcal bacteria species or strains, such as a sample taken from an individual, for example, from one's blood, saliva, 45 tissues, bone, muscle, cartilage, or skin. Following isolation of the sample, diagnostic assays utilizing the polypeptides, proteins, peptides, and/or antibodies of the present invention may be carried out to detect the presence of staphylococci, and such assay techniques for determining such presence in a 50 sample are well known to those skilled in the art and include methods such as radioimmunoassay, western blot analysis and ELISA assays. In general, in accordance with the invention, a method of diagnosing an infection is contemplated wherein a sample suspected of being infected with staphylo-55 cocci has added to it the polypeptide, protein, peptide, antibody, or monoclonal antibody in accordance with the present invention, and staphylococci are indicated by antibody binding to the polypeptides, proteins, and/or peptides, or polypeptides, proteins, and/or peptides binding to the antibodies in 60 the sample.

Accordingly, antibodies in accordance with the invention may be used for the prevention of infection from staphylococcal bacteria (i.e., passive immunization), for the treatment of an ongoing infection, or for use as research tools. The term 65 "antibodies" as used herein includes monoclonal, polyclonal, chimeric, single chain, bispecific, simianized, and humanized

or primatized antibodies as well as Fab fragments, such as those fragments which maintain the binding specificity of the antibodies, including the products of an Fab immunoglobulin expression library. Accordingly, the invention contemplates the use of single chains such as the variable heavy and light chains of the antibodies. Generation of any of these types of antibodies or antibody fragments is well known to those skilled in the art. Specific examples of the generation of an antibody to a bacterial protein can be found in U.S. Patent Application Pub. No. 20030153022, which is incorporated herein by reference in its entirety.

Any of the above described polypeptides, proteins, peptides, and/or antibodies may be labeled directly with a detectable label for identification and quantification of staphylococcal bacteria. Labels for use in immunoassays are generally known to those skilled in the art and include enzymes, radioisotopes, and fluorescent, luminescent and chromogenic substances, including colored particles such as colloidal gold or latex beads. Suitable immunoassays include enzyme-linked immunosorbent assays (ELISA).

C. Protective Immunity

In some embodiments of the invention, proteinaceous compositions confer protective immunity to a subject. Protective immunity refers to a body's ability to mount a specific immune response that protects the subject from developing a particular disease or condition that involves the agent against which there is an immune response. An immunogenically effective amount is capable of conferring protective immunity to the subject.

As used herein in the specification and in the claims section that follows, the term polypeptide or peptide refer to a stretch of amino acids covalently linked there amongst via peptide bonds. Different polypeptides have different functionalities according to the present invention. While according to one aspect, a polypeptide is derived from an immunogen designed to induce an active immune response in a recipient, according to another aspect of the invention, a polypeptide is derived from an antibody which results following the elicitation of an active immune response in, for example, an animal, and which can serve to induce a passive immune response in the recipient. In both cases, however, the polypeptide is encoded by a polynucleotide according to any possible codon usage.

As used herein the phrase "immune response" or its equivalent "immunological response" refers to the development of a humoral (antibody mediated), cellular (mediated by antigen-specific T cells or their secretion products) or both humoral and cellular response directed against a protein, peptide, carbohydrate, or polypeptide of the invention in a recipient patient. Such a response can be an active response induced by administration of immunogen or a passive response induced by administration of antibody, antibody containing material, or primed T-cells. A cellular immune response is elicited by the presentation of polypeptide epitopes in association with Class I or Class II MHC molecules, to activate antigen-specific CD4 (+) T helper cells and/or CD8 (+) cytotoxic T cells. The response may also involve activation of monocytes, macrophages, NK cells, basophils, dendritic cells, astrocytes, microglia cells, eosinophils or other components of innate immunity. As used herein "active immunity" refers to any immunity conferred upon a subject by administration of an antigen.

As used herein "passive immunity" refers to any immunity conferred upon a subject without administration of an antigen to the subject. "Passive immunity" therefore includes, but is not limited to, administration of activated immune effectors including cellular mediators or protein mediators (e.g., monoclonal and/or polyclonal antibodies) of an immune response. A monoclonal or polyclonal antibody composition may be used in passive immunization for the prevention or treatment of infection by organisms that carry the antigen recognized by the antibody. An antibody composition may include antibodies that bind to a variety of antigens that may 5 in turn be associated with various organisms. The antibody component can be a polyclonal antiserum. In certain aspects the antibody or antibodies are affinity purified from an animal or second subject that has been challenged with an antigen(s). Alternatively, an antibody mixture may be used, which is a 10 mixture of monoclonal and/or polyclonal antibodies to antigens present in the same, related, or different microbes or organisms, such as gram-positive bacteria, gram-negative bacteria, including but not limited to *staphylococcus* bacteria.

Passive immunity may be imparted to a patient or subject 15 by administering to the patient immunoglobulins (Ig) and/or other immune factors obtained from a donor or other nonpatient source having a known immunoreactivity. In other aspects, an antigenic composition of the present invention can be administered to a subject who then acts as a source or 20 donor for globulin, produced in response to challenge with the antigenic composition ("hyperimmune globulin"), that contains antibodies directed against Staphylococcus or other organism. A subject thus treated would donate plasma from which hyperimmune globulin would then be obtained, via 25 conventional plasma-fractionation methodology, and administered to another subject in order to impart resistance against or to treat staphylococcus infection. Hyperimmune globulins according to the invention are particularly useful for immunecompromised individuals, for individuals undergoing inva- 30 sive procedures or where time does not permit the individual to produce their own antibodies in response to vaccination. See U.S. Pat. Nos. 6,936,258, 6,770,278, 6,756,361, 5,548, 066, 5,512,282, 4,338,298, and 4,748,018, each of which is incorporated herein by reference in its entirety, for exemplary 35 methods and compositions related to passive immunity.

For purposes of this specification and the accompanying claims the terms "epitope" and "antigenic determinant" are used interchangeably to refer to a site on an antigen to which B and/or T cells respond or recognize. B-cell epitopes can be 40 formed both from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents whereas epitopes formed by tertiary folding are typically lost on treatment with 45 denaturing solvents. An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation. Methods of determining spatial conformation of epitopes include, for example, x-ray crystallography and 2-dimensional nuclear magnetic resonance. See, e.g., 50 Epitope Mapping Protocols (1996). Antibodies that recognize the same epitope can be identified in a simple immunoassay showing the ability of one antibody to block the binding of another antibody to a target antigen. T-cells recognize continuous epitopes of about nine amino acids for CD8 cells 55 or about 13-15 amino acids for CD4 cells. T cells that recognize the epitope can be identified by in vitro assays that measure antigen-dependent proliferation, as determined by 3H-thymidine incorporation by primed T cells in response to an epitope (Burke et al., 1994), by antigen-dependent killing 60 (cytotoxic T lymphocyte assay, Tigges et al., 1996) or by cytokine secretion.

The presence of a cell-mediated immunological response can be determined by proliferation assays (CD4 (+) T cells) or CTL (cytotoxic T lymphocyte) assays. The relative contributions of humoral and cellular responses to the protective or therapeutic effect of an immunogen can be distinguished by

separately isolating IgG and T-cells from an immunized syngeneic animal and measuring protective or therapeutic effect in a second subject.

As used herein and in the claims, the terms "antibody" or "immunoglobulin" are used interchangeably and refer to any of several classes of structurally related proteins that function as part of the immune response of an animal or recipient, which proteins include IgG, IgD, IgE, IgA, IgM and related proteins.

Under normal physiological conditions antibodies are found in plasma and other body fluids and in the membrane of certain cells and are produced by lymphocytes of the type denoted B cells or their functional equivalent. Antibodies of the IgG class are made up of four polypeptide chains linked together by disulfide bonds. The four chains of intact IgG molecules are two identical heavy chains referred to as H-chains and two identical light chains referred to as L-chains.

In order to produce polyclonal antibodies, a host, such as a rabbit or goat, is immunized with the antigen or antigen fragment, generally with an adjuvant and, if necessary, coupled to a carrier. Antibodies to the antigen are subsequently collected from the sera of the host. The polyclonal antibody can be affinity purified against the antigen rendering it monospecific.

Monoclonal antibodies can be produced by hyperimmunization of an appropriate donor with the antigen or ex-vivo by use of primary cultures of splenic cells or cell lines derived from spleen (Anavi, 1998; Huston et al., 1991; Johnson et al., 1991; Mernaugh et al., 1995).

As used herein and in the claims, the phrase "an immunological portion of an antibody" includes a Fab fragment of an antibody, a Fv fragment of an antibody, a heavy chain of an antibody, a light chain of an antibody, a heterodimer consisting of a heavy chain and a light chain of an antibody, a variable fragment of a light chain of an antibody, a variable fragment of a heavy chain of an antibody, and a single chain variant of an antibody, which is also known as scFv. In addition, the term includes chimeric immunoglobulins which are the expression products of fused genes derived from different species, one of the species can be a human, in which case a chimeric immunoglobulin is said to be humanized. Typically, an immunological portion of an antibody competes with the intact antibody from which it was derived for specific binding to an antigen.

Optionally, an antibody or preferably an immunological portion of an antibody, can be chemically conjugated to, or expressed as, a fusion protein with other proteins. For purposes of this specification and the accompanying claims, all such fused proteins are included in the definition of antibodies or an immunological portion of an antibody.

As used herein the terms "immunogenic agent" or "immunogen" or "antigen" are used interchangeably to describe a molecule capable of inducing an immunological response against itself on administration to a recipient, either alone, in conjunction with an adjuvant, or presented on a display vehicle.

VI. TREATMENT METHODS

A method of the present invention includes treatment for a disease or condition caused by a *staphylococcus* pathogen. An immunogenic polypeptide of the invention can be given to induce an immune response in a person infected with *staphylococcus* or suspected of having been exposed to *staphylococcus*. Methods may be employed with respect to individu-

als who have tested positive for exposure to *staphylococcus* or who are deemed to be at risk for infection based on possible exposure.

In particular, the invention encompasses a method of treatment for staphylococcal infection, particularly hospital 5 acquired nosocomial infections. The immunogenic compositions and vaccines of the invention are particularly advantageous to use in cases of elective surgery. Such patients will know the date of surgery in advance and could be inoculated in advance. The immunogenic compositions and vaccines of ¹⁰ the invention are also advantageous to use to inoculate health care workers.

In some embodiments, the treatment is administered in the presence of adjuvants or carriers or other staphylococcal antigens. Furthermore, in some examples, treatment comprises ¹⁵ administration of other agents commonly used against bacterial infection, such as one or more antibiotics.

The use of peptides for vaccination can require, but not necessarily, conjugation of the peptide to an immunogenic carrier protein, such as hepatitis B surface antigen, keyhole ²⁰ limpet hemocyanin, or bovine serum albumin. Methods for performing this conjugation are well known in the art.

VII. VACCINE AND OTHER PHARMACEUTICAL COMPOSITIONS AND ADMINISTRATION

The present invention includes methods for preventing or ameliorating staphylococcal infections, particularly hospital acquired nosocomial infections. As such, the invention con-30 templates vaccines for use in both active and passive immunization embodiments. Immunogenic compositions, proposed to be suitable for use as a vaccine, may be prepared from immunogenic SpA polypeptide(s), such as a SpA domain D variant, or immunogenic coagulases. In other 35 embodiments SpA or coagulases can be used in combination with other secreted virulence proteins, surface proteins or immunogenic fragments thereof. In certain aspects, antigenic material is extensively dialyzed to remove undesired small molecular weight molecules and/or lyophilized for more 40 ready formulation into a desired vehicle.

Other options for a protein/peptide-based vaccine involve introducing nucleic acids encoding the antigen(s) as DNA vaccines. In this regard, recent reports described construction of recombinant vaccinia viruses expressing either 10 contigu-45 ous minimal CTL epitopes (Thomson, 1996) or a combination of B cell, cytotoxic T-lymphocyte (CTL), and T-helper (Th) epitopes from several microbes (An, 1997), and successful use of such constructs to immunize mice for priming protective immune responses. Thus, there is ample evidence 50 in the literature for successful utilization of peptides, peptidepulsed antigen presenting cells (APCs), and peptide-encoding constructs for efficient in vivo priming of protective immune responses. The use of nucleic acid sequences as vaccines is exemplified in U.S. Pat. Nos. 5,958,895 and 5,620, 55 896.

The preparation of vaccines that contain polypeptide or peptide sequence(s) as active ingredients is generally well understood in the art, as exemplified by U.S. Pat. Nos. 4,608, 251; 4,601,903; 4,599,231; 4,599,230; 4,596,792; and 4,578, 60 770, all of which are incorporated herein by reference. Typically, such vaccines are prepared as injectables either as liquid solutions or suspensions: solid forms suitable for solution in or suspension in liquid prior to injection may also be prepared. The preparation may also be emulsified. The active 65 immunogenic ingredient is often mixed with excipients that are pharmaceutically acceptable and compatible with the

active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, or adjuvants that enhance the effectiveness of the vaccines. In specific embodiments, vaccines are formulated with a combination of substances, as described in U.S. Pat. Nos. 6,793,923 and 6,733,754, which are incorporated herein by reference.

Vaccines may be conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers may include, for example, polyalkalene glycols or triglycerides: such suppositories may be formed from mixtures containing the active ingredient in the range of about 0.5% to about 10%, preferably about 1% to about 2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain about 10% to about 95% of active ingredient, preferably about 25% to about 70%.

The polypeptides and polypeptide-encoding DNA constructs may be formulated into a vaccine as neutral or salt forms. Pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the peptide) and those that are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like.

Typically, vaccines are administered in a manner compatible with the dosage formulation, and in such amount as will be therapeutically effective and immunogenic. The quantity to be administered depends on the subject to be treated, including the capacity of the individual's immune system to synthesize antibodies and the degree of protection desired. Precise amounts of active ingredient required to be administered depend on the judgment of the practitioner. However, suitable dosage ranges are of the order of several hundred micrograms of active ingredient per vaccination. Suitable regimes for initial administration and booster shots are also variable, but are typified by an initial administration followed by subsequent inoculations or other administrations.

The manner of application may be varied widely. Any of the conventional methods for administration of a vaccine are applicable. These are believed to include oral application within a solid physiologically acceptable base or in a physiologically acceptable dispersion, parenterally, by injection and the like. The dosage of the vaccine will depend on the route of administration and will vary according to the size and health of the subject.

In certain instances, it will be desirable to have multiple administrations of the vaccine, e.g., 2, 3, 4, 5, 6 or more administrations. The vaccinations can be at 1, 2, 3, 4, 5, 6, 7, 8, to 5, 6, 7, 8, 9, 10, 11, 12 twelve week intervals, including all ranges there between. Periodic boosters at intervals of 1-5 years will be desirable to maintain protective levels of the antibodies. The course of the immunization may be followed by assays for antibodies against the antigens, as described in U.S. Pat. Nos. 3,791,932; 4,174,384 and 3,949,064.

A given composition may vary in its immunogenicity. It is often necessary therefore to boost the host immune system, as may be achieved by coupling a peptide or polypeptide to a carrier. Exemplary and preferred carriers are keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA). Other albumins such as ovalbumin, mouse serum albumin, or rabbit serum albumin can also be used as carriers. Means for conjugating a polypeptide to a carrier protein are well known in the art and include glutaraldehyde, m-maleimidobencoyl-Nhydroxysuccinimide ester, carbodiimyde, and bis-biazotized benzidine.

The immunogenicity of polypeptide or peptide compositions can be enhanced by the use of non-specific stimulators of the immune response, known as adjuvants. Suitable adju-10 vants include all acceptable immunostimulatory compounds, such as cytokines, toxins, or synthetic compositions. A number of adjuvants can be used to enhance an antibody response against a Ebh, variant SpA polypeptide or coagulase, or any other bacterial protein or combination contemplated herein. 15 Adjuvants can (1) trap the antigen in the body to cause a slow release; (2) attract cells involved in the immune response to the site of administration; (3) induce proliferation or activation of immune system cells; or (4) improve the spread of the antigen throughout the subject's body. 20

Adjuvants include, but are not limited to, oil-in-water emulsions, water-in-oil emulsions, mineral salts, polynucleotides, and natural substances. Specific adjuvants that may be used include IL-1, IL-2, IL-4, IL-7, IL-12, γ -interferon, GMCSP, BCG, aluminum salts, such as aluminum hydroxide 25 or other aluminum compound, MDP compounds, such as thur-MDP and nor-MDP, CGP (MTP-PE), lipid A, and monophosphoryl lipid A (MPL). RIBI, which contains three components extracted from bacteria, MPL, trehalose dimycolate (TDM), and cell wall skeleton (CWS) in a 2% squalene/ 30 Tween 80 emulsion. MHC antigens may even be used. Others adjuvants or methods are exemplified in U.S. Pat. Nos. 6,814, 971, 5,084,269, 6,656,462, each of which is incorporated herein by reference).

Various methods of achieving adjuvant affect for the vac- 35 cine includes use of agents such as aluminum hydroxide or phosphate (alum), commonly used as about 0.05 to about 0.1% solution in phosphate buffered saline, admixture with synthetic polymers of sugars (Carbopol®) used as an about 0.25% solution, aggregation of the protein in the vaccine by 40 heat treatment with temperatures ranging between about 70° to about 101° C. for a 30-second to 2-minute period, respectively. Aggregation by reactivating with pepsin-treated (Fab) antibodies to albumin; mixture with bacterial cells (e.g., C. parvum), endotoxins or lipopolysaccharide components of 45 Gram-negative bacteria; emulsion in physiologically acceptable oil vehicles (e.g., mannide mono-oleate (Aracel A)); or emulsion with a 20% solution of a perfluorocarbon (Fluosol-DA®) used as a block substitute may also be employed to produce an adjuvant effect.

Examples of and often preferred adjuvants include complete Freund's adjuvant (a non-specific stimulator of the immune response containing killed *Mycobacterium tuberculosis*), incomplete Freund's adjuvants, and aluminum hydroxide.

In some aspects, it is preferred that the adjuvant be selected to be a preferential inducer of either a Th1 or a Th2 type of response. High levels of Th1-type cytokines tend to favor the induction of cell mediated immune responses to a given antigen, while high levels of Th2-type cytokines tend to favor the 60 induction of humoral immune responses to the antigen.

The distinction of Th1 and Th2-type immune response is not absolute. In reality an individual will support an immune response which is described as being predominantly Th1 or predominantly Th2. However, it is often convenient to consider the families of cytokines in terms of that described in murine CD4+ T cell clones by Mosmann and Coffman (Mos-

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mann, and Coffman, 1989). Traditionally, Th1-type responses are associated with the production of the INF- γ and IL-2 cytokines by T-lymphocytes. Other cytokines often directly associated with the induction of Th1-type immune responses are not produced by T-cells, such as IL-12. In contrast, Th2-type responses are associated with the secretion of IL-4, IL-5, IL-6, IL-10.

In addition to adjuvants, it may be desirable to co-administer biologic response modifiers (BRM) to enhance immune responses. BRMs have been shown to upregulate T cell immunity or downregulate suppresser cell activity. Such BRMs include, but are not limited to, Cimetidine (CIM; 1200 mg/d) (Smith/Kline, PA); or low-dose Cyclophosphamide (CYP; 300 mg/m2) (Johnson/Mead, NJ) and cytokines such as γ -interferon, IL-2, or IL-12 or genes encoding proteins involved in immune helper functions, such as B-7.

In certain embodiments, the present invention concerns compositions comprising one or more lipids associated with a nucleic acid or a polypeptide/peptide. A lipid is a substance that is insoluble in water and extractable with an organic solvent. Compounds other than those specifically described herein are understood by one of skill in the art as lipids, and are encompassed by the compositions and methods of the present invention. A lipid component and a non-lipid may be attached to one another, either covalently or non-covalently.

A lipid may be a naturally occurring lipid or a synthetic lipid. However, a lipid is usually a biological substance. Biological lipids are well known in the art, and include for example, neutral fats, phospholipids, phosphoglycerides, steroids, terpenes, lysolipids, glycosphingolipids, glucolipids, sulphatides, lipids with ether and ester-linked fatty acids and polymerizable lipids, and combinations thereof.

A nucleic acid molecule or a polypeptide/peptide, associated with a lipid may be dispersed in a solution containing a lipid, dissolved with a lipid, emulsified with a lipid, mixed with a lipid, combined with a lipid, covalently bonded to a lipid, contained as a suspension in a lipid or otherwise associated with a lipid. A lipid or lipid-poxvirus-associated composition of the present invention is not limited to any particular structure. For example, they may also simply be interspersed in a solution, possibly forming aggregates which are not uniform in either size or shape. In another example, they may be present in a bilayer structure, as micelles, or with a "collapsed" structure. In another non-limiting example, a lipofectamine(Gibco BRL)-poxvirus or Superfect (Qiagen)poxvirus complex is also contemplated.

In certain embodiments, a composition may comprise about 1%, about 2%, about 3%, about 4% about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 11%, about 12%, about 13%, about 14%, about 15%, about 16%, about 17%, about 18%, about 19%, about 20%, about 21%, about 22%, about 23%, about 24%, about 25%, about 26%, about 27%, about 28%, about 29%, about 30%, about 31%, about 32%, about 33%, about 34%, about 35%, about 36%, about 37%, about 38%, about 39%, about 40%, about 41%, about 42%, about 43%, about 44%, about 45%, about 46%, about 47%, about 48%, about 49%, about 50%, about 51%, about 52%, about 53%, about 54%, about 55%, about 56%, about 57%, about 58%, about 59%, about 60%, about 61%, about 62%, about 63%, about 64%, about 65%, about 66%, about 67%, about 68%, about 69%, about 70%, about 71%, about 72%, about 73%, about 74%, about 75%, about 76%, about 77%, about 78%, about 79%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or any range therebetween, of a particular lipid, lipid type, or non-lipid component such as an adjuvant, antigen, peptide, polypeptide, sugar, nucleic acid or other material disclosed herein or as would be known to one of skill in the art. In a non-limiting example, a composition may comprise about 10% to about 20% neutral 5 lipids, and about 33% to about 34% of a cerebroside, and about 1% cholesterol. In another non-limiting example, a liposome may comprise about 4% to about 12% terpenes, wherein about 1% of the micelle is specifically lycopene, leaving about 3% to about 11% of the liposome as comprising 10 other terpenes; and about 10% to about 35% phosphatidyl choline, and about 1% of a non-lipid component. Thus, it is contemplated that compositions of the present invention may comprise any of the lipids, lipid types or other components in any combination or percentage range. 15

The compositions and related methods of the present invention, particularly administration of a secreted virulence factor or surface protein, including a variant SpA polypeptide or peptide, and/or other bacterial peptides or proteins to a patient/subject, may also be used in combination with the 20 administration of traditional therapies. These include, but are not limited to, the administration of antibiotics such as streptomycin, ciprofloxacin, doxycycline, gentamycin, chloramphenicol, trimethoprim, sulfamethoxazole, ampicillin, tetracycline or various combinations of antibiotics. 25

In one aspect, it is contemplated that a polypeptide vaccine and/or therapy is used in conjunction with antibacterial treatment. Alternatively, the therapy may precede or follow the other agent treatment by intervals ranging from minutes to weeks. In embodiments where the other agents and/or a pro- 30 teins or polynucleotides are administered separately, one would generally ensure that a significant period of time did not expire between the time of each delivery, such that the agent and antigenic composition would still be able to exert an advantageously combined effect on the subject. In such 35 instances, it is contemplated that one may administer both modalities within about 12-24 h of each other or within about 6-12 h of each other. In some situations, it may be desirable to extend the time period for administration significantly, where several days (2, 3, 4, 5, 6 or 7) to several weeks (1, 2, 3, 4, 5, 40 6, 7 or 8) lapse between the respective administrations.

Various combinations may be employed, for example antibiotic therapy is "A" and the immunogenic molecule given as part of an immune therapy regime, such as an antigen, is "B":

A/B/A B/A/B B/B/A A/A/B A/B/B B/A/A A/B/B/B B/A/ 45 B/B

B/B/B/A B/B/A/B A/A/B/B A/B/A/B A/B/B/A B/B/A/A B/A/B/A B/A/A/B A/A/A/B B/A/A/A A/B/A/A A/A/B/A

Administration of the immunogenic compositions of the present invention to a patient/subject will follow general pro- 50 tocols for the administration of such compounds, taking into account the toxicity, if any, of the SpA composition, or other compositions described herein. It is expected that the treatment cycles would be repeated as necessary. It also is contemplated that various standard therapies, such as hydration, 55 may be applied in combination with the described therapy.

In some embodiments, pharmaceutical compositions are administered to a subject. Different aspects of the present invention involve administering an effective amount of a composition to a subject. In some embodiments of the present ⁶⁰ invention, staphylococcal antigens, members of the Ess pathway, including polypeptides or peptides of the Esa or Esx class, and/or members of sortase substrates may be administered to the patient to protect against infection by one or more *staphylococcus* pathogens. Alternatively, an expression vector encoding one or more such polypeptides or peptides may be given to a patient as a preventative treatment. Additionally,

such compounds can be administered in combination with an antibiotic or an antibacterial. Such compositions will generally be dissolved or dispersed in a pharmaceutically acceptable carrier or aqueous medium.

In addition to the compounds formulated for parenteral administration, such as those for intravenous or intramuscular injection, other pharmaceutically acceptable forms include, e.g., tablets or other solids for oral administration; time release capsules; and any other form currently used, including creams, lotions, mouthwashes, inhalants and the like.

The active compounds of the present invention can be formulated for parenteral administration, e.g., formulated for injection via the intravenous, intramuscular, subcutaneous, or even intraperitoneal routes. The preparation of an aqueous composition that contains a compound or compounds that increase the expression of an MHC class I molecule will be known to those of skill in the art in light of the present disclosure. Typically, such compositions can be prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for use to prepare solutions or suspensions upon the addition of a liquid prior to injection can also be prepared; and, the preparations can also be emulsified.

Solutions of the active compounds as free base or pharmacologically acceptable salts can be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions; formulations including sesame oil, peanut oil, or aqueous propylene glycol; and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In all cases the form must be sterile and must be fluid to the extent that it may be easily injected. It also should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi.

The proteinaceous compositions may be formulated into a neutral or salt form. Pharmaceutically acceptable salts, include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like.

The carrier also can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and vegetable oils. The proper fluidity can be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion, and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions are prepared by incorporating the active compounds in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the various 5 sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum-drying and 10 freeze-drying techniques, which yield a powder of the active ingredient, plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Administration of the compositions according to the present invention will typically be via any common route. 15 This includes, but is not limited to oral, nasal, or buccal administration. Alternatively, administration may be by orthotopic, intradermal, subcutaneous, intramuscular, intraperitoneal, intranasal, or intravenous injection. In certain embodiments, a vaccine composition may be inhaled (e.g., 20 U.S. Pat. No. 6,651,655, which is specifically incorporated by reference). Such compositions would normally be administered as pharmaceutically acceptable compositions that include physiologically acceptable carriers, buffers or other excipients. As used herein, the term "pharmaceutically 25 tic applications. acceptable" refers to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem complications 30 commensurate with a reasonable benefit/risk ratio. The term "pharmaceutically acceptable carrier," means a pharmaceutically acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting a chemical 35 agent.

For parenteral administration in an aqueous solution, for example, the solution should be suitably buffered, if necessary, and the liquid diluent first rendered isotonic with sufficient saline or glucose. These particular aqueous solutions are 40 especially suitable for intravenous, intramuscular, subcutaneous, and intraperitoneal administration. In this connection, sterile aqueous media which can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage could be dissolved in isotonic NaCl 45 solution and either added to hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, Remington's Pharmaceutical Sciences, 1990). Some variation in dosage will necessarily occur depending on the condition of the subject. The person responsible for administration will, in any 50 event, determine the appropriate dose for the individual subject.

An effective amount of therapeutic or prophylactic composition is determined based on the intended goal. The term "unit dose" or "dosage" refers to physically discrete units 55 suitable for use in a subject, each unit containing a predetermined quantity of the composition calculated to produce the desired responses discussed above in association with its administration, i.e., the appropriate route and regimen. The quantity to be administered, both according to number of 60 treatments and unit dose, depends on the protection desired.

Precise amounts of the composition also depend on the judgment of the practitioner and are peculiar to each individual. Factors affecting dose include physical and clinical state of the subject, route of administration, intended goal of 65 treatment (alleviation of symptoms versus cure), and potency, stability, and toxicity of the particular composition.

Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically or prophylactically effective. The formulations are easily administered in a variety of dosage forms, such as the type of injectable solutions described above.

As used herein, the term in vitro administration refers to manipulations performed on cells removed from or outside of a subject, including, but not limited to cells in culture. The term ex vivo administration refers to cells which have been manipulated in vitro, and are subsequently administered to a subject. The term in vivo administration includes all manipulations performed within a subject.

In certain aspects of the present invention, the compositions may be administered either in vitro, ex vivo, or in vivo. In certain in vitro embodiments, autologous B-lymphocyte cell lines are incubated with a virus vector of the instant invention for 24 to 48 hours or with a variant SpA and/or cogaulase and/or any other composition described herein for two hours. The transduced cells can then be used for in vitro analysis, or alternatively for ex vivo administration. U.S. Pat. Nos. 4,690,915 and 5,199,942, both incorporated herein by reference, disclose methods for ex vivo manipulation of blood mononuclear cells and bone marrow cells for use in therapeutic applications.

VIII. ANTIBODIES AND PASSIVE IMMUNIZATION

Another aspect of the invention is a method of preparing an immunoglobulin for use in prevention or treatment of staphylococcal infection comprising the steps of immunizing a recipient or donor with the vaccine of the invention and isolating immunoglobulin from the recipient or donor. An immunoglobulin prepared by this method is a further aspect of the invention. A pharmaceutical composition comprising the immunoglobulin of the invention and a pharmaceutically acceptable carrier is a further aspect of the invention which could be used in the manufacture of a medicament for the treatment or prevention of staphylococcal disease. A method for treatment or prevention of staphylococcal infection comprising a step of administering to a patient an effective amount of the pharmaceutical preparation of the invention is a further aspect of the invention.

Inocula for polyclonal antibody production are typically prepared by dispersing the antigenic composition in a physiologically tolerable diluent such as saline or other adjuvants suitable for human use to form an aqueous composition. An immunostimulatory amount of inoculum is administered to a mammal and the inoculated mammal is then maintained for a time sufficient for the antigenic composition to induce protective antibodies.

The antibodies can be isolated to the extent desired by well known techniques such as affinity chromatography (Harlow and Lane, 1988). Antibodies can include antiserum preparations from a variety of commonly used animals, e.g. goats, primates, donkeys, swine, horses, guinea pigs, rats or man.

An immunoglobulin produced in accordance with the present invention can include whole antibodies, antibody fragments or subfragments. Antibodies can be whole immunoglobulins of any class (e.g., IgG, IgM, IgA, IgD or IgE), chimeric antibodies or hybrid antibodies with dual specificity to two or more antigens of the invention. They may also be fragments (e.g., F(ab')2, Fab', Fab, Fv and the like) including hybrid fragments. An immunoglobulin also includes natural, synthetic, or genetically engineered proteins that act like an antibody by binding to specific antigens to form a complex.

A vaccine of the present invention can be administered to a recipient who then acts as a source of immunoglobulin, produced in response to challenge from the specific vaccine. A subject thus treated would donate plasma from which hyperimmune globulin would be obtained via conventional plasma 5 fractionation methodology. The hyperimmune globulin would be administered to another subject in order to impart resistance against or treat staphylococcal infection. Hyperimmune globulins of the invention are particularly useful for treatment or prevention of staphylococcal disease in infants, 10 immune compromised individuals, or where treatment is required and there is no time for the individual to produce antibodies in response to vaccination.

An additional aspect of the invention is a pharmaceutical composition comprising two of more monoclonal antibodies 15 (or fragments thereof; preferably human or humanised) reactive against at least two constituents of the immunogenic composition of the invention, which could be used to treat or prevent infection by Gram positive bacteria, preferably staphylococci, more preferably S. aureus or S. epidermidis. Such pharmaceutical compositions comprise monoclonal antibodies that can be whole immunoglobulins of any class, chimeric antibodies, or hybrid antibodies with specificity to two or more antigens of the invention. They may also be fragments 25 (e.g., F(ab')2, Fab', Fab, Fv and the like) including hybrid fragments.

Methods of making monoclonal antibodies are well known in the art and can include the fusion of splenocytes with myeloma cells (Kohler and Milstein, 1975; Harlow and Lane, 1988). Alternatively, monoclonal Fv fragments can be obtained by screening a suitable phage display library (Vaughan et al., 1998). Monoclonal antibodies may be humanized or part humanized by known methods.

IX. EXAMPLES

The following examples are given for the purpose of illustrating various embodiments of the invention and are not 40 meant to limit the present invention in any fashion. One skilled in the art will appreciate readily that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those objects, ends 15 and advantages inherent herein. The present examples, along with the methods described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein and other uses which are encompassed within the 50 spirit of the invention as defined by the scope of the claims will occur to those skilled in the art.

Example 1

Non-Toxigenic Protein A Variants as Subunit Vaccines to Prevent Staphylococcus aureus Infections

Results

An animal model for S. aureus infection BALB/c mice were infected by intravenous injection with 1×10^7 CFU of the human clinical isolate S. aureus Newman (Baba et al., 2007). Within 6 hours following infection, 99.999% of staphylo- 65 cocci disappeared from the blood stream and were distributed via the vasculature. Staphylococcal dissemination to periph106

eral tissues occurred rapidly, as the bacterial load in kidney and other peripheral organ tissues reached 1×10^5 CFU g⁻¹ within the first three hours. The staphylococcal load in kidney tissues increased by 1.5 log CFU within twenty-four hours. Forty-eight hours following infection, mice developed disseminated abscesses in multiple organs, detectable by light microscopy of hematoxylin-eosin stained, thin-sectioned kidney tissue. The initial abscess diameter was 524 μ M (±65 µM); lesions were initially marked by an influx of polymorphonuclear leukocytes (PMNs) and harbored no discernable organization of staphylococci, most of which appeared to reside within PMNs. On day 5 of infection, abscesses increased in size and enclosed a central population of staphylococci, surrounded by a layer of eosinophilic, amorphous material and a large cuff of PMNs. Histopathology revealed massive necrosis of PMNs in proximity to the staphylococcal nidus at the center of abscess lesions as well as a mantle of healthy phagocytes. A rim of necrotic PMNs were observed at the periphery of abscess lesions, bordering eosinophilic, amorphous material that separates healthy renal tissue from lesions. Abscesses eventually reached a diameter of $\geq 1,524$ µM on day 15 or 36. At later time intervals, the staphylococcal load was increased to 10^4 - 10^6 CFU g⁻¹ and growing abscess lesions migrated towards the organ capsule. Peripheral lesions were prone to rupture, thereby releasing necrotic material and staphylococci into the peritoneal cavity or the retroperitoneal space. These events resulted in bacteremia as well as a secondary wave of abscesses, eventually precipitating a lethal outcome.

To enumerate staphylococcal load in renal tissue, animals were killed, their kidneys excised and tissue homogenate spread on agar media for colony formation. On day 5 of 35 infection, a mean of 1×10^6 CFU g⁻¹ renal tissue for S. aureus Newman was observed. To quantify abscess formation, kidneys were visually inspected, and each individual organ was given a score of one or zero. The final sum was divided by the total number of kidneys to calculate percent surface abscesses (Table 4). In addition, randomly chosen kidneys were fixed in formalin, embedded, thin sectioned, and stained with hematoxylin-eosin. For each kidney, four sagittal sections at 200 µM intervals were viewed by microscopy. The numbers of lesions were counted for each section and averaged to quantify the number of abscesses within the kidneys. S. aureus Newman caused 4.364±0.889 abscesses per kidney, and surface abscesses were observed on 14 out of 20 kidneys (70%) (Table 4).

When examined by scanning electron microscopy, S. aureus Newman was located in tightly associated lawns at the center of abscesses. Staphylococci were contained by an amorphous pseudocapsule that separated bacteria from the 55 cuff of abscesses leukocytes. No immune cells were observed in these central nests of staphylococci, however occasional red blood cells were located among the bacteria. Bacterial populations at the abscess center, designated staphylococcal abscess communities (SAC), appeared homogenous and coated by an electron-dense, granular material. The kinetics of the appearance of infectious lesions and the morphological attributes of abscesses formed by S. aureus Newman were similar to those observed following mouse infection with S. aureus USA300 (LAC), the current epidemic communityacquired methicillin-resistant S. aureus (CA-MRSA) clone in the United States (Diep et al., 2006).

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	Geneti	c requirements	for S. aureus Newm	an abscess forma	tion in mice			
Abscess formation in kidney tis						iey tissue		
	Staphylococcal load in kidney tissue				"Number of			
Genotype	^{<i>a</i>} log ₁₀ CFU g ⁻¹ tissue	^b Significance (P-value)	^c Reduction (log ₁₀ CFU g ⁻¹)	^d Surface abscesses (%)	abscesses per kidney	^f Significance (P-value)		
wild-type ∆srtA Spa	6.141 ± 0.192 4.095 ± 0.347 5.137 ± 0.374	 6.7 × 10 ⁻⁶ 0.0144	2.046 1.004	70 0 13	$\begin{array}{c} 4.364 \pm 0.889 \\ 0.000 \pm 0.000 \\ 0.375 \pm 0.374 \end{array}$	0.0216 0.0356		

TABLE 3

^aMeans of staphylococcal load calculated as $\log_{10} \text{CFU g}^{-1}$ in homogenized renal tissues 5 days following infection in cohorts of fifteen BALB/c mice per challenge strain. Standard error of the means (±SEM) is indicated. ^bStatistical significance was calculated with the Students t-test and P-values recorded; P-values < 0.05 were deemed significant.

^cReduction in bacterial load calculated as \log_{10} CFU g⁻¹.

^dAbscess formation in kidney tissues five days following infection was measured by macroscopic inspection (% positive)

"Histopathology of hematoxylin-eosin stained, thin sectioned kidneys from eight to ten animals; the average number of abscesses per kidney

The plant is given in the set of the final mean (\pm SEM). 'Statistical significance was calculated with the Students t-test and P-values recorded; P-values < 0.05 were deemed significant.

S. aureus Protein A (spa) mutants are avirulent and cannot form abscesses Sortase A is a transpeptidase that immobilizes nineteen surface proteins in the envelope of S. aureus strain Newman (Mazmanian et al., 1999; Mazmanian et al., 2000). Earlier work identified sortase A as a virulence factor in 25 multiple animal model systems, however the contributions of this enzyme and its anchored surface proteins to abscess formation or persistence have not yet been revealed (Jonsson et al., 2002; Weiss et al., 2004). Compared to the wild-type parent (Baba et al., 2007), an isogenic srtA variant (Δ srtA) ₃₀ failed to form abscess lesions on either macroscopic or histopathology examination on days 2, 5, or 15. In mice infected with the strA mutant, only 1×10^4 CFU g⁻ was recovered from kidney tissue on day 5 of infection, which is a 2.046 \log_{10} CFU g^{-1} reduction compared to the wild-type parent strain 35 $(P=6.73\times10^{-6})$. A similar defect was observed for the srtA mutant of MRSA strain USA300 (data not shown). Scanning electron microscopy showed that srtA mutants were highly dispersed and often associated with leukocytes in otherwise healthy renal tissue. On day fifteen following infection, srtA 40 mutants were cleared from renal tissues, $a \ge 3.5 \log_{10} CFU g^{-1}$ reduction compared to the wild-type. Thus, sortase A anchored surface proteins enable the formation of abscess lesions and the persistence of bacteria in host tissues, wherein staphylococci replicate as communities embedded in an 45 extracellular matrix and shielded from surrounding leukocytes by an amorphous pseudocapsule.

Sortase A anchors a large spectrum of proteins with LPXTG motif sorting signals to the cell wall envelope, thereby providing for the surface display of many virulence 50 factors (Mazmanian et al., 2002). To identify surface proteins required for staphylococcal abscess formation, bursa aurealis insertions were introduced in 5' coding sequences of genes that encode polypeptides with LPXTG motif proteins (Bae et al., 2004) and these mutations were transduced into S. aureus 55 Newman. Mutations in the structural gene for Protein A (spa) reduced the staphylococcal load in infected mouse kidney tissues by 1.004 log₁₀ (P=0.0144). When analyzed for their ability to form abscesses in kidney tissues by histopathology, the inventors observed that the spa mutants were unable to 60 form abscesses as compared with the wild-type parent strain S. aureus Newman (wild-type S. aureus Newman 4.364±0.889 abscesses per kidney vs. the isogenic spa mutant with 0.375±0.374 lesions; P=0.0356).

Protein A blocks innate and adaptive immune responses. 65 Studies identified Protein A as a critical virulence factor during the pathogenesis of *S. aureus* infections. Earlier work

demonstrated that Protein A impedes phagocytosis of staphylococci by binding the Fc component of immunoglobulin (Jensen 1958; Uhlen et al., 1984), activates platelet aggregation via the von Willebrand factor (Hartleib et al., 2000), functions as a B cell superantigen by capturing the F(ab)2 region of VH3 bearing IgM (Roben et al., 1995), and, through its activation of TNFR1, can initiate staphylococcal pneumonia (Gomez et al., 2004). Due to the fact that Protein A captures immunoglobulin and displays toxic attributes, the possibility that this surface molecule may function as a vaccine in humans has not been rigorously pursued. The inventors demonstrate for the first time that Protein A variants no longer able to bind to immunoglobulins, vWF and TNFR-1 are removed of their toxigenic potential and are able to stimulate humoral immune responses that protect against staphylococcal disease.

Molecular basis of Protein A surface display and function. Protein A is synthesized as a precursor in the bacterial cytoplasm and secreted via its YSIRK signal peptide at the cross wall, i.e., the cell division septum of staphylococci (FIG. 1). (DeDent et al., 2007; DeDent et al, 2008). Following cleavage of the C-terminal LPXTG sorting signal, Protein A is anchored to bacterial peptidoglycan crossbridges by sortase A (Schneewind et al., 1995; Mazmanian et al., 1999; Mazmanian et al., 2000). Protein A is the most abundant surface protein of staphylococci; the molecule is expressed by virtuallv all S. aureus strains (Saïd-Salim et al., 2003; Cespedes et al., 2005; Kennedy et al., 2008). Staphylococci turn over 15-20% of their cell wall per division cycle (Navarre and Schneewind 1999). Murine hydrolases cleave the glycan strands and wall peptides of peptidoglycan, thereby releasing Protein A with its attached C-terminal cell wall disaccharide tetrapeptide into the extracellular medium (Ton-That et al., 1999). Thus, by physiological design, Protein A is both anchored to the cell wall and displayed on the bacterial surface but also released into surrounding tissues during host infection (Marraffini et al., 2006).

Protein A captures immunoglobulins on the bacterial surface and this biochemical activity enables staphylococcal escape from host innate and acquired immune responses (Jensen 1958; Goodyear and Silverman 2004). Interestingly, region X of Protein A (Guss et al, 1984), a repeat domain that tethers the IgG binding domains to the LPXTG sorting signal/ cell wall anchor, is perhaps the most variable portion of the staphylococcal genome (Schneewind et al., 1992; Saïd-Salim et al., 2003). Each of the five immunoglobulin binding domains of Protein A (SpA), formed from three helix bundles and designated E, D, A, B, and C, exerts similar structural and functional properties (Sjödahl 1977; Jansson et al., 1998). The solution and crystal structure of domain D has been solved both with and without the Fc and VH3 (Fab) ligands, which bind Protein A in a non-competitive manner at distinct 5 sites (Graille et al., 2000).

In the crystal structure complex, the Fab interacts with helix II and helix III of domain D via a surface composed of four VH region P-strands (Graille et al., 2000). The major axis of helix II of domain D is approximately 50° to the orientation 10 of the strands, and the interhelical portion of domain D is most proximal to the CO strand. The site of interaction on Fab is remote from the Ig light chain and the heavy chain constant region. The interaction involves the following domain D residues: Asp-36 of helix II as well as Asp-37 and Gln-40 in the 15 loop between helix II and helix III, in addition to several other residues with SpA-D (Graille et al., 2000). Both interacting surfaces are composed predominantly of polar side chains, with three negatively charged residues on domain D and two positively charged residues on the 2A2 Fab buried by the 20 interaction, providing an overall electrostatic attraction between the two molecules. Of the five polar interactions identified between Fab and domain D, three are between side chains. A salt bridge is formed between Arg-H19 and Asp-36 and two hydrogen bonds are made between Tyr-H59 and 25 Asp-37 and between Asn-H82a and Ser-33. Because of the conservation of Asp-36 and Asp-37 in all five IgG binding domains of Protein A, these residues were selected for mutagenesis.

The SpA-D sites responsible for Fab binding are structur- 30 ally separate from the domain surface that mediates Fcy binding. The interaction of Fcy with domain B primarily involves residues in helix I with lesser involvement of helix II (Deisenhofer 1981; Gouda et al, 1992). With the exception of the Gln-32, a minor contact in both complexes, none of the resi- 35 dues that mediate the Fcy interaction are involved in Fab binding. To examine the spatial relationship between these different Ig-binding sites, the SpA domains in these complexes have been superimposed to construct a model of a complex between Fab, the SpA-domain D, and the Fcy mol- 40 ecule. In this ternary model, Fab and Fcy form a sandwich about opposite faces of the helix II without evidence of steric hindrance of either interaction. These findings illustrate how, despite its small size (i.e., 56-61 aa), a SpA domain can simultaneously display both activities, explaining experi- 45 mental evidence that the interactions of Fab with an individual domain are noncompetitive. Residues for the interaction between SpA-D and Fcy are Gln-9 and Gln-10.

In contrast, occupancy of the Fc portion of IgG on the domain D blocks its interaction with vWF A1 and probably 50 also TNFR1 (O'Seaghdha et al., 2006). Mutations in residues essential for IgG Fc binding (F5, Q9, Q10, S11, F13, Y14, L17, N28, I31 and K35) are also required for vWF A1 and TNFR1 binding (Cedergren et al., 1993; Gomez et al., 2006; O'Seaghdha et al 2006), whereas residues critical for the VH3 55 interaction (Q26, G29, F30, S33, D36, D37, Q40, N43, E47) have no impact on the binding activities of IgG Fc, vWFA1 or TNFR1 (Jansson et al., 1998; Graille et al., 2000). The Protein A immunoglobulin Fab binding activity targets a subset of B cells that express VH3 family related IgM on their surface, i.e. 60 these molecules function as VH3 type B cell receptors (Roben et al., 1995). Upon interaction with SpA, these B cells rapidly proliferate and then commit to apoptosis, leading to preferential and prolonged deletion of innate-like B lymphocytes (i.e. marginal zone B cells and follicular B2 cells) (Goodyear 65 and Silverman 2003; Goodyear and Silverman 2004). It is important to note that more than 40% of circulating B cells are

targeted by the Protein A interaction and the VH3 family represents the largest family of human B cell receptors to impart protective humoral responses against pathogens (Goodyear and Silverman 2003; Goodyear and Silverman 2004). Thus, Protein A functions analogously to staphylococcal superantigens (Roben et al, 1995), albeit that the latter class of molecules, for example SEB, TSST-1, TSST-2, form complexes with the T cell receptor to inappropriately stimulate host immune responses and thereby precipitating characteristic disease features of staphylococcal infections (Roben et al., 1995; Tiedemann et al., 1995). Together these findings document the contributions of Protein A in establishing staphylococcal infections and in modulating host immune responses.

Non-toxigenic variant of Protein A. The inventors have developed a non-toxigenic variant of staphylococcal Protein A and, with this reagent in hand, aimed for the first time to measure the immune response of animals to Protein A immunization. Further, the inventors address whether immunization of animals with a non-toxigenic variant of Protein A could generate immune responses that raise protective immunity against staphylococcal infection.

To perturb the IgG Fc, vWF A1 and TNFR1 binding activities of Protein A, glutamine (Q) residues 9 and 10 [the numbering here is derived from that established for the SpA domain D] were modified generating lysine or glycine substitutions for both glutamines with the expectation that these substitutions abolish the ion bonds formed between wild-type Protein A and its ligands. The added effect of the dual lysine substitutions may be that these positively charged residues institute a repellent charge for immunoglobulins. To perturb IgM Fab VH3 binding, the inventors selected the aspartate (D) residues 36 and 37 of SpA-D, each of which is required for the association of Protein A with the B cell receptor. D36 and D37 were both substituted with alanine. The Q9,10K and D36,37A mutations were combined in the recombinant molecule SpA-D $_{Q9,10K;D36,37A}$ and examined for the binding attributes of Protein A.

In brief, the Protein A (spa) genomic sequence of Staphylococcus aureus N315 was PCR amplified with the primers (GCTGCACATATGGCGCAACACGATGAAGCTCAAC [5' primer] (SEQ ED No:156) and AGTGGATCCTTAT-GCTTTGTTAGCATCTGC [3' primer] (SEQ ED No:157)), cloned into the pET15b vector (pYSJ1, codons 48-486) (Stranger-Jones, et al., 2006) and recombinant plasmid transformed into E. coli BL21(DE3) (Studier et al., 1990). The Protein A product derived from pYSJ1 harbors SpA residues 36-265 fused to the N-terminal His tag (MGSSHHHHHH-SSGLVPRGS (SEQ ID No:158)). Following IPTG inducible expression, recombinant N-terminal His6-tagged SpA was purified by affinity chromatography on Ni-NTA resin (Stranger-Jones et al., 2006). The domain D of SpA (SpA-D) was PCR amplified with a pair of specific primers (AA-CATATGTTCAACAAAGATCAACAAAGC [5' primer] (SEQ ID No:159) and AAGGATCCAGATTCGTT-TAATTTTTTAGC [3' primer] (SEQ ID No:160)), sub-cloned into the pET15b vector (pHAN1, spa codons 212-261) and recombinant plasmid transformed into E. coli BL21(DE3) to express and purify recombinant N-terminal His6-tagged protein. To generate mutations in the SpA-D coding sequence, sets of two pairs of primers were synthesized (for D to A substitutions: CTTCATTCAAAGTCTTAAAGCCGC-CCCAAGCCAAAGCACTAAC [5' primer] (SEQ ID No:161) and GTTAGTGCTTTGGCTTGGGGGGGGGCTT-

TAAGACTTTGAATGAAG [3' primer] (SEQ ID No:162); for Q to K substitutions CATATGTTCAACAAA-GATAAAAAAAGCGCCTTCTATGAAATC [5' primer] (SEQ ID No:163) No:164); for Q to G substitutions CATAT-GTTCAACAAAGATGGAGGAAGCGCCTTC-

TATGAAATC [5' primer] (SEQ ED No:165) and GATTTCATAGAAGGCGCTTCCTC-

CATCTTTGTTGAACATATG' [3' primer] (SEQ ID NO: 166). Primers were used for quick-change mutagenesis pro- 10 tocols. Following mutagenesis, DNA sequences were confirmed for each of the recombinant proteins: SpA, SpA-D and SpA-D_{Q9,10G;D36,37A} and SpA-D_{Q9,10K;D36,37A}. All proteins were purified from lysates of recombinant *E. coli* using Ni-NTA chromatography and subsequently dialyzed against ¹⁵ PBS and stored at 4° C.

To measure binding of immunoglobulin to Protein A and its variants, 200 µg of purified protein was diluted into a 1 ml volume using column buffer (50 mM Tris-HCl, 150 mM 20 NaCl, pH7.5) and then loaded onto a pre-equilibrated Ni-NTA column (1 ml bed volume). Columns were washed with 10 ml of column buffer. 200 µg of purified human IgG was diluted in a total volume of 1 ml column buffer and then applied to each of the columns charged with Protein A and its 25 variants. The columns were subsequently washed with 5 ml wash buffer (10 mM imidazole in column buffer) and 5 ml column buffer. Protein samples were eluted with 2 ml elution buffer (500 mM imidazole in column buffer), fractions collected and aliquots subjected to SDS-PAGE gel electrophoresis, followed by Coomassie-Blue staining. As shown in FIG. 3, wild-type Protein A (SpA) and its SpA-domain D both retained immunogobulin during chromatography. In contrast, the SpA-D_{O9,10K;D36,37A} variant did not bind to immunoglo- 35 bulin.

To quantify the binding of Protein A and its variants to the Fc portion of immunoglobulin and the VH3 domain of Fab, HRP conjugated human immunoglobulin G [hIgG], the Fc portion of human IgG [hFc] and the F(ab)2 portion of human IgG [hF(ab)2] as well as ELISA assays were used to quantify the relative amount binding to Protein A and its variants. The data in FIG. 4 demonstrate the binding of SpA and SpA-D to hIgG and hFc, whereas SpA-D_{Q9,10G;D36,37A} and SpA- 45 D_{09,10K;D36,37A} displayed only background binding activities. SpA bound similar amounts of hFc and hF(ab)2, however the binding of SpA-D to hF(ab)2 was reduced compared to full length SpA. This result suggests that the presence of multiple IgG binding domains may cooperatively increase the ability of Protein A to bind to the B cell receptor. When compared with the reduced binding power of SpA-D for hF(ab)2, of the two variants only SpA-D_{Q9,10K;D36,37A} displayed a significant reduction in the ability to bind the VH3 55 domain of immunoglobulin. To examine the toxigenic attributes of SpA-D and its variants, purified proteins were injected into mice, which were sacrificed after 4 hours to remove their spleens. Organ tissue was homogenized, capsular material removed and B cells stained with fluorescent CD19 antibodies. Following FACS analysis to quantify the abundance of B cells in splenic tissues, it was observed that SpA-D caused a 5% drop in the B cell count compared to a mock (PBS) control (FIG. 5). In contrast, SpA- 65 D_{09,10K:D36,37A} did not cause a reduction in B-cell counts, indicating that the mutant molecule had lost its toxigenic

attributes of stimulating B cell proliferation and death (FIG. **5**). In summary, amino acid substitutions in the SpA-D residues Q9, Q10, D36, and D37 abolished the ability of Protein A domains to bind immunoglobulins or exert toxigenic functions in human and animal tissues.

Non-toxigenic Protein A variants elicit vaccine protection. To test whether or not Protein A and its variants can function as vaccine antigens, SpA, SpA-D, SpA-D_{Q9,10K;D36,37A}, and SpA-D_{Q9,10K;D36,37A} were emulsified with complete or incomplete Freund's adjuvant and immunized 4 week old BALB/c mice on day 1 and day 11 with 50 µg of purified protein. Cohort of animals (n=5) were analyzed for humoral immune responses to immunization by bleeding the animals before (day 0) and after the immunization schedule (day 21). Table 5 indicates that immunized mice generated only a modest humoral immune response directed at wild-type Protein A or its SpA-D module, whereas the amount of antibody raised following immunization with ${\rm SpA-D}_{Q9,10K;D36,37A}$ or ${\rm SpA-}$ D_{Q9,10K;D36,37A} was increased four to five fold. Following intravenous challenge with 1×107 CFU S. aureus Newman, animals were killed on day 4, their kidneys removed and either analyzed for staphylococcal load (by plating tissue homogenate on agar plates and enumerating colony forming units, CFU) or histopathology. As expected, mock (PBS) immunized mice (n=19) harbored 6.46 log₁₀ (±0.25) CFU in kidney tissue and infectious lesions were organized into 3.7 (±1.2) abscesses per organ (n=10)(Table 5). Immunization of animals with SpA led to a 2.51 log10 CFU reduction on day 5 (P=0.0003) with 2.1 (± 1.2) abscesses per organ. The latter data indicate that there was no significant reduction in abscess formation (P=0.35). Immunization with SpA-D generated similar results: a 2.03 log_{10} CFU reduction on day 5 $(P{\pm}0.0001)$ with 1.5 $({\pm}0.8)$ abscesses per organ (P=0.15). In contrast, immunization with SpA-D_{09,10K;D36,374} or SpA- $D_{Q9,10G;D36,37A}$ created increased protection, with 3.07 log₁₀ and 3.03 log₁₀ CFU reduction on day 4, respectively (statistical significance P<0.0001 for both observations). Further, immunization with both SpA-D_{Q9,10K;D36,37A} and SpA- $D_{Q9,10G;D36,37A}$ generated significant protection from staphylococcal abscess formation, as only 0.5 (±0.4) and 0.8 (±0.5) infectious lesions per organ (P=0.02 and P=0.04) were identified. Thus, immunization with non-toxigenic Protein A variants generates increased humoral immune responses for Protein A and provides protective immunity against staphylococcal challenge. These data indicate that Protein A is an ideal candidate for a human vaccine that prevents S. aureus disease.

These exciting results have several implications for the design of a human vaccine. First, the generation of substitution mutations that affect the ability of the immunoglobulin binding domains of Protein A, either alone or in combination of two or more domains, can generate non-toxigenic variants suitable for vaccine development. It seems likely that a combination of mutant IgG binding domains closely resembling the structure of Protein A can generate even better humoral immune responses as is reported here for the SpA-domain D alone. Further, a likely attribute of Protein A specific antibodies may be that the interaction of antigen binding sites with the microbial surface can neutralize the ability of staphylococci to capture immunoglobulins via their Fc portion or to stimulate the B cell receptor via the VH3 binding activities.

	Bacterial load in kidney (n = number of mice)				Abscess formation in mice (n = number of mice)					
Antigen	^{<i>a</i>} log ₁₀ CFU g ⁻¹	^b Reduction	^c P value	IgG titer	^d Surface abscess	Reduction	"Histopathology	Reduction	۶ _P value	
Mock	6.46 ± 0.25 (n = 19)	_	—	<100	14/19 (70%)	_	3.7 ± 1.2 (n = 10)	_	_	
SpA	3.95 ± 0.56 (n = 20)	2.51	0.0003	1706 ± 370	10/20 (50%)	32%	2.1 ± 1.2 (n = 10)	2.2	0.35	
SpA-D	4.43 ± 0.41 (n = 18)	2.03	0.0001	381 ± 27	10/18 (55%)	25%	1.5 ± 0.8 (n = 10)	2.2	0.15	
SpA-D1	3.39 ± 0.50 (n = 19)	3.07	< 0.0001	5600 ± 801	6/20 (30%)	59%	0.5 ± 0.4 (n = 10)	3.2	0.02	
SpA-D2	3.43 ± 0.46 (n = 19)	3.03	<0.0001	3980 ± 676	6/19 (32%)	57%	0.8 ± 0.5 (n = 10)	2.9	0.04	

^aMeans of staphylococcal load calculated as \log_{10} CFU g⁻¹ in homogenized renal tissues 4 days following infection in cohorts of 18 to 20 BALB/c mice. Standard error of the means (±SEM) is indicated. ^cStatistical significance was calculated with the Students t-test and P-values recorded; P-values < 0.05 were deemed significant.

^bReduction in bacterial load calculated as log₁₀ CFU g⁻¹

^dAbscess formation in kidney tissues four days following infection was measured by macroscopic inspection (% positive)

"Histopathology of hematoxylin-cosin stained, thin sectioned kidneys from ten animals; the number of abscesses per kidney was recorded and averaged for the final mean (±SEM). "Statistical significance was calculated with the Students t-test and P-values recorded; P-values < 0.05 were deemed significant.

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SpA-D1 and SpA-D2 represent SpA-D_{Q9,10K;D36,37A} and SpA-D_{Q9,10G;D36,37A}, respectively.

Vaccine protection in murine abscess, murine lethal infection, and murine pneumonia models. Three animal models have been established for the study of S. aureus infectious disease. These models are used here to examine the level of protective immunity provided via the generation of Protein A 30 specific antibodies.

Murine Abscess

BALB/c mice (24-day-old female, 8-10 mice per group, Charles River Laboratories, Wilmington, Mass.) are immunized by intramuscular injection into the hind leg with purified protein (Chang et al., 2003; Schneewind et al., 1992). Purified SpA, SpA-D or SpA-D_{Q9,10K;D36,374} (50 µg protein) is administered on days 0 (emulsified 1:1 with complete Freund's adjuvant) and 11 (emulsified 1:1 with incomplete Freund's adjuvant). Blood samples are drawn by retroorbital 40 bleeding on days 0, 11, and 20. Sera are examined by ELISA for IgG titers for specific SpA-D and SpA-D_{Q9,10K;D36,374} binding activity. Immunized animals are challenged on day 21 by retroorbital injection of 100 µl of S. aureus Newman or S. aureus USA300 suspension $(1 \times 10^7 \text{ cfu})$. For this, overnight cultures of S. aureus Newman are diluted 1:100 into fresh 45 tryptic soy broth and grown for 3 h at 37° C. Staphylococci are centrifuged, washed twice, and diluted in PBS to yield an A_{600} of 0.4 (1×10⁸ cfu per ml). Dilutions are verified experimentally by agar plating and colony formation. Mice are anesthetized by intraperitoneal injection of 80-120 mg of 50 ketamine and 3-6 mg of xylazine per kilogram of body weight and infected by retroorbital injection. On day 5 or 15 following challenge, mice are euthanized by compressed CO2 inhalation. Kidneys are removed and homogenized in 1% Triton X-100. Aliquots are diluted and plated on agar medium for 55 triplicate determination of cfu. For histology, kidney tissue is incubated at room temperature in 10% formalin for 24 h. Tissues are embedded in paraffin, thin-sectioned, stained with hematoxylinleosin, and examined by microscopy.

Murine Lethal Infection

BALB/c mice (24-day-old female, 8-10 mice per group, Charles River Laboratories, Wilmington, Mass.) are immunized by intramuscular injection into the hind leg with purified SpA, SpA-D or SpA-D_{Q9,10K;D36,37A} (50 µg protein). Vaccine is administered on days 0 (emulsified 1:1 with complete Freund's adjuvant) and 11 (emulsified 1:1 with incom- 65 plete Freund's adjuvant). Blood samples are drawn by retroorbital bleeding on days 0, 11, and 20. Sera are examined by

ELISA for IgG titers with specific SpA-D and SpA-D_{09,10K;D36,37A} binding activity. Immunized animals are challenged on day 21 by retroorbital injection of 100 μ l of S. aureus Newman or S. aureus USA300 suspension (15×107 cfu). For this, overnight cultures of S. aureus Newman are diluted 1:100 into fresh tryptic soy broth and grown for 3 h at 37° C. Staphylococci are centrifuged, washed twice, diluted in PBS to yield an A_{600} of 0.4 (1 $\times 10^8$ cfu per ml) and concentrated. Dilutions are verified experimentally by agar plating and colony formation. Mice are anesthetized by intraperitoneal injection of 80-120 mg of ketamine and 3-6 mg of xylazine per kilogram of body weight. Immunized animals are challenged on day 21 by intraperitoneal inject with 2×10^{10} cfu of S. aureus Newman or 3-10×10⁹ cfu of clinical S. aureus isolates. Animals are monitored for 14 days, and lethal disease is recorded.

Murine Pneumonia Model

S. aureus strains Newman or USA300 (LAC) are grown at 37° C. in tryptic soy broth/agar to OD₆₆₀ 0.5. 50-ml culture aliquots are centrifuged, washed in PBS, and suspended in 750 μl PBS for mortality studies (3-4×10⁸ CFU per 30-μl volume), or 1,250 ul PBS (2×10⁸ CFU per 30-ul volume) for bacterial load and histopathology experiments. For lung infection, 7-wk-old C57BL/6J mice (The Jackson Laboratory) are anesthetized before inoculation of 30 µl of S. aureus suspension into the left nare. Animals are placed into the cage in a supine position for recovery and observed for 14 days. For active immunization, 4-wk-old mice receive 20 µg SpA-D or SpA-D_{Q9,10K;D36,37A} in CFA on day 0 via the i.m. route, followed by a boost with 20 µg SpA-D or SpA-D_{Q9,10K;D36,37A} in incomplete Freund's adjuvant (IFA) on day 10. Animals are challenged with S. aureus on day 21. Sera are collected before immunization and on day 20 to assess specific antibody production. For passive immunization studies, 7-wk-old mice receive 100 µl of either NRS (normal rabbit serum) or SpA-D-specific rabbit antisera via i.p. injection 24 h before challenge. To assess the pathological correlates of pneumonia, infected animals are killed via forced CO₂ inhalation before removal of both lungs. The right lung is homogenized for enumeration of lung bacterial load. The left lung is placed in 1% formalin and paraffin embedded, thin sectioned, stained with hematoxylin-eosin, and analyzed by microscopy.

Rabbit Antibodies

Purified 200 μ g SpA-D or SpA-D_{Q9,10K;D36,37A} is used as an immunogen for the production of rabbit antisera. 200 μ g protein is emulsified with CFA for injection at day 0, followed by booster injections with 200 μ g protein emulsified with 5 EFA on days 21 and 42. Rabbit antibody titers are determined by ELISA. Purified antibodies are obtained by affinity chromatography of rabbit serum on SpA-D or SpA-D_{Q9,10K;D36,37A} sepharose. The concentration of eluted antibodies is measured by absorbance at A280 and specific anti-10 body titers are determined by ELISA.

Active Immunization with SpA-Domain D Variants

To determine vaccine efficacy, animals are actively immunized with purified SpA-D or SpA-D_{Q9,10K;D36,374}. As a control, animals are immunized with adjuvant alone. Antibody 15 titers against Protein A preparations are determined using SpA-D or SpA-D_{Q9,10K;D36,374} as antigens; note that the SpA-D_{Q9,10K;D36,374} variant cannot bind the Fc or Fab portion of IgG. Using infectious disease models described above, any reduction in bacterial load (murine abscess and pneumonia), histopathology evidence of staphylococcal disease (murine abscess and pneumonia) and protection from lethal disease (murine lethal challenge and pneumonia) is measured.

Passive immunization with affinity purified rabbit polyclonal antibodies generated against SpA-domain D variants. To determine protective immunity of Protein A specific rabbit 25 antibodies, mice are passively immunized with 5 mg/kg of purified SpA-D or SpA-D_{Q9,10K;D36,37A} derived rabbit antibodies. Both of these antibody preparations are purified by affinity chromatography using immobilized SpA-D or SpA- $D_{Q^{9,10K;D36,37,4}}$. As a control, animals are passively immu-nized with rV10 antibodies (a plague protective antigen that has no impact on the outcome of staphylococcal infections). Antibody titers against all Protein A preparations are determined using SpA-D_{Q9,10K;D36,37A} as an antigen, as this variant cannot bind the Fc or Fab portion of IgG. Using the $_{35}$ infectious disease models described above, the reduction in bacterial load (murine abscess and pneumonia), histopathology evidence of staphylococcal disease (murine abscess and pneumonia), and the protection from lethal disease (murine lethal challenge and pneumonia) is measured. 40

Example 2

Non-Toxigenic Protein a Vaccine for Methicillin-Resistant *Staphylococcus Aureus* Infection

Clinical isolates of S. aureus express protein A (Shopsin et al., 1999, whose primary translational product is comprised of an N-terminal signal peptide (DeDent et al., 2008), five Ig-BDs (designated E, D, A, B and C)(Sjodahl, 1977), region 50 X with variable repeats of an eight residue peptide (Guss et al., 1984), and C-terminal sorting signal for the cell wall anchoring of SpA (Schneewind et al., 1992; Schneewind et al., 1995) (FIG. 6). Guided by amino acid homology (Uhlen et al., 1984), the triple α -helical bundle structure of IgBDs 55 (Deisenhofer et al., 1978; Deisenhofer et al, 1981) and their atomic interactions with Fab VH3 (Graille et al., 2000) or Fcy (Gouda et al, 1998), glutamine 9 and 10 were selected as well as aspartate 36 and 37 as critical for the association of SpA with antibodies or B cell receptor, respectively. Substitutions Gln9Lys, Gln10Lys, Asp36Ala and Asp37Ala were introduced into the D domain to generate SpA-D_{KKAA} (FIG. 6). The ability of isolated SpA-D or SpA-D_{KK4A} to bind human IgG was analyzed by affinity chromatography (FIG. 6). Polyhistidine tagged SpA-D as well as full-length SpA retained human IgG on Ni-NTA, whereas SpA-D_{KKAA} and a negative 65 control (SrtA) did not (FIG. 6). A similar result was observed with von Willebrand factor (Hartleib et al., 2000), which,

along with tumor necrosis factor receptor 1 (TNFR1)(Gomez et al., 2004), can also bind protein A via glutamine 9 and 10 (FIG. **6**). Human immunoglobulin encompasses 60-70% VH3-type IgG. The inventors distinguish between Fc domain and B cell receptor activation of Igs and measured association of human Fc γ and F(ab)₂ fragments, both of which bound to full-length SpA or SpA-D, but not to SpA-D_{*KKAA*} (FIG. **6**). Injection of SpA-D into the peritoneal cavity of mice resulted in B cell expansion followed by apoptotic collapse of CD19+ lymphocytes in spleen tissue of BALB/c mice (Goodyear and Silverman, 2003)(FIG. **6**). B cell superantigen activity was not observed following injection with SpA-D_{*KKAA*}, and TUNEL-staining of splenic tissue failed to detect the increase in apoptotic cells that follows injection of SpA or SpA-D (FIG. **6**).

Naive six week old BALB/c mice were injected with 50 µg each of purified SpA, SpA-D or SpA-D_{KKAA} emulsified in CFA and boosted with the same antigen emulsified in IFA. In agreement with the hypothesis that SpA-D promotes the apoptotic collapse of activated clonal B cell populations, the inventors observed a ten-fold higher titer of SpA-D_{KKAA} specific antibodies following immunization of mice with the non-toxigenic variant as compared to the B cell superantigen (Spa-D vs. SpA-D_{KKAA} P<0.0001, Table 6). Antibody titers raised by immunization with full-length SpA were higher than those elicited by SpA-D (P=0.0022), which is likely due to the larger size and reiterative domain structure of this antigen (Table 6). Nevertheless, even SpA elicited lower antibody titers than SpA-D_{KKAA} (P=0.0003), which encompasses only 50 amino acids of protein A (520 residues, SEQ ID NO:33). Immunized mice were challenged by intravenous inoculation with S. aureus Newman and the ability of staphylococci to seed abscesses in renal tissues was examined by necropsy four days after challenge. In homogenized renal tissue of mock (PBS/adjuvant) immunized mice, an average staphylococcal load of 6.46 log10 CFU g⁻¹ was enumerated (Table 6). Immunization of mice with SpA or SpA-D led to a reduction in staphylococcal load, however SpA-D_{KKAA} vaccinated animals displayed an even greater, $3.07 \log_{10} CFU g^{-1}$ reduction of S. aureus Newman in renal tissues (P<0.0001, Table 6). Abscess formation in kidneys was analyzed by histopathology (FIG. 7). Mock immunized animals harbored an average of $3.7 (\pm 1.2)$ abscesses per kidney (Table 6). Vaccination with SpA-D_{*KKAA*} reduced the average number of abscesses to 0.5 (\pm 0.4)(P=0.0204), whereas immunization with SpA or SpA-D did not cause a significant reduction in 45 the number of abscess lesions (Table 6). Lesions from SpA- D_{KKAA} vaccinated animals were smaller in size, with fewer infiltrating PMNs and characteristically lacked staphylococcal abscess communities (Cheng et al, 2009)(FIG. 7). Abscesses in animals that had been immunized with SpA or SpA-D displayed the same overall structure of lesions in mock immunized animals (FIG. 7).

The inventors examined whether SpA-D_{*KKAA*} immunization can protect mice against MRSA strains and selected the USA300 LAC isolate for animal challenge (Diep et al., 2006). This highly virulent CA-MRSA strain spread rapidly throughout the United States, causing significant human morbidity and mortality (Kennedy et al., 2008). Compared to adjuvant control mice, SpA-D_{*KKAA*} immunized animals harbored a 1.07 log)₁₀ CFU g⁻¹ reduction in bacterial load of infected kidney tissues. Histopathology examination of renal tissue following *S. aureus* USA300 challenge revealed that the average number of abscesses was reduced from 4.04 (±0.8) to 1.6 (±0.6)(P=0.02774). In contrast, SpA or SpA-D immunization did not cause a significant reduction in bacterial load or abscess formation (Table 6).

Rabbits were immunized with SpA-D_{*KKAA*} and specific antibodies were purified on SpA-D_{*KKAA*} affinity column followed by SDS-PAGE (FIG. 8). SpA-D_{*KKAA*} specific IgG was

cleaved with pepsin to generate Fcy and F(ab)2 fragments, the latter of which were purified by chromatography on SpA-D_{KK4A} column (FIG. 8). Binding of human IgG or vWF to SpA or SpA-D was perturbed by SpA-D_{KK4A} specific F(ab)2, indicating that SpA-D_{KKAA} derived antibodies neutralize the 5 B cell superantigen function of protein A as well as its interactions with Ig (FIG. 8).

To further improve the vaccine properties for non-toxigenic protein A, the inventors generated SpAKKAA, which includes all five IgBDs with four amino acid substitutionssubstitutions corresponding to Gln9Lys, Gln10Lys, Asp36Ala and Asp37Ala of domain D-in each of its five domains (E, D, A, B and C). Polyhistidine tagged SpA_{KKAA} was purified by affinity chromatography and analyzed by Coomassie Blue-stained SDS-PAGE (FIG. 9). Unlike fulllength SpA, SpA_{*KKAA*} did not bind human IgG, Fc and $F(ab)_2$ or vWF (FIG. 9). SpA_{*KKAA*} failed to display B cell superan-tigen activity, as injection of the variant into BALB/c mice did not cause a depletion of CD19+ B cells in splenic tissue (FIG. 9). SpA_{*KKAA*} vaccination generated higher specific antibody titers than SpA-D_{KKAA} immunization and provided mice with

elevated protection against S. aureus USA300 challenge (Table 6). Four days following challenge, SpA_{KKAA} vaccinated animals harbored 3.54 log₁₀ CFU g⁻¹ fewer staphylococci in renal tissues (P=0.0001) and also caused a greater reduction in the number of abscess lesions (P=0.0109) (Table 6).

 $\mathrm{SpA}_{K\!K\!A\!A}$ was used to immunize rabbits. Rabbit antibodies specific for SpA-D_{*KKAA*} or SpA_{*KKAA*} were affinity purified on matrices with immobilized cognate antigen and injected at a concentration of 5 mg kg⁻¹ body weight into the peritoneal cavity of BALB/c mice (Table 7). Twenty-four hours later, specific antibody titers were determined in serum and animals challenged by intravenous inoculation with S. aureus Newman. Passive transfer reduced the staphylococcal load in kidney tissues for SpA-D_{*KKAA*} (P=0.0016) or SpA_{*KKAA*</sup> (P=0.0005) specific antibodies. On histopathology examina-} tion, both antibodies reduced the abundance of abscess lesions in the kidneys of mice challenged with S. aureus Newman (Table 7). Together these data reveal that vaccine protection following immunization with SpA-D_{KK4A} or SpA_{KKAA} is conferred by antibodies that neutralize protein A.

TABLE 5

		Staphylococ	cal load and abscess	formation in ren	al tissue	
Antigen	a log ₁₀ CFU g ⁻¹	^b P-value	^c Reduction (log ₁₀ CFU g ⁻¹)	^d IgG Titer	"Number of abscesses	^b P-value
		S. au	<i>reus</i> Newman challe	nge		
Mock	6.46 ± 0.25	_	_	<100	3.7 ± 1.2	_
SpA	3.95 ± 0.56	0.0003	2.51	1706 ± 370	2.1 ± 1.2	0.3531
SpA-D	4.43 ± 0.41	0.0001	2.03	381 ± 27	1.5 ± 0.8	0.1430
SpA-D _{KKAA}	3.39 ± 0.50	< 0.0001	3.07	5600 ± 801	0.5 ± 0.4	0.0204
1 10020		S. aureus	USA300 (LAC) ch	allenge		
Mock	7.20 ± 0.24	_	_	<100	4.0 ± 0.8	_
SpA	6.81 ± 0.26	0.2819	0.39	476 ± 6 0	3.3 ± 1.0	0.5959
SpA-D	6.34 ± 0.52	0.1249	0.86	358 ± 19	2.2 ± 0.6	0.0912
SpA-D _{KKAA}	6.00 ± 0.42	0.0189	1.20	3710 ± 1147	1.6 ± 0.6	0.0277
SpA _{KKAA}	3.66 ± 0.76	0.0001	3.54	10200 ± 2476	1.2 ± 0.5	0.0109

^aMeans of staphylococcal load calculated as \log_{10} CFU g⁻¹ in homogenized renal tissues 4 days following infection in cohorts of fifteen to twenty BALB/c mice per immunization. Representative of two independent and reproducible animal experiments is shown. Standard error of the means (±SEM) is indicated. ^bStatistical significance was calculated with the unpaired two-tailed Students t-test and P-values recorded; P-values < 0.05 were

deemed significant.

Reduction in bacterial load calculated as $\log_{10} ext{CFU} extbf{g}^{-1}$.

^dMeans of five randomly chosen serum IgG titers were measured prior to staphylococcal infection by ELISA.

"Histopathology of hematoxylene-eosin stained, thin sectioned kidneys from ten animals; the average number of abscesses per kidney was recorded and averaged again for the final mean (±SEM).

TABLE 6

	Passive immu	nization of	mice with antibodie	es against prote	in A.	
	St	aphylococo	cal load and abscess	formation in r	enal tissue	
^a Antibody	^b log ₁₀ CFU g ⁻¹	^c P-value	d Reduction (log ₁₀ CFU g ⁻¹)	eIgG Titer	^f Number of abscesses	^c P-value
Mock α-SpA-D _{KK44} α-SpA _{KK44}	7.10 ± 0.14 5.53 ± 0.43 5.69 ± 0.34	 0.0016 0.0005	 1.57 1.41	<100 466 ± 114 1575 ± 152	4.5 ± 0.8 1.9 ± 0.7 1.6 ± 0.5	 0.0235 0.0062

^aAffinity purified antibodies were injected into the peritoneal cavity of BALB/c mice at a concentration of 5 mg \cdot kg⁻¹ twenty-four hours prior to intravenous challenge with 1 × 10⁷ CFU *S. aureus* Newman. ^bMeans of staphylococcal load calculated as log₁₀ CFU g⁻¹ in homogenized renal tissues 4 days following infection in cohorts of fifteen BALB/c mice per immunization. Representative of two independent and reproducible animal experiments is shown.

Standard error of the means (\pm SEM) is indicated. "Statistical significance was calculated with the unpaired two-tailed Students t-test and P-values recorded; P-values < 0.05

were deemed significant. "Reduction in bacterial load calculated as \log_{10} CFU g⁻¹.

"Means of five randomly chosen serum IgG titers were measured prior to staphylococcal infection by ELISA

^fHistopathology of hematoxylene-eosin stained, thin sectioned kidneys from ten animals; the average number of abscesses per orded and averaged again for the final mean (±SEM). was rec

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Following infection with virulent S. aureus, mice do not develop protective immunity against subsequent infection with the same strain (Burts et al., 2008)(FIG. 10). The average abundance of SpA-D_{KKAA} specific IgG in these animals was determined by dot blot as 0.20 μ g ml⁻¹ (±0.04) and 0.14 μ g -5 ml⁻¹ (±0.01) for strains Newman and USA300 LAC, respectively (FIG. 9). The minimal concentration of protein A-specific IgG required for disease protection in SpA_{KKAA} or SpA-D_{KK4A} vaccinated animals (P .0.05 log₁₀ reduction in staphylococcal CFU g^{-1} renal tissue) was calculated as 4.05 10 $\mu g m l^{-1}$ (±0.88). Average serum concentration of SpA-specific IgG in adult healthy human volunteers (n=16) was 0.21 $\mu g m l^{-1}$ (±0.02). Thus, S. aureus infections in mice or humans are not associated with immune responses that raise significant levels of neutralizing antibodies directed against protein 15 A, which is likely due to the B cell superantigen attributes of this molecule. In contrast, the average serum concentration of IgG specific for diphtheria toxin in human volunteers, 0.068 $\mu g m l^{-1}$ (±0.20), was within range for protective immunity against diphtheria (Behring, 1890; Lagergard et al., 1992). 20

Clinical S. aureus isolates express protein A, an essential virulence factor whose B cell surperantigen activity and evasive attributes towards opsono-phagocytic clearance are absolutely required for staphylococcal abscess formation (Palmqvist et al., 2005; Cheng et al., 2009; Silverman and 25 Goodyear, 2006). Protein A can thus be thought of as a toxin, essential for pathogenesis, whose molecular attributes must be neutralized in order to achieve protective immunity. By generating non-toxigenic variants unable to bind Igs via Fcy or VH3-Fab domains, the inventors measure here for the first 30 time protein A neutralizing immune responses as a correlate for protective immunity against S. aureus infection. In contrast to many methicillin-sensitive strains, CA-MRSA isolate USA300 LAC is significantly more virulent (Cheng et al., 2009). For example, immunization of experimental animals 35 with the surface protein IsdB (Kuklin et al., 2006; Stranger-Jones et al, 2006) raises antibodies that confer protection against S. aureus Newman (Stranger-Jones et al., 2009) but not against USA300 challenge.

The methods utilized include:

Bacterial strains and growth. *Staphylococcus aureus* strains Newman and USA300 were grown in tryptic soy broth (TSB) at 37° C. *Escherichia coli* strains DH5 α and BL21 (DE3) were grown in Luria-Bertani (LB) broth with 100 µg ml⁻¹ ampicillin at 37° C.

Rabbit Antibodies. The coding sequence for SpA was PCR-amplified with two primers, gctgcacatatggcgcaacacgatgaagetcaac (SEQ ID NO:35) and agtggatecttatgettgagetttgttagcatctgc (SEQ ID NO:36) using S. aureus Newman template DNA. SpA-D was PCR-amplified with two primers, 50 aacatatgttcaacaaagatcaacaaagc (SEQ ID NO:38) and aaggatccagattcgtttaattttttagc (SEQ ID NO:39). The sequence for SpA-D_{KK44} was mutagenized with two sets of primers catatgttcaacaaagataaaaaagcgccttctatgaaatc (SEQ ED NO:42) and gamcatagaaggcgctttttttatctttgttgaacatatg (SEQ ID 55 NO:43) for Q9K, Q10K as well as cttcattcaaagtcttaaagccgccccaagccaaagcactaac (SEQ ID NO:40) and gttagtgctttggcttggggcggctttaagactttgaatgaag (SEQ ID NO:41) for D36A, D37A. The sequence of SpA_{KK44} was synthesized by Integrated DNA Technologies, Inc. PCR products were 60 cloned into pET-15b generating N-terminal His6 tagged recombinant protein. Plasmids were transformed into BL21 (DE3). Overnight cultures of transformants were diluted $1{:}100$ into fresh media and grown at $37^\circ\,\mathrm{C}.$ to an OD600 0.5, at which point cultures were induced with 1 mM isopropyl 65 β-D-1-thiogalatopyranoside (IPTG) and grown for an additional three hours. Bacterial cells were sedimented by cen-

trifugation, suspended in column buffer (50 mM Tris-HCl, pH 7.5, 150 mM NaCl) and disrupted with a French pressure cell at 14,000 psi. Lysates were cleared of membrane and insoluble components by ultracentrifugation at $40,000 \times g$. Proteins in the soluble lysate were subjected to nickel-nitrilotriacetic acid (Ni-NTA, Qiagen) affinity chromatography. Proteins were eluted in column buffer containing successively higher concentrations of imidazole (100-500 mM). Protein concentrations were determined by bicinchonic acid (BCA) assay (Thermo Scientific). For antibody generation, rabbits (6 month old New-Zealand white, female, Charles River Laboratories) were immunized with 500 µg protein emulsified in Complete Freund's Adjuvant (Difco) by subscapular injection. For booster immunizations, proteins emulsified in Incomplete Freund's Adjuvant and injected 24 or 48 days following the initial immunization. On day 60, rabbits were bled and serum recovered.

Purified antigen (5 mg protein) was covalently linked to HiTrap NHS-activated HP columns (GE Healthcare). Antigen-matrix was used for affinity chromatography of 10-20 ml of rabbit serum at 4° C. Charged matrix was washed with 50 column volumes of PBS, antibodies eluted with elution buffer (1 M glycine, pH 2.5, 0.5 M NaCl) and immediately neutralized with 1M Tris-HCl, pH 8.5. Purified antibodies were dialyzed overnight against PBS at 4° C.

 $F(ab)_2$ fragments. Affinity purified antibodies were mixed with 3 mg of pepsin at 37° C. for 30 minutes. The reaction was quenched with 1 M Tris-HCl, pH 8.5 and F(ab)2 fragments were affinity purified with specific antigen-conjugated HiTrap NHS-activated HP columns. Purified antibodies were dialyzed overnight against PBS at 4° C., loaded onto SDS-PAGE gel and visualized with Coomassie Blue staining.

Active and passive immunization. BALB/c mice (3 week old, female, Charles River Laboratories) were immunized with 50 µg protein emulsified in Complete Freund's Adjuvant (Difco) by intramuscular injection. For booster immunizations, proteins were emulsified in Incomplete Freund's Adjuvant and injected 11 days following the initial immunization. On day 20 following immunization, 5 mice were bled to obtain sera for specific antibody titers by enzyme-linked immunosorbent assay (ELISA).

Affinity purified antibodies in PBS were injected at a concentration 5 mg kg⁻¹ of experimental animal weight into the peritoneal cavity of BALB/c mice (6 week old, female, Charles River Laboratories) 24 hours prior to challenge with *S. aureus*. Animal blood was collected via periorbital vein puncture. Blood cells were removed with heparinized microhematocrit capillary tubes (Fisher) and Z-gel serum separation micro tubes (Sarstedt) were used to collect and measure antigen specific antibody titers by ELISA.

Mouse renal abscess. Overnight cultures of S. aureus Newman or USA300 (LAC) were diluted 1:100 into fresh TSB and grown for 2 hours at 37° C. Staphylococci were sedimented, washed and suspended PBS at OD600 of 0.4 (~1×10⁸ CFU ml^{-1}). Inocula were quantified by spreading sample aliquots on TSA and enumerating colonies formed. BALB/c mice (6 week old, female, Charles River Laboratories) were anesthetized via intraperitoneal injection with 100 mg ml⁻¹ ketamine and 20 mg ml⁻¹ xylazine per kilogram of body weight. Mice were infected by retro-obital injection with 1×10^7 CFU of S. aureus Newman or 5×10⁶ CFU of S. aureus USA300. On day 4 following challenge, mice were killed by CO₂ inhalation. Both kidneys were removed, and the staphylococcal load in one organ was analyzed by homogenizing renal tissue with PBS, 1% Triton X-100. Serial dilutions of homogenate were spread on TSA and incubated for colony formation. The remaining organ was examined by histopathology. Briefly, kidneys were fixed in 10% formalin for 24 hours at room temperature. Tissues were embedded in paraffin, thin-sectioned, stained with hematoxylin-eosin, and inspected by light microscopy to enumerate abscess lesions. All mouse experiments were performed in accordance with the institu-5 tional guidelines following experimental protocol review and approval by the Institutional Biosafety Committee (IBC) and the Institutional Animal Care and Use Committee (IACUC) at the University of Chicago.

Protein A binding. For human IgG binding, Ni-NTA affin- 10 ELISA, and B cell superantigen data. ity columns were pre-charged with 200 µg of purified proteins (SpA, SpA-D, SpA-D_{KKAA}, and SrtA) in column buffer. After washing, 200 µg of human IgG (Sigma) was loaded onto the column. Protein samples were collected from washes and elutions and subjected to SDS-PAGE gel electrophoresis, 15 followed by Coomassie Blue staining. Purified proteins (SpA, SpA_{*KKAA*}, SpA-D and SpA-D_{*KKAA*}) were coated onto MaxiSorp ELISA plates (NUNC) in 0.1M carbonate buffer (pH 9.5) at 1 µg ml⁻¹ concentration overnight at 4° C. Plates were next blocked with 5% whole milk followed by incuba- 20 tion with serial dilutions of peroxidase-conjugated human IgG, Fc or F(ab)2 fragments for one hour. Plates were washed and developed using OptEIA ELISA reagents (BD). Reactions were quenched with 1 M phosphoric acid and A_{450} readings were used to calculate half maximal titer and percent 25 binding

von Willebrand Factor (vWF) binding assays. Purified proteins (SpA, SpA, SpA D and SpA-D_{KKAA}) were coated and blocked as described above. Plates were incubated with human vWF at 1 μ g ml⁻¹ concentration for two hours, then 30 washed and blocked with human IgG for another hour. After washing, plates were incubated with serial dilution of peroxidase-conjugated antibody directed against human vWF for one hour. Plates were washed and developed using OptEIA ELISA reagents (BD). Reactions were quenched with 1 M 35 phosphoric acid and A450 readings were used to calculate half maximal titer and percent binding. For inhibition assays, plates were incubated with affinity purified F(ab)2 fragments specific for SpA-D_{KKAA} at 10 μ g ml⁻¹ concentration for one hour prior to ligand binding assays.

Splenocyte apoptosis. Affinity purified proteins (150 μg of SpA, SpA-D, SpA $_{KKAA}$, and SpA-D $_{KKAA}$) were injected into the peritoneal cavity of BALB/c mice (6 week old, female, Charles River Laboratories). Four hours following injection, animals were killed by CO₂ inhalation. Their spleens were 45 removed and homogenized. Cell debris were removed using cell strainer and suspended cells were transferred to ACK lysis buffer (0.15 M NH4Cl, 10 mM KHCO3, 0.1 mM EDTA) to lyse red blood cells. White blood cells were sedimented by centrifugation, suspended in PBS and stained with 1:250 50 diluted R-PE conjugated anti-CD19 monoclonal antibody (Invitrogen) on ice and in the dark for one hour. Cells were washed with 1% FBS and fixed with 4% formalin overnight at 4° C. The following day, cells were diluted in PBS and analyzed by flow cytometry. The remaining organ was examined 55 for histopathology. Briefly, spleens were fixed in 10% formalin for 24 hours at room temperature. Tissues were embedded in paraffin, thin-sectioned, stained with the Apoptosis detection kit (Millipore), and inspected by light microscopy.

Antibody quantification. Sera were collected from healthy 60 human volunteers or BALB/c mice that had been either infected with S. aureus Newman or USA300 for 30 days or that had been immunized with SpA-D_{KK44}/SpA_{KK44} as described above. Human/mouse IgG (Jackson Immunology Laboratory), SpAKKAA, and CRM197 were blotted onto nitro-65 cellulose membrane. Membranes were blocked with 5% whole milk, followed by incubation with either human or

mouse sera. IRDye 700DX conjugated affinity purified antihuman/mouse IgG (Rockland) was used to quantify signal intensities using the OdysseyTM infrared imaging system (Licor). Experiments with blood from human volunteers involved protocols that were reviewed, approved and performed under regulatory supervision of The University of Chicago's Institutional Review Board (IRB).

Statistical Analysis. Two tailed Student's t tests were performed to analyze the statistical significance of renal abscess,

Example 3

Active Immunization Using Subunit Vaccine Including Multiple Antigens

BALB/c mice (n=18-20) were either mock immunized with PBS/adjuvant or injected with 25 µg of each antigen (Combo 1, ClfA+SdrD+FnBPB; Combo 2, Combo 1+ SpA_{KK4A}). Immunized mice were challenged by intravenous inoculation with 1×10^7 CFU S. aureus Newman. Bacterial loads in kidney tissues were examined at day 4 (FIG. 13A) and day 18 (FIG. 13B) post challenge. Statistical significance was calculated with the unpaired two-tailed Students t-test and P-values recorded; P-values <0.05 were deemed significant. Combo 1 and Combo 2 showed significant reduction in bacterial load at 4 and 18 days post challenge.

Bacterial Strains and Culturing Conditions. Staphylococci were cultured on tryptic soy agar or broth at 37° C. E. coli strains DH5a and BL21(DE3) (Studier et al., (1990) Methods Enzymol. 185, 60-89) were cultured on Luria agar or broth at 37° C. Ampicillin (100 μg ml-1), erythromycin (200 μg ml-1) and spectinomycin (200 µg ml-1) were used for pET15b (Studier et al., (1990) Methods Enzymol. 185, 60-89), transposon mutant (Bae et al., (2004) Proc. Natl. Acad. Sci. USA 101, 12312-12317) and protein A mutant (Kim et al., J Exp Med 207, 1863-70) selection, respectively.

Cloning and Purification. Coding sequences for ClfA, SdrD, and FnBPB were PCR amplified using S. aureus New-40 man template DNA (Stranger-Jones et al., (2006) Proc. Nat. Acad. Sci. USA 103, 16942-16947). PCR products were cloned into pET15b to express recombinant proteins with N-terminal His6-tag fusion. Cloning of non-toxigenic protein A was described previously (Kim et al., J Exp Med 207, 1863-70). Plasmids were transformed into BL21(DE3). Overnight cultures of transformants were diluted 1:100 into fresh media and grown at 37° C. to an OD600 0.5, at which point cultures were induced with 1 mM isopropyl β-D-1thiogalatopyranoside (IPTG) and grown for an additional three hours. Bacterial cells were sedimented by centrifugation, suspended in column buffer (50 mM Tris-HCl, pH 7.5, 150 mM NaCl) and disrupted with a French pressure cell at 14,000 psi. Lysates were cleared of membrane and insoluble components by ultracentrifugation at 40,000×g. Proteins in the soluble lysate were subjected to nickel-nitrilotriacetic acid (Ni-NTA, Qiagen) affinity chromatography. Proteins were eluted in column buffer containing successively higher concentrations of imidazole (100-500 mM). Protein concentrations were determined by bicinchonic acid (BCA) assay (Thermo Scientific).

Active Immunization. BALB/c mice (3 week old, female, Charles River Laboratories) were immunized with 25 µg protein emulsified in Complete Freund's Adjuvant (Difco) by intramuscular injection. For booster immunizations, proteins were emulsified in Incomplete Freund's Adjuvant and injected 11 days following the initial immunization. On day 20 following immunization, 5 mice were bled to obtain sera for specific antibody titers by enzyme-linked immunosorbent assay (ELISA). On day 21, all mice were challenged with 1×10^7 CFU *S. aureus* Newman. Four and eighteen days following challenge, kidneys were removed during necropsy, and renal tissue was analyzed for staphylococcal load or 5 histopathology. Also, hyper-immune sera were collected via cardiac puncture and analyzed against components of the staphylococcal antigen matrix.

Statistical Analysis. Unpaired two-tailed Student's t tests were performed to analyze the statistical significance. Linear ¹⁰ regression analysis was performed using Graphpad Prism.

Example 4

EBH Confers Complement Resistance to Staphylococcus Aureus

The methicillin-resistant *Staphylococcus aureus* isolate USA300 LAC expresses the Ebh protein on its surface. Mutations that disrupt the ebh reading frame increase the volume 20 of staphylococcal cells and alter the dimensions of their crosswall septa. These ebh variants display increased susceptibility to methicillin as well as complement-mediated killing, which is associated with reduced survival of mutant staphylococci in blood and diminished virulence during animal 25 infection. Immunization of mice with the N-terminal domain of Ebh (residues 12524) elicits humoral immune responses that confer protection against staphylococcal challenge.

Results

Growth Characteristics of Staphylococcal ebh Mutants

Mutations in ebh were generated by constructing either a chromosomal deletion of the ebh gene in S. aureus Newman or introducing a transposon insertion into the 5' portion of the ebh gene in S. aureus USA300 (FIG. 14). The mutational lesions were verified by DNA sequencing, and the predictive 35 disruption of ebh expression was verified by immunoblotting and immunofluorescence of ebh variant staphylococci. For immunoblotting experiments, mid-log staphylococcal cultures were treated with lysostaphin and proteins in the total cell lysate were precipitated with 10% tricarboxylic acid, 40 washed with acetone and solubilized in sample buffer. Proteins were separated on a 6% polyacrylamide gel, electrotransferred to PVDF membrane and immunoblotted with rabbit antibodies (α -EbhN) that had been raised against recombinant Ebh (residues 1-2524). In agreement with the 45 extraordinary size of Ebh, the inventors observed immunoreactive material near the well and stacking portion of the 6% SDS-PAGE gel. This immunoreactive material was absent in lysates derived from the S. aureus Newman and USA300 ebh mutants.

For immunofluorescence detection of Ebh, staphylococci grown to mid log in tryptic soy broth were fixed in paraformaldehyde and stained with α -EbhN antibodies. To eliminate protein A background signals, the inventors stained for Ebh in a Δ spa and Δ spa/ Δ ebh mutant. Antibodies against Ebh were 55 distributed on the surface of the Δ spa mutants of S. aureus Newman and USA300 but not in the envelope of $\Delta spa/\Delta ebh$ variants. Staphylococci with positive signals displayed a hemispherical distribution of immuno-reactive Ebh signals, similar to that of other surface proteins secreted via YSIRK/ 60 GS type signal peptides (DeDent et al., 2007; Marraffini et al., 2006). BODIPY-vancomycin binds to cell wall pentapeptides in the staphylocococcal peptidoglycan; while the entire envelope displays diffuse BODIPY-vancomycin staining, the increased abundance of fluorescence signals in cross walls, 65 the cell division septa, is indicative of the greater abundance of pentapeptides at this location. BODIPY-vancomycin stain-

ing also revealed that ebh variants of S. aureus Newman and S. aureus USA300 display increased cell sizes over wild-type staphylococci. The inventors sought to quantify the increased cell size of ebh mutant staphylococci. Bacteria from mid-log cultures were sedimented by centrifugation, suspended in PBS and fixed in glutaraldehyde. Samples were embedded in epoxy, thin-sectioned and stained with uranyl acetate prior to viewing by transmission electron microscopy (FIG. 15). To compare individual coccal cells for an analysis of their cell diameter, only those staphylococci were selected for measurement that had completed their cell division septum (cross wall) and that displayed equal volumes of both daughter cells. In this manner, the inventors could ensure that the cells had been cut at midpoint, using the cross wall as a landmark for 15 mid-axial sectioning. By calculating the average (±standard error of the mean) cell diameter in µm, the inventors learned that ebh mutants are 0.2 µm (approximately 20%) larger in size than wild-type staphylococci (FIG. 15). Of note, S. aureus USA300 cells were larger in diameter (1.1 µm±0.2) than S. aureus Newman (0.9 um±0.2).

Oxacillin and Lysostaphin Sensitivity

S. aureus USA300 is resistant to methicillin, a penicillinase-resistant β -lactam compound, however methicillin is no longer commercially available. Over the past decade, oxacillin has been used as a surrogate for methicillin; this β -lactam is also resistant to cleavage by penicillinase and expression of PBP2A (mecA) in S. aureus USA300 confers resistance to both methicillin and oxacillin. Growth of the wild-type MRSA parent in tryptic soy broth was not inhibited following the addition of 2 µg/ml oxacillin to culture media (Kuroda et al., 2008). By comparison, addition of 2 (µg/ml oxacillin had a profound impact on the growth of the ebh mutant (FIG. 16), which exhibited at least a 3 hour delay until the bacteria resumed growth, likely due to the depletion of the antimicrobial below its minimal inhibitory concentration. USA300 mutants with bursa aurealis insertions in the middle (Δ ebh 15727) and final third (Aebh 10853) of ebh exhibited intermediate phenotypes of oxacillin sensitivity (data not shown), in agreement with the conjecture that all segments of ebh are required for function but that the 5' portions of the gene exert partial activity. This gradient in phenotype suggests that Ebh is directly responsible for mediating resistance to beta lactam antibiotics.

Electron microscopy of wild-type and ebh mutant staphylococci grown in the presence of 2 μ g/ml oxacillin revealed differences in cell wall integrity and cell structure. The vast majority of wild-type MRSA strain USA300 cells displayed physiological cell and cell wall envelope structures (FIG. 16). In contrast, most cells of the ebh mutants had lysed and displayed defects in the integrity of their cell wall envelope. These defects occurred in small segments of the peripheral cell walls as well as large deviations of the cross wall (FIG. 16). These images therefore suggest that Ebh is required for the physiological assembly, integrity and separation of the staphylococcal cell wall envelope as these cells divide.

Previous studies have shown that oxacillin-sensitivity of MRSA strains is associated with alterations in cell wall structure (Komatsuzawa et al., 2000; Komatsuzawa et al, 1997; Berger-Bachi, 1983). For example, mutations in the femAB genes display an oxacillin-sensitive phenotype as the variants synthesize altered cell wall crossbridges and a reduced degree of peptidoglycan crosslinking (Berger-Bachi et al., 1989; Berger-Bachi Et al., 1998). Such mutational phenotypes are associated with resistance to lysostaphin, a bacteriocin protease that cleaves the peptidoglycan crossbridges of wildtype staphylococci, but not of femAB mutant staphylococci. The inventors tested whether ebh mutations confer resistance

to lysostaphin onto the mutant staphylococci. Suspensions of wild-type and ebh mutant staphylococci were incubated with increasing concentrations of lysostaphin for 30 minutes and the absorbance at 600 nm determined as a measure for cell density and integrity of the cell wall envelope. The ebh mutants did not exhibit a significant difference in lysostaphin sensitivity as compared to the wild-type strain (FIG. 17).

Susceptibility of Staphylococci to Killing by Complement The inventors wondered whether the observed structural changes to the envelope of ebh mutant staphylococci impact their ability to survive and replicate in blood or host tissues. To address these issues, the inventors inoculated wild-type and ebh mutant staphylococci into fresh mouse blood that had been treated with lepirudin to prevent coagulation. Aliquots of blood with staphylococci were spread on agar media at timed intervals; by measuring colony formation, the ability of staphylococci to survive in blood was enumerated. Over a period of 30 and 60 minutes, wild-type MRSA strain USA300 remained viable and did not display a significant drop in colony forming units. In contrast, 60% of ebh mutant staphy-²⁰ lococci were killed within 30 min of their inoculation into mouse blood (FIG. 18).

Bacterial killing in mouse blood may be a feature of phagocytic cells that recognize opsonized staphylococci and, following uptake via phagocytosis, engage oxygen radicals and 25 lysosomal vesicles to remove the invading pathogen. At least for Gram-negative bacteria, complement deposition in the bacterial envelope can trigger the formation of membrane attack complexes (MAC) that kill these microbes without the assistance of phagocytic cells. To distinguish between such 30 possibilities for the killing of ebh variants, mouse blood was centrifuged to remove all cells and incubated staphylococci in the presence of plasma. MRSA strain USA300 replicated in plasma, in agreement with the general hypothesis that staphylococci escape complement mediated killing and replicate in blood. In contrast, 30-40% of the ebh variant population was killed in mouse plasma (FIG. 18). As a test whether this killing required complement, plasma was treated for 20 minutes at 60° C., a condition that inactivates C3 convertases required to promote complement deposition and activate the formation of MACs. Of note, both wild-type and ebh mutant ⁴⁰ staphylococci replicated in heat-treated plasma (FIG. 18), in agreement with a model whereby complement deposition into the envelope of ebh mutant staphylococci triggers their killing in blood.

Complement-mediated killing can be initiated with the 45 deposition of antibody, C3b, and C5 binding to bacterial surfaces, which triggers a series of proteolytic cascades that ultimately result in the formation of a MAC pore complex (Gros et al., 2008). As is alluded to above, complement proteins are effective at lysing Gram-negative bacteria, whereas 50 the thick peptidoglycan envelope of Gram-positive pathogens prevents the access of MACs to membranes (Laarman et al., 2010). S. aureus isolates are particularly resistant to complement mediated killing as these microbes secrete SCIN, Sak, and CHIPS-proteins that neutralize, or destroy complement 55 (Jongerius et al., 2007; Rooijakkers et al., 2005; Rooijakkers et al., 2006; Rooijakkers et al., 2009; van Wamel et al., 2006). Cell wall associated (Eap, Efb) or sortase anchored (IsdH, SpA) proteins in the staphylococcal envelope bind to and sequester complement (Lee et al., 2004; Harraghy et al, 2003; 60 Hammel et al., 2007; Visai et al., 2009; Jongerius et al., 2009). The sum of these reactions prevents the deposition on complement on the staphylococcal surface. Ebh is presumed to lie across the staphylococcal surface and strengthen the peptidoglycan. If so, the loss of this protein could increase 65 plasma membrane exposure to complement and trigger increased deposition of C3 and C5 convertases and eventually

MAC. This was tested and the invenotors first measured C3b deposition on wild-type or ebh mutant cells with FACS analysis and immunoblotting. Mid-log wild-type and ebh mutant staphylococci were incubated with human plasma and aliquots were collected at 5 min intervals. Samples were stained with anti-human C3b FITC conjugated antibody and viewed with a FACS sorter. The inventors observed significantly increased labeling of ebh mutants as compared to the wildtype strain (FIG. 19). The ebh mutant staphylococci displayed increased staining at all time points, although the overall amount of labeling increased at the same rate as occurs for wild-type staphylococci.

Ebh and Biofilms

Christner et al. reported that a gene fragment of Ebh appears to contribute to the formation of biofilms by Staphylococcus epidermidis, albeit that this phenotype was only observed in the absence of other biofilm producing factors-PIA and Aap. The inventors therefore wondered whether Ebh contributes also to biofilm growth of S. aureus. MRSA strain USA300 and its isogenic ebh variant were grown in still cultures overnight on fibronectin pre-coated 96 well plates. Under these conditions, USA300 is known to consistently form a biofilm (FIG. 20). These plates were then washed three times with PBS and the biofilms stained with safranin. The amount of safranin staining is measured as absorbance at 450 nm and corresponds with the thickness of the biofilm layer formed on the bottom of the well. FIG. 20 shows that mutations in ebh or icaA do not affect biofilm formation. As a control, a mutation in srtA (sortase A) abrogated the ability of USA300 staphylococci to grow as a biofilm. The inventors also examined whether antibodies against the repeat region of Ebh could perturb biofilm formation. USA300 biofilm formation was monitored in the presence or absence of increasing concentrations of normal rabbit sera and immunoreactive sera specific for PIA or the repeat region of Ebh, i.e., the very domain that has been assigned a biofilm contributory role in S. epidermidis (Christner et al., 2010). Of note, Ebh specific antibodies did not perturb the ability of USA300 staphylococci to grow as a biofilm (FIG. 20). Taken together, these experiments indicate that Ebh does not contribute to S. aureus biofilm growth in laboratory media or on fibronectin-coated plates.

Ebh and Staphylococcal Virulence

The inventors wondered whether ebh contributes to the virulence of the MSSA isolate S. aureus Newman or MRSA strain USA300 and infected cohorts of BALB/c mice with either the wild-type parent or the corresponding ebh variants (FIG. **21**). At a challenge dose of 5×10^7 CFU, all BALB/c mice that had been infected with the USA300 wild-type died within 24 hours. In contrast, animals infected with the same dose of the ebh variant displayed a delayed time-to-death for up to 108 hours (P<0.005, wild-type vs. ebh-statistical significance analyzed via the log-rank test, FIG. 21). Following intravenous challenge with 5×10⁶ CFU, all BALB/c mice infected with the USA300 wild-type strain displayed abscesses in kidneys and other internal organs. When renal tissues were analyzed for the load of wild-type staphylococci on day 5 following challenge, the inventors observed an average of 6.2 log₁₀ CFU g⁻¹ tissue (FIG. 21). In contrast, the ebh variant displayed a 1.4 log₁₀ reduction in CFU g⁻¹ tissue (FIG. 21). A similar defect (1.2 \log_{10} reduction in CFU g⁻¹ tissue) in staphylococcal replication was observed for the ebh variant of the MSSA strain Newman (FIG. 21). In summary, mutations that affect the expression of ebh in either the MSSA strain Newman or the MRSA strain USA300 diminish the ability of staphylococci to replicate in host tissues and also reduce their virulence in a murine lethal sepsis model.

TABLE 7	
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			Virulence of Aebl	1			
				Abscess formation in kidney tissue			
Staphylococcal load in kidney tissue					"Number of		
Genotype	^{<i>a</i>} log ₁₀ CFU g ⁻¹ tissue	^b Significance (P-value)	^c Reduction (log ₁₀ CFU g ⁻¹)	^d Surface abscesses (%)	abscesses per kidney	^f Significance (P-value)	
Newman	5.767 ± 0.325	_	_	50	ND	ND	
∆ebh KO	4.525 ± 0.444	0.0409	1.24	55	ND	ND	
USA300	6.126 ± 0.223			65	ND	ND	
∆ebh 9044	4.719 ± 0.430	0.0103	2.046	45	ND	ND	

^aMeans of staphylococcal load calculated as \log_{10} CFU g⁻¹ in homogenized renal tissues 5 days following infection in cohorts of 10 BALB/c mice per challenge strain, each strain was tested at least twice and the data were combined to obtain the final averages. Standard error of mean (±SEM) indicated statistical significance was calculated with the Students t-test and P-values (-0.05 are significant.^b Statistical significant is statistical significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 are significant.^b Statistical significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significance was calculated with the Students t-test and P-values (-0.05 were deemed significant.^b Statistical significant (-0.05 were deemed si

^cReduction in bacterial load calculated as \log_{10} CFU g⁻¹

^dAbscess formation in kidney tissues five days following infection was measured by macroscopic inspection (% positive)

Histopathology of hematoxylene-cosin stained, thin sectioned kidneys from eight to ten animals; the average number of abscesses per kidney was recorded and average again for the final mean (\pm SEM). 'Statistical significance was calculated with the non-parametric Mann-Whitney test (MWT) and P-values recorded; P-values < 0.05 were deemed significant.

Ebh Vaccines

Secreted antigens that are required for the establishment of staphylococcal infections may exert humoral immune responses that can prevent their associated diseases (protec- 25 tive immunity). To ascertain whether or not Ebh, a secreted

 g^{-1} tissue when challenged with strains Newman or USA300, respectively. Although Ebh40-2544 immunization reduced the load of staphylococci in infected tissues, this vaccine did not cause a significant reduction in the number of abscess lesions in renal tissues (Table 9, FIG. 22).

TABLE 8

	Sta	phylococcal loa	d in kidney tis	sue*	Abscess fe	ormation in kidi	ney tissue*
Antigen	^{<i>a</i>} log ₁₀ CFU g ⁻¹ of kidney tissue	^b Significance (P-value) t-test	^c Reduction in ^a log ₁₀ CFU g ⁻¹	^d IgG titers	^e Surface abscess (%)	^f Number of abscesses per kidney	^g Significance (P-value) MWT
			Newm	an challenge			
PBS	4.382 ± 0.545	_	_	<100	50	1.8 ± 0.6	_
Ebh	1.767 ± 0.676	0.0008	2.615 USA 3	14,500 ± 5,000 00 challenge	15	0.3 ± 0.3	0.1216
PBS	6.960 ± 0.070	_		<100	100	5.0 ± 1.4	
Ebh	6.580 ± 0.174	0.0683	0.380	$14,500 \pm 5,000$	85	2.8 ± 0.6	0.282

*BALB/c mice (n = 10, 2 repeat trials) were injected with 50 µg each of purified Ebh N₄₀₋₂₅₄₄ emulsified in CFA on day 0 and boosted with the same antigen emulsified in IFA on day 11. On day 20, three animals were examined for IgG antibody titers and on day 21 animals were challenged by intravenous inoculation with either 1 × 10⁷ colony forming units (CFU). S. *aureus* Newman. On day 25 (day 5 post challenge) or 35 (day 15 post challenge), animals were killed and both kidneys removed. One kidney was fixed in formaldehyde, embedded in parafin, thin sectioned, hemaotoxylin-cosin stained and four saggital sections per kidney were analyzed for abscess formation. The other kidney was homogenized in PBS buffer, homogenate spread on agar medium for colony formation, and staphylococcal load enumerated as CFU. "Means of staphylococcal load calculated as log₁₀ CFU g⁻¹ in homogenized renal tissues 5 or 15 days following infection in cohorts of 10 BALB/c mice per immunization. Standard error (±SE) is indicated. "Statistical significance was calculated with the unpaired two-tailed Students t-test (t-test) and P-values recorded; P-values < 0.05 were deemed significant.

significant. c Reduction in bacterial load calculated as $\log_{10} \text{CFU g}^{-1}$.

 d Means of three randomly chosen serum IgG titers were measured prior to staphylococcal infection by ELISA with purified recombinant antigen

"Means of mee randomly chosen setuin 1gG mers were measured prior to supproceedent meeting y interval (1 ug m^{-1}) by dilution of serum. (1 $\mu \text{g} \text{m}^{-1})$ by dilution of serum. "Histopathology of hemaloxylene-cosin stained, thin sectioned kidneys from ten animals; the average number of abscesses per kidney was recorded and averaged again for the final mean (\pm SEM). "Statistical significance was calculated with the non-parametric Mann-Whitney test (MWT) and P-values recorded; P-values < 0.05 were

deemed significant.

surface protein, can be used as a protective antigen, Ebh $N_{\rm 40\text{-}2544},$ a recombinant protein spanning the first 2540 resi- 55 dues of mature Ebh, was purified by affinity chromatography from the lysate of E. coli. Purified Ebh N₄₀₋₂₅₄₄ was emulsified in CFA and injected into mice to raise antibodies. Immunized animals were challenged by intravenous inoculation with 1×10^7 CFU S. *aureus* Newman or MRSA strain USA300. Five days after challenge, animals were killed and their kidneys were either analyzed by histopathology for abscess formation or tissue homogenates were spread on agar media to enumerate the bacterial load as CFU. As compared to an adjuvant control (PBS), Ebh immunized mice, which 65 harbored an average titer of 1:150,000 of IgG specific for Ebh N₄₀₋₂₅₄₄, displayed a 2.616 and 0.584 log₁₀ reduction in CFU

The N-terminal domain of Ebh is more than 2500 residues in length and the current vaccine experiments have not determined the types of antibodies that are elicited following immunization and where these antibodies bind. Rather than mapping the binding sites of antibodies that reduce the staphylococcal load, the inventors asked whether specific subdomains of Ebh N40-2544, defined by secondary structure prediction algorithms, can lead to recombinant antigens that achieve equal or greater protection from staphylococcal challenge than the first 2514 residues. Four peptides were tested as vaccines: Ebh1 (40-471), Ebh3 (920-119), Ebh5 (1855-2705), and Ebh₆ (2087-2544). Antibodies raised by immunization of Ebh₁ and Ebh₆ but not antibodies generated by Ebh₃ or Ebh₅-caused a significant reduction in staphylococcal load and a reduction in abscess formation (FIG. 23, Table 10).

TABLE	9
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	Staphylococcal load in kidney tissue*			Abscess formation in kidney tissue*		
Antigen	[⊿] log ₁₀ CFU g ^{−1} of kidney tissue	^b Significance (P-value) t-test	^c Reduction in ^a log ₁₀ CFU g ⁻¹	^e Surface abscesses (%)	^f Number of abscesses per kidney	^g Significance (P-value) MWT
PBS	5.860 ± 0.536	_	_	60	2.3 ± 0.6	_
E1	4.230 ± 0.507	0.0158	1.630	25	0.0 ± 0.0	0.0201
E3	5.045 ± 0.390	0.1417	0.815	15	1.0 ± 1.0	0.2338
E5	4.908 ± 0.458	0.1195	0.952	35	1.5 ± 0.9	0.3719
E6	4.147 ± 0.380	0.0042	1.713	15	0.8 ± 0.5	0.1342

*BALB/c mice (n = 10) were injected with 50 μ g each with purified fragments of Ebh N₄₀₋₂₅₄₄ (E1, E3, E5, E6) emulsified in CFA on day 0 and boosted with the same antigen emulsified in IFA on day 11. On day 20, three animals were examined for IgG antibody titers and on day 21 animals were challenged by intravenous inoculation with either 1 × 10' colony forming units (CFU) *S. aureus* Newman. On day 25 (day 5 post challenge) or 35 (day 15 post challenge), animals were kilded and both kidneys removed. One kidney was fixed in formaldehyde, embedded in paraffin, thin sectioned, hemaotoxylin-cosin stained and four saggital sections per kidney were analyzed for abscess formation. The other kidney was homogenized in PBS buffer, homogenate spread on agar medium for colony formation, and staphylococcal load enumerated as CFU. "Means of staphylococcal load calculated as log₁₀ CFU g⁻¹ in homogenized real tissues 5 or 15 days following infection in colonts of 10 BALB/c mice per immunization. Standard error (45E) is indicated. "Statistical significance was calculated with the unpaired two-tailed Students t-test (t-test) and P-values recorded; P-values <0.05

were deemed significant. "Reduction in bacterial load calculated as \log_{10} CFU g⁻¹.

^dMeans of three randomly chosen serum IgG titers were measured prior to staphylococcal infection by ELISA with purified

recombinant antigen (1 µg ml⁻¹) by dilution of serum. "Histopathology of hematoxylene-cosin stained, thin sectioned kidneys from ten animals; the average number of abscesses per kidney was recorded and averaged again for the final mean (45EM). 'Statistical significance was calculated with the students t-test and P-values recorded; P-values < 0.05 were deemed significant.

Taken together, these data suggest that antibodies against the N-terminal domain of Ebh, specifically residues 40-471 and 2087-2544, can elicit immune responses that confer protection against staphylococcal replication in murine organ 30 tissues and against the establishment of staphylococcal abscess lesions.

I. Materials and Methods

Protein Analysis, Bacterial Strains and Growth

Staphylococcus aureus strains were cultured on tryptic soy 35 agar or in tryptic soy broth at 37° C. Escherichia coli strains DH5 α and BL21 (DE3) were cultured on Luria agar or in Luria broth at 37° C., Ampicillin (100 µg/ml) and erythromycin (10 µg/ml) were used for plasmid and transposon mutant selection, respectively. Protein sequence comparisons were ⁴⁰ done using BLAST on NCBI and EMBL.

Transposon Mutagenesis

Insertional mutations NMTN-9044, 10853, and 15727 from the Phoenix library were transduced into S. aureus Newman (Bae et al., 2004). Each mutant carries the transposon bursa aurealis containing an erythromycin resistance cassette in the gene of interest and mutations were verified as previously described (Bae et al., 2004). Briefly, chromosomal DNA was extracted (Promega Wizard Kit), digested with Acil (NEB), religated with T4 Ligase (Promega) to form individual plasmids, and PCR amplified using Martn-F and Martn-R, primers specific to the transposon bursa aurealis. PCR products were sequenced to verify the site of transposon insertion in the target gene.

Deletion Mutagenesis

DNA sequences 1 kb upstream and downstream of ebh were PCR amplified using the primers attB1_ebh, ebh1 BamHI, ebh2 BamHI, attbB2 ebh (Table 10). The fragments were exchanged onto pKOR1 using the BP clonase II kit (Invitrogen) (Bae et al., 2005). These vectors were electroporated into S. aureus Newman and subjected to temperature shift, which induced allelic exchange to generate the corresponding deletion (Bae et al., 2005). Mutants were verified by PCR amplification of the gene locus, DNA sequencing, and immunoblot analysis.

TABLE 10

	Primers (SEQ ID NO: 167 to SEQ ID NO: 209)
Primer name	sequence
BamHI_emp_F	aaGGATCCgatgaaaaagaaattattagttttaac
BamHI_emp_R	aaGGATCCttatactcgtggtgctggtaag
BamHI_cap_RC_F	aaGGATCCgatgaaatttaagtcattgattacaac
BamHI_cap_R	aaGGATCCgatttattttttttttgatttagtg
P_BamHI_eapRC_F	aaGGTACCgttaaaagtctccagtttggatac
P_PstI_eapR	aaCTGCAGgatttatttattttttttgatttagtg
P_BamHI_empF	aaGGATCCcatggctgcaaagcaaataatg
P_PstI_empR	aaCTGCAGttatactcgtggtgctggtaag
attB1_Coa	GGGGACAAGTTTGTACAAAAAAGCAGGCTgatgactaagttgaaaaaagaag

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TABLE 10-continued

Primers (SEQ ID NO: 167 to SEQ ID NO: 209)					
Primer name					
Coal_BamHI	aaGGATCCcctccaaaatgtaattgccc				
Coa2_BamHI	aaGGATCCgtttgtaactctatccaaagac				
attbB2_Coa	GGGGACCACTTTGTACAAGAAAGCTGGGTgacacctattgcacgattcg				
attB1_vWF	GGGGACAAGTTTGTACAAAAAAGCAGGCTcagatagcgattcagattcag				
vWF1_BamHI	aaGGATCCctgtattttctccttaattttcc				
vWF2_BamHI	aaGGATCCcatggctgcaaagcaaataatg				
attbB2_vWF	GGGGACCACTTTGTACAAGAAAGCTGGGTgccctggtgtaacaaatttatg				
Coa_promoter_BamHI_F	gaaGGATCCgtttattctagttaatatatagttaatg				
Coa_out_PstI_R	gaaCTGCAGctgtatgtctttggatagagttac				
vWbp_promoter_BamHI_F	gaaGGATCCggtggcttttttacttggattttc				
vWbp_out_PstI_R	gaaCTGCAGcgacaaactcattatttgctttgc				
Coa_foward_XhoI	GAACTCGAGTCTAGCTTATTTACATGG				
Coa_Xho_factorXa_F	GAACTCGAGatagaaggcagaatagtaacaaaggattatagtggg				
Coa_reverse_BamHI	GTAGGATCCTGGGATAGAGTTACAAAC				
vWbp_forward_XhoI	GAACTCGAGgcattatgtgtatcacaaatttggg				
vWbp_Xho_factorXa_F	GAACTCGAGatagaaggcagagtggtttctggggagaagaatc				
vWbp_reverse_BamHI	GAACTCGAGgcagccatgcattaattattgcc				
Ebh-1 Fwd XhoI	gaaCTCGAGgctgaaacaaatcaaccagc				
Ebh-1 Rev BglII	agtAGATCTaccattaatatattcaaaattttg				
Ebh-3 Fwd XhoI	gaaCTCGAGggaataaatgccaaatactatc				
Ebh-3 Rev BglII	agtAGATCTaataggttgtccattacttaaag				
Ebh-5 Fwd XhoI	gaaCTCGAGtctgtgacatataaagcagg				
Ebh-5 Rev BglII	agtAGATCTccatgctgcagtgatacc				
Ebh-6 Fwd XhoI	gaaCTCGAGggcgtgcaacatttaaatgtc				
Ebh-6 Rev BglII	agtAGATCTctgcgtaattgtacctggc				
Ebh NT Fwd XhoI	gaaCTCGAGgetgaaacaaateaaceage				
Ebh NT 1st 1/2 BglIIR	agtAGATCTttgtgggaaattaacccaacg				
Ebh NT 2nd 1/2 XhoI	gaaCTCGAGcgttgggttaatttcccacaa				
Ebh NT Fwd Overlap	ccatataactgctacaaatgcg				
Ebh 300 NT++ BglII R	agtAGATCTtttaacagtatttacgccagc				
attB1 EbH	GGGGACAAGTTTGTACAAAAAAGCAGGCTgttagatcaaggctattaacgc				
EbH1 BamHI	ggttCCGCGGggagcaccgattgacatcac				
EbH2 BamHI	ggttCCGCGGctccttatcttgttgttatgtc				
attbB2 EbH	GGGGACCACTTTGTACAAGAAAGCTGGGTqatcaqaattaqqtqtaacctc				

Cloning, Purification, and Antibody Generation

For vaccination studies, full-length coding sequence of Ebh₄₀₋₂₅₄₄ was cloned into pET15b vector using the primers Ebh NT Fwd Xhol, Ebh NT 1st ½ BglIIR, Ebh NT 2nd ½ 65 Xhol, Ebh NT Fwd Overlap, Ebh 300 NT++ BglII R (Table 9) to obtain His6-EbhN. The remaining Ebh primers from Table

9 were used to clone the four fragments of the N terminus (E1, E3, E5, E6). *E. coli* BL21 (DE3) harboring expression vectors were grown at 37° C. and induced with 1 mM IPTG after two hours. Four hours after induction, cells were centrifuged at 6,000×g, supended in 1× column buffer (0.1 M Tris-HCl pH 7.5, 0.5 M NaCl) and lysed in a French press at 14,0000 lb/in².

Lysates were subjected to ultracentrifugation at 40,000×g for 30 min and the supernatant was subjected to Ni-NTA chromatography, washed with column buffer containing 25 µM imidazole, followed by elution with 500 µM imidazole. Eluate was dialyzed against 1×PBS. To remove endotoxin, 1:1, 5 000 Triton-X 114 was added and the solution was chilled for 5 min, incubated at 37° C. for 10 min, and centrifuged at 13,000×g. Supernatant was loaded onto a HiTrap desalting column to remove remnants of Triton-X114. Rabbits (6 month old NewZealand white, female animals) were pur- 10 chased from Charles River Laboratories and immunized with 500 µg protein emulsified in Complete Freund's Adjuvant (Difco) for initial immunization or emulsified in Incomplete Freund's Adjuvant for booster immunizations on day 24 and 48). On day 60, rabbits were bled and serum was recovered 15 after centrifugation of blood at 6,000 rpm for 10 minutes.

Immunoblotting

For immunoblot analysis, overnight cultures of staphylococci grown in tryptic soy broth (Difco) were refreshed 1:100 and grown with shaking at 37° C. until they reached OD_{600} of 20 0.4. One ml of each culture was lysed with addition of 5 µl of lysostaphin from a 2 mg/ml stock, followed by addition of 75 µl of 100% w/v trichloroacetic acid solution. Samples were incubated on ice for 10 min, followed by centrifugation and wash with 1 ml ice-cold 100% acetone. Samples were air dried overnight and solubilized in 50 µl sample buffer (4% SDS, 50 mM Tris-HCl, pH 8.0, 10% glycerol, and bromophenol blue). Protein samples were separated on a 6% acrylamide gel and immunoblotted for Ebh using a primary rabbit antibody and a secondary mouse anti-rabbit alexa fluor-680 conjugated. Gels were viewed using a Li-Cor Odessey machine.

Immunofluorescence Microscopy

For visualization of Ebh, overnight cultures of staphylococci were refreshed and grown to mid-log phase (OD₆₀₀ of 0.4). One ml of culture was centrifuged to sediment bacteria, 35 staphylococci washed in 1×PBS, and fixed (2.5% paraformaldehyde, 0.006% glutaraldehyde in 1×PBS, pH 7.4) for 20 min at room temperature. Cells were washed 3 times with PBS, suspended in 100 µl PBS and a 30 µl droplet was added to a coverslip pre-coated with poly-L Lysine. To pre-coat, 60 40 µl of poly-L lysine solution (Fisher) was placed on glass coverslip (Fisher) for 5 minutes, followed by 3 washes with water. Cells adhering to the coverslip were washed 3 times with 60 µl droplets of PBS (all volumes used hereafter are 60 µl and all washes are with 1×PBS) and placed in blocking 45 solution [3% BSA, 1:200 Human IgG (Sigma), PBS] for 30 minutes. Blocking solution containing specific rabbit antibody (1:1,000) was added to cells and cover slips were incubated for one hour. Cover slips were washed ten times and secondary antibody solution [3% BSA, 1:200 Alexa-Fluor 50 647 mouse anti-rabbit IgG), was added for 1 hour, followed by ten washes. PBS1:200 BOOPIY-vancomycin and 1:1,000 Hoechst dye was added to the cover slips and allowed to incubate for 5 min. Cover slips were washed three times, then mounted on glass slides with N-propylgallate and sealed with 55 nail polish. Slides were stored at 4° C. and images collected with a Leica SP5 AOBS spectral two-photon confocal microscope.

Transmission Electron Microscopy

Staphylococcal cells were cultured to mid-log, centri- 60 fuged, fixed in 3% paraformaldehyde, embedded in epoxy and thin sectioned. Sections were stained with uranyl acetate and then viewed under with a transmission electron microscope.

Oxacillin and Lysostaphin Sensitivity

Overnight cultures of *S. aureus* were normalized to OD₆₀₀ 4.0 and diluted 1:1,000 into TSB containing 2 ng/ml oxacillin. The absorbance at 600 nm was measured for 18 hours in a 96 well plate reader, at 37° C. with constant shaking. For lysostaphin-sensitivity experiments, lysostaphin was purchased from AMBI Products LLC (Lawrence, N.Y.) and stored frozen as a 2 mg/ml stock solution in 0.02 M sodium acetate buffer, pH 4.5. Overnight cultures of staphylococci were washed twice with 50 mM Tris-HCl, pH 8.0, and suspended at an OD₆₀₀ of 1.6. Following addition of 10 μ l of a 100-, 50-, 25-, 12.5-, or 6.25- μ g/ml lysostaphin stock solution to 100 μ l of culture, the decline in optical density was recorded.

Biofilm Formation

USA300 S. aureus strains were grown overnight in TSB at 37° C. without shaking, then refreshed 1:10 into fresh media in 96 well flat-bottomed plates (Costar) fibronectin precoated plates. Plates were coated with 1 µg/ml fibronectin (Fisher stock) in coating buffer (10 mM Na₂HCO₃, pH 8.3) at 4° C. overnight. These plates were incubated statically at 37° C. in 24 hours. S. aureus Newman strains were grown in Chelex (Sigma) treated RPMI 1640 (Gibco) supplemented with 10% RPMI 1640 and 1% casamino acids (Difco). Overnight cultures were grown without rotation at 37° C. in 6% CO₂, then inoculated 1:10 in quadruplicate into 96-well flatbottomed tissue culture plates (Costar) containing fresh media. These plates were incubated statically at 37° C. in 6% CO₂ for 24 hours. For all plates, wells were washed three times with 1×PBS, dried for 2 hours at 37° C., and stained with 1% safranin. Absorbance at 450 nm was measured to quantify biofilm formation. Each strain was tested in triplicate wells for at least 3 separate experiments and a two-tailed Student t test was employed.

Blood and Plasma Survival Assays

Overnight cultures of staphylococcal strains were diluted 1:100 into fresh TSB and grown at 37° C. until they reached an OD₆₀₀ 0.4. One ml of culture was washed and suspended in 1 ml PBS to obtain a 1×10^8 cfu/ml bacterial stock. Whole blood from naive 6 week old BALB/c mice was collected and REFLUDAN™ (lepirudin, Bayer) was added to a final concentration 50 µg/ml. To obtain plasma, whole blood was centrifuged at 8,000 rpm for 3 min to sediment host cells, supernatant was collected as fresh plasma. Some plasma was heat inactivated at 60° C. for 30 minutes with occasional mixing. 450 µL blood or plasma was aliquoted into a 1 ml eppendorf tube and mixed with 50 µl bacterial stock to a final concentration of 5×10⁶ CFU/ml. Samples were incubated at 37° C. with slow rotation. 50 µl aliquots were removed at times 0 min and 30 min, mixed 1:1 with 2% saponin/PBS and incubated on ice for 30 minutes. Five 1:10 serial dilutions were prepared and 10 µl aliquots spread on TSA agar for colony formation and enumeration.

Complement Deposition Assay

S. aureus suspension $(1 \times 10^7 \text{ cfu/ml} \text{ from previously})$ described bacterial stock solution) was incubated in PBS containing 10% human plasma at a final volume of 1 ml. Reactions were incubated at 37° C. with end over end rotation and aliquots of 100 µl were removed and quenched 1:10 in ice-cold PBS at 5 min intervals. Samples were washed three times with PBS labeled with anti-C3 FITC tagged antibody, washed three more times, fixed in 4% formalin, and viewed with a LSRII FACS machine.

Renal Abscess Model and Lethal Challenge

Overnight cultures of staphylococcal strains were diluted 1:100 into fresh TSB and grown until they reached an OD_{600} of 0.4. Cells were centrifuged at 7,500×g, washed, and resuspended in 1×PBS. Six week-old female BALB/c mice (Charles River) were injected retro-orbitally with 5×10⁶ CFU (USA300) staphylococcal suspension in 100 µl of PBS.

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Cohorts of 10 mice were used. On the fifth or fifteenth day post infection, these mice were killed by CO₂ asphyxiation and their kidneys were excised. All organs were examined for surface lesions and 8-10 right kidneys were analyzed for histopathology by staining thin-sectioned paraffin-embedded 5 tissues with hematoxylin-eosin. These slides were examined by light microscopy for abscess formation. For the lethal challenge model, all experimental conditions remain the same except that 5×10^7 CFU (USA300) staphylococci were administered and that the mice were monitored for 10 days 10 post infection for survival.

Active Immunization

Three week old BALB/c mice were injected with 50 µg protein each emulsified in 100 µl CFA. Cohorts of 10 mice were used, with 5 mice reserved for bleeding and antibody 15 titers. Eleven days post vaccination these mice were boosted with 50 µg protein each emulsified in 100 µl IFA. On day 20, 3 randomly chosen mice per cohort were bled for antibody titers. On day 21, mice were injected with 1×10^7 CFU of staphylococci for the renal abscess model or 1×10^8 CFU for 20lethal challenge. At the time of infection, 5 mice were bled to obtain antibody titers.

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	450 Lys	Ile	Tyr	Arg		455 Pro	Glu	Gly	Tyr		460 Leu	Asn	Lys	Gly	-	
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-				485	-		Gln	-	490		-			495		
-			500	-			Met	505				-	510	-	-	
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Leu	Thr 770	Thr	Thr	Gly	Val	Ile 775	Asn	Gly	Ala	Asp	Asn 780	Met	Thr	Leu	Asp
Ser 785	Gly	Phe	Tyr	Lya	Thr 790	Pro	Lys	Tyr	Asn	Leu 795	Gly	Asn	Tyr	Val	Trp 800
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Ser	Asn 1025	-	a yab	ρ Glչ	/ Lуа	Gli 103		∋p S∢	er Th	nr G		ys (035	Gly :	Ile 1	Lys
Asp	Val 1040	-	8 Val	L Il€	e Leu	1 Leu 104		en G	lu Ly	∕s Gi	-	lu ' 050	Val :	Ile (Gly
Thr	Thr 1059	-	; Thi	r Asī	Glu	1 Ası 106		ly Ly	ya Ty	yr A:	-	he 2 065	Aap i	Asn 1	Leu
Asp	Ser 1070		и Гле	з Туз	: Lys	9 Va 10		le Pl	ne Gl	lu Ly		ro ' 080	Thr (Gly 1	Leu
Thr	Gln 1085		r Gly	/ Thi	: Asr	n Thi 109		nr G	lu A:	ap Ai		ys 1 095	Asp i	Ala i	Asp
Gly	Gly 1100		ı Val	l Asp	va]	. Th: 110		le Tì	nr Af	зр Н:		sp 1	Asp 1	Phe '	Thr

Leu Asp Asn Gly Tyr Tyr Glu Glu Glu Thr Ser Asp Ser Asp Ser 1115 1120 1125	
Asp Ser Asp Ser Asp Ser Asp Ser Asp Ser Asp Ser Asp 1130 1135 1140	
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Asp Ser Asp Ser Asp Ser Asp Ser Asp Ser Asp Ser Asp 1160 1165 1170	
Ser Asp Ser 1175 1180 1185	
Asp Ser Asp 1190 1195 1200	
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Asp Ser Asp Ser Asp Ser Asp Ser Asp Ser Asp Ser Asp 1250 1255 1260	
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Glv	450 Ser	Gln	Val	Asp	Asp	455 Tyr	Glv	Asn	Ile	Lvs	460 Leu	Glv	Asn	Gly	Ser
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Glu Asp Val Thr Ser Gln Phe Asp Asn Lys Lys Ser Phe Ser Asn 515 520 525	ı Asn
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Gln Gly Thr Ser Met Arg Thr Thr Asp Lys Tyr Gly Tyr Tyr Asr 565 570 579	-
Ala Gly Tyr Ser Asn Phe Ile Val Thr Ser Asn Asp Thr Gly Gly 580 585 590	/ Gly
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Glu Lys Pro Met Ala Asn Val Leu Val Thr Leu Thr Tyr Pro Asp 625 630 635	Gly 640
Thr Thr Lys Ser Val Arg Thr Asp Ala Asn Gly His Tyr Glu Phe 645 650 659	
Gly Leu Lys Asp Gly Glu Thr Tyr Thr Val Lys Phe Glu Thr Pro 660 665 670	> Ala
Gly Tyr Leu Pro Thr Lys Val Asn Gly Thr Thr Asp Gly Glu Lys 675 680 685	a Yab
Ser Asn Gly Ser Ser Ile Thr Val Lys Ile Asn Gly Lys Asp Asp 690 695 700) Met
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Tyr Val Trp Glu Asp Thr Asn Lys Asp Gly Ile Gln Asp Ala Asp 725 730 739	
Pro Gly Ile Lys Asp Val Lys Val Thr Leu Lys Asp Ser Thr Gly 740 745 750	/ Lys
Val Ile Gly Thr Thr Thr Thr Asp Ala Ser Gly Lys Tyr Lys Phe 755 760 765	e Thr
Asp Leu Asp Asn Gly Asn Tyr Thr Val Glu Phe Glu Thr Pro Ala 770 775 780	a Gly
Tyr Thr Pro Thr Val Lys Asn Thr Thr Ala Glu Asp Lys Asp Ser 785 790 795	7 Asn 800
Gly Leu Thr Thr Gly Val Ile Lys Asp Ala Asp Asn Met Thu 805 810 815	
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Gln Thr Val Thr Asn Thr Thr Glu Asp Asp Lys Asp Ala Asp Gly 900 905 910	/ Gly

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Ser	Asp 1025		: Asj	p Sei	r Asp	Sei 103		ap Se	er A	ap S		4ap 035	Ser	Asp	Ser
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Lys	His 1085		r Pro	o Val	l Lys	9 Pro 109		et Se	er Tl	hr T		ув .095	Asp	His	His
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His Thr Gln Ser Gln Asn Asn Lys Asn Thr Gln Glu Asn Lys Ala Lys Ser Leu Pro Gln Thr Gly Glu Glu Ser Asn Lys Asp Met Thr Leu Pro Leu Met Ala Leu Leu Ala Leu Ser Ser Ile Val Ala Phe Val Leu Pro Arg Lys Arg Lys Asn <210> SEQ ID NO 17 <211> LENGTH: 80 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 17 Met Asn Gln His Val Lys Val Thr Phe Asp Phe Thr Asn Tyr Asn Tyr Gly Thr Tyr Asp Leu Ala Val Pro Ala Tyr Leu Pro Ile Lys Asn Leu 20 25 30 Ile Ala Leu Val Leu Asp Ser Leu Asp Ile Ser Ile Phe Asp Val Asn Thr Gln Ile Lys Val Met Thr Lys Gly Gln Leu Leu Val Glu Asn Asp Arg Leu Ile Asp Tyr Gln Ile Ala Asp Gly Asp Ile Leu Lys Leu Leu <210> SEQ ID NO 18 <211> LENGTH: 877 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 18 Met Lys Lys Arg Ile Asp Tyr Leu Ser Asn Lys Gln Asn Lys Tyr Ser Ile Arg Arg Phe Thr Val Gly Thr Thr Ser Val Ile Val Gly Ala Thr Ile Leu Phe Gly Ile Gly Asn His Gln Ala Gln Ala Ser Glu Gln Ser Asn Asp Thr Thr Gln Ser Ser Lys Asn Asn Ala Ser Ala Asp Ser Glu Lys Asn Asn Met Ile Glu Thr Pro Gln Leu Asn Thr Thr Ala Asn Asp Thr Ser Asp Ile Ser Ala Asn Thr Asn Ser Ala Asn Val Asp Ser Thr Thr Lys Pro Met Ser Thr Gln Thr Ser Asn Thr Thr Thr Glu Pro Ala Ser Thr Asn Glu Thr Pro Gln Pro Thr Ala Ile Lys Asn Gln Ala Thr Ala Ala Lys Met Gln Asp Gln Thr Val Pro Gln Glu Ala Asn Ser Gln Val Asp Asn Lys Thr Thr Asn Asp Ala Asn Ser Ile Ala Thr Asn Ser Glu Leu Lys Asn Ser Gln Thr Leu Asp Leu Pro Gln Ser Ser Pro Gln Thr Ile Ser Asn Ala Gln Gly Thr Ser Lys Pro Ser Val Arg Thr

Arg	Ala	Val 195	Arg	Ser	Leu	Ala	Val 200	Ala	Glu	Pro	Val	Val 205	Asn	Ala	Ala
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Phe	Thr	Ala	Lys 260	Leu	Pro	Asp	Ser	Leu 265	Thr	Gly	Asn	Gly	Asp 270	Val	Asp
Tyr	Ser	Asn 275	Ser	Asn	Asn	Thr	Met 280	Pro	Ile	Ala	Asp	Ile 285	ГЛа	Ser	Thr
Asn	Gly 290	Asp	Val	Val	Ala	Lys 295	Ala	Thr	Tyr	Asp	Ile 300	Leu	Thr	ГÀа	Thr
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Gly	Gln	Phe	Ser	Leu 325	Pro	Leu	Phe	Thr	Asp 330	Arg	Ala	ГЛЗ	Ala	Pro 335	Lys
Ser	Gly	Thr	Tyr 340	Asp	Ala	Asn	Ile	Asn 345	Ile	Ala	Asp	Glu	Met 350	Phe	Asn
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Ile	Phe	Glu 435	Val	Asn	Asp	Thr	Ser 440	Lys	Leu	Ser	Asp	Ser 445	Tyr	Tyr	Ala
Asp	Pro 450	Asn	Asp	Ser	Asn	Leu 455	ГЛЗ	Glu	Val	Thr	Asp 460	Gln	Phe	Lys	Asn
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Asp	Ser	Glu 675	Ser	Asp	Ser	Asp	Ser 680	Aap	Ser	Aap	Ser	Asp 685	Ser	Asp	Ser
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Asp	Ser 770	Asp	Ser	Asp	Ser	Asp 775	Ser	Aab	Ser	Asp	Ser 780	Asp	Ser	Asp	Ser
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Ser	Asn	Pro	Lys 820	Gly	Glu	Val	Asn	His 825	Ser	Asn	Lys	Val	Ser 830	Lys	Gln
His	Lys	Thr 835	Asp	Ala	Leu	Pro	Glu 840	Thr	Gly	Asp	Lys	Ser 845	Glu	Asn	Thr
Asn	Ala 850	Thr	Leu	Phe	Gly	Ala 855	Met	Met	Ala	Leu	Leu 860	Gly	Ser	Leu	Leu
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Lys 65	Leu	Tyr	Val	Gln	Ile 70	Thr	Val	Asn	His	Ser 75	His	Trp	Ile	Thr	Gly 80
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Larc	Acr	G1.,	۸ra		Sor	G1.,	Dho	G1.,		Sor	Larc	Ler	Agr		Lare
пуя	чаh	GIU	Arg 100	1111	ser	GIU	FIIG	Glu 105	vai	Set	пув	цец	Asn 110	σтү	цур

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Ile	Asp	Gly 115	Lys	Ile	Asp	Val	Tyr 120	Ile	Asp	Glu	Гла	Val 125	Asn	Gly	Гуз
Pro	Phe 130	Lys	Tyr	Asp	His	His 135	Tyr	Asn	Ile	Thr	Tyr 140	Гла	Phe	Asn	Gly
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Ser	Ala	Ser	Gly	Ser 165	Asp	ГЛа	Gly	Ser	Asp 170	Gly	Thr	Thr	Thr	Gly 175	Gln
Ser	Glu	Ser	Asn 180	Ser	Ser	Asn	Гла	Asp 185	Lys	Val	Glu	Asn	Pro 190	Gln	Thr
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Tyr	Asb	Ala 35	Gln	Ala	Ala	Ser	Glu 40	Lys	Asp	Thr	Glu	Ile 45	Ser	ГÀа	Glu
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	Ala			85					90					95	
	Lys		100					105					110		
		115		-			120		-		-	125	_		
	Lys 130					135					140				
145	Gly				150				-	155	_				160
Ala	Thr	Thr	Lys	Tyr 165	Gly	Glu	Lys	Asp	Asp 170	Lys	Asn	Asp	Glu	Ala 175	Met
Val	Asn	Lys	Ala 180	Leu	Glu	Asp	Leu	Asp 185	His	Leu	Asn	Gln	Gln 190	Ile	His
Lys	Ser	Lys 195	Asp	Ala	Leu	Lys	Asp 200	Ala	Ser	Lys	Asp	Pro 205	Ala	Val	Ser

Thr Thr Asp Ser Asn His Glu Val Ala Lys Thr Pro Asn Asn Asp Gly Ser Gly His Val Val Leu Asn Lys Phe Leu Ser Asn Glu Glu Asn Gln

Ser His Ser Asn Gln Leu Thr Asp Lys Leu Gln Gly Ser Asp Lys Ile

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Glu 305	Val	Asn	Lys	Thr	Lys 310	Glu	Arg	Ile	Lys	Ser 315	Gln	Arg	Asn	Ile	Ile 320
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Lys	Ala 450	Ile	Leu	Asn	Asn	Ala 455	Lys	Asp	Lys	ГÀа	Gln 460	Ala	Ile	Glu	Thr
Ile 465	Leu	Ala	Thr	Arg	Ile 470	Glu	Arg	Gln	Lys	Ala 475	Lys	Leu	Leu	Ala	Asp 480
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Val	Asn 530	Arg	Pro	Ser	Leu	Leu 535	Asp	Arg	Leu	Asn	Lys 540	Asn	Gly	Lys	Thr
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Ser	Pro	Gln 115	Asn	Ala	Thr	Ala	Ser 120	Gln	Ser	Thr	Thr	Gln 125	Thr	Ser	Asn
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-															
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Ala	Lys	Ala 915	Leu	Pro	Glu	Thr	Gly 920	Ser	Glu	Asn	Asn	Asn 925	Ser	Asn	Asn
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		35			-		40	Glu				45			-
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Ala	Thr 130	Thr	Gln	Ser	Ser	Asn 135	Thr	Asn	Ala	Glu	Glu 140	Leu	Val	Asn	Gln
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Vol	ጥሎ~	T] -	N an	Cor	a 1	mlari	mla r-	17-7	m ••••	Date	The c	01 m	71.0	a 1	(T)= 1.00

Val Thr Ile Asp Ser Gly Thr Thr Val Tyr Pro His Gln Ala Gly Tyr

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Ser Asp Ser Asp

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Val	His	Val	Pro	Tyr	Ala	Ile	Thr	Val	Asn	Gly	Thr	Ser	Gln	Asn	Ile

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Asp	Arg	Gly	Ile 420	Gly	Glu	Arg	Glu	Leu 425	Lys	Tyr	Ala	Гла	Lys 430	Ala	Thr
Tyr	Thr	Val 435	His	Phe	Lys	Asn	Gly 440	Thr	Lys	Lys	Val	Ile 445	Asn	Ile	Asn
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Val Pro Tyr Thr Ile Ala Val Asn Gly Thr Ser Thr Pro Ile Leu Ser Lys Leu Lys Ile Ser As
n Lys Gl
n Leu Ile Ser Tyr Lys Tyr Leu As
n $% \left({{\mathbb{F}} {\mathbb{F}} {\mathbb{F}}$ Asp Lys Val Lys Ser Val Leu Lys Ser Glu Arg Gly Ile Ser Asp Leu Asp Leu Lys Phe Ala Lys Gln Ala Lys Tyr Thr Val Tyr Phe Lys Asn Gly Lys Lys Gln Val Val Asn Leu Lys Ser Asp Ile Phe Thr Pro Asn Leu Phe Ser Ala Lys Asp Ile Lys Lys Ile Asp Ile Asp Val Lys Gln Tyr Thr Lys Ser Lys Lys Asn Lys <210> SEQ ID NO 24 <211> LENGTH: 10419 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 24 Met Asn Tyr Arg Asp Lys Ile Gln Lys Phe Ser Ile Arg Lys Tyr Thr Val Gly Thr Phe Ser Thr Val Ile Ala Thr Leu Val Phe Leu Gly Phe Asn Thr Ser Gln Ala His Ala Ala Glu Thr Asn Gln Pro Ala Ser Val Val Lys Gln Lys Gln Gln Ser Asn Asn Glu Gln Thr Glu Asn Arg Glu Ser Gln Val Gln Asn Ser Gln Asn Ser Gln Asn Gly Gln Ser Leu Ser Ala Thr His Glu Asn Glu Gln Pro Asn Ile Ser Gln Ala Asn Leu Val Asp Gln Lys Val Ala Gln Ser Ser Thr Thr Asn Asp Glu Gln Pro Ala Ser Gln Asn Val Asn Thr Lys Lys Asp Ser Ala Thr Ala Ala Thr Thr Gln Pro Asp Lys Glu Gln Ser Lys His Lys Gln Asn Glu Ser Gln Ser Ala Asn Lys Asn Gly Asn Asp Asn Arg Ala Ala His Val Glu Asn His Glu Ala Asn Val Val Thr Ala Ser Asp Ser Ser Asp Asn Gly Asn Val Gln His Asp Arg Asn Glu Leu Gln Ala Phe Phe Asp Ala Asn Tyr His Asp Tyr Arg Phe Ile Asp Arg Glu Asn Ala Asp Ser Gly Thr Phe Asn Tyr Val Lys Gly Ile Phe Asp Lys Ile Asn Thr Leu Leu Gly Ser Asn Asp Pro Ile Asn Asn Lys Asp Leu Gln Leu Ala Tyr Lys Glu Leu Glu Gln Ala Val Ala Leu Ile Arg Thr Met Pro Gln Arg Gln Gln Thr Ser Arg Arg Ser Asn Arg Ile Gln Thr Arg Ser Val Glu Ser Arg Ala Ala

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			260					265					270			
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Asn	Gln 1055		n Ile	e Arg	g Gly	7 Ty: 106		eu Al	la Se	er Tl		ap 1 065	Pro N	/al '	Ihr
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Thr	Val 1625	Pro	Asn	Arg	Ser	Tyr 1630	Ala	Arg	Ala	Ser	Ala 1635	Asn	Glu	Ile
Thr	Ser 1640	-	Thr	Val	Ser	Asn 1645		Ser	Arg	Thr	Gly 1650	Asn	Asn	Ala
Asn	Val 1655	Thr	Val	Thr	Val	Thr 1660	-	Gln	Asp	Gly	Thr 1665	Thr	Ser	Thr
Val	Thr 1670	Val	Pro	Val	ГЛа	His 1675	Val	Ile	Pro	Glu	Ile 1680	Val	Ala	His
Ser	His 1685	-	Thr	Val	Gln	Gly 1690	Gln	Asp	Phe	Pro	Ala 1695	Gly	Asn	Gly
Ser	Ser 1700	Ala	Ser	Asp	Tyr	Phe 1705	-	Leu	Ser	Asn	Gly 1710	Ser	Asp	Ile
Ala	Asp 1715	Ala	Thr	Ile	Thr	Trp 1720	Val	Ser	Gly	Gln	Ala 1725	Pro	Asn	Lys
	1730					Glu 1735					1740			
	1745	-	•			Thr 1750				•	1755			-
-	1760		0			Pro 1765	•				1770			
-	1775		-		-	Val 1780				-	1785		-	
-	1790	-				Asn 1795					1800			
	1805					Gly 1810		-	-		1815	-	_	
Val	Gly 1820				Ū	Leu 1825					1830	-		-
Gln	Thr 1835	Glu	Asp	Leu	Thr	Ile 1840	Leu	Ser	Lys	Val	Lys 1845	Pro	Asp	Pro
Pro	Arg 1850	Ile	Asp	Ala	Asn	Ser 1855	Val	Thr	Tyr	ГÀа	Ala 1860	Gly	Leu	Thr
Asn	Gln 1865	Glu	Ile	Lys	Val	Asn 1870	Asn	Val	Leu	Asn	Asn 1875	Ser	Ser	Val
Lys	Leu 1880	Phe	Lys	Ala	Asp	Asn 1885	Thr	Pro	Leu	Asn	Val 1890	Thr	Asn	Ile

Iner Higs Gly Ser Gly Pe Ser Val Val Val Th Yas Ser Arp Ala Leu Pio An Gly Gly Ile Lys Ala Lys Ser Ser Ile Ser Met Asn Man Yas Thr Tyr Thr Th Gln Arp Ser Asn Ap Ser Ala Thr Val Yas Thr Arg An Glu Ser Yal Arp Arn Glu Ser Yal Arp Arn Glu Glu Ha Yal Yas Thr Pro Glu Arp Arp Arn Glu Ser Yal Arp Arn Glu Glu Glu Arp Arp Arn Glu Ser Yal Arp Arp Arn Glu Ser Yal Arp Arp Arn Glu Ser Yal Yal Yal Glu Arp Pro Yal	_														
1910 1915 1920 Asn Yal Thr Tyr Thr Thr Glu His Glu Glu His His <t< td=""><td>Thr</td><td></td><td>Gly</td><td>Ser</td><td>Gly</td><td>Phe</td><td></td><td>Ser</td><td>Val</td><td>Val</td><td>Thr</td><td></td><td>Ser</td><td>Asp</td><td>Ala</td></t<>	Thr		Gly	Ser	Gly	Phe		Ser	Val	Val	Thr		Ser	Asp	Ala
1925 1930 1933 1935 Val Årg <	Leu		Asn	Gly	Gly	Ile		Ala	Гла	Ser	Ser		Ser	Met	Asn
1940 1945 1950 Thr Yab Thr Pro Gln Leu Gln Ala Thr Thr Gln Gln <td>Asn</td> <td></td> <td>Thr</td> <td>Tyr</td> <td>Thr</td> <td>Thr</td> <td></td> <td>Asp</td> <td>Glu</td> <td>His</td> <td>Gly</td> <td></td> <td>Val</td> <td>Val</td> <td>Thr</td>	Asn		Thr	Tyr	Thr	Thr		Asp	Glu	His	Gly		Val	Val	Thr
1965 1960 1965 1965 11e 1969 619 619 619 619 619 619 610 743	Val		Arg	Asn	Glu	Ser		Asp	Ser	Asn	Asp		Ala	Thr	Val
1970 1975 1980 11e Gln Asn Pro Pro His Gly Ala Thr Val Ala Trp His Asp Ser Pro Asp Thr Lup Asn Thr Quo Thr Thr Lup Asn Thr Ala Asp Thr Asp Ser Val Val Thr Lup Pro Asn Gly Gln Gly Thr Arg Asp Val Gly Gln Asp Ala Asp Ala Asp Ala Asp Ala Asp Ala Met Asp 2030 Ur Gly Gln Asp Leu Asp	Thr		Thr	Pro	Gln	Leu		Ala	Thr	Thr	Glu		Ala	Val	Phe
1995 1996 1995 Pro Åsop Thr Trp Lys Asn Thr Suo Suo Thr His Lys Thr Asn Thr Suo Suo </td <td>Ile</td> <td></td> <td>Gly</td> <td>Gly</td> <td>Asp</td> <td>Gly</td> <td></td> <td>Asp</td> <td>Phe</td> <td>Gly</td> <td>His</td> <td></td> <td>Glu</td> <td>Arg</td> <td>Phe</td>	Ile		Gly	Gly	Asp	Gly		Asp	Phe	Gly	His		Glu	Arg	Phe
2000 2005 2010 Val Val Thr Leu Pro Asn Gly Gln Gly Thr Arg Asn Val Yal Glu Val Pro Val Lys Val Tyr Pro Val Ala Asn Ala Lys Ala Pro Ser Arg 2030 Us Gly Gln Asn Lys Ala Pro Ser Arg 2045 Lys Gly Gln Asn Lys Thr Asn <	Ile		Asn	Pro	Pro	His		Ala	Thr	Val	Ala		His	Asp	Ser
2015 2020 2025 Pro Val Lys Val Tyr Pro Val Aas Ass Ala Lys Ala Pro Ser Arg Asp Val Lys Gly Gln Ass Leu Thr Ass Gly Thr Ass Ala Lys Ala Met Ass Tyr Lle Thr Pro Ass Chr Ass Gly Thr Ala Met Ass Ala Trp Ala Ass Arg Cols Thr Ass Gly Thr Ass Ass Cols Thr Ass Gly Thr Tyr Fo Gly Thr Ass Gly Thr Thr Thr Thr <	Pro		Thr	Trp	Lys	Asn		Val	Gly	Asn	Thr		Lya	Thr	Ala
2030 2035 2040 2040 Asp Val Lys Gly Gln Asn Leu Thr Asn Gly Gl Thr Asn Thr Asn Gly Gln Ala Asn Asn Close Asn Gl Gln Asn Gln Asn Close Asn Asn Close Asn Asn Close Asn Ala Close Asn Asn Close Asn Ala Close Ala Asn Close Ala Asn Close Ala Asn Close Ala Ala Close Ala Ala Close Ala Ala Close Ala Sloe Close Close Close Clos	Val		Thr	Leu	Pro	Asn		Gln	Gly	Thr	Arg		Val	Glu	Val
2045 2050 2057 Tyr Ile Thr Phe Asp Pro Asn Thr Asn Thr Asn Gly Ile Thr Ala Ala Trp Ala Asn Arg Gln Gln 2000 Pro Asn Asn Gln Gln Gln 2070 Ile Thr Ala Gly 2080 Pro Asn Asn Gly 2080 Pro Asn Asn Gly 2080 Pro 2010 Pro 2010 Pro 2110 Pro 2110 Pro 2110	Pro		Гла	Val	Tyr	Pro		Ala	Asn	Ala	Гла		Pro	Ser	Arg
2060 2065 2070 Ala Trp 2075 Ala Asn Arg Gln Gln 2080 Pro Asn Asn Gln Gln 2085 Ala Gln 2085 Ala Gln 2085 Ala Gln 2085 Asn Asn Gln Gln 2085 Ala Gln 2085 Ala Ala Ala Ala Gln 2090 Cu Asn Val Asp 2095 Thr Tyr Pro Gly 11e Ser Ala Ala Lys Arg 2090 Val Pro Val Thr Thr 2010 Asn Val Tyr Bin 2095 Thr Tyr Gly 2110 Ser Ala Ala Ala Lys Arg 2005 Val Pro Val Thr Thr 101 Asn Tyr Ann Gly 2115 Gly 2115 Gly 2115 Gly 2115 Ala Ser Gly 2115 Thr 2120 Thr 30 Asn 3 Fyr 41a Asn 7yr 41a His 8 Gly 214 Gly 214 Gly 2145	Asp		Гла	Gly	Gln	Asn		Thr	Asn	Gly	Thr		Ala	Met	Asn
2075 2080 2085 Gln His Leu Asn Val Asp 2095 Thr Tyr Pro Gly Ile Ser Ala Ala Lys Arg Val Pro Val Thr Val Asn Val Tyr Gln Phe Glu Phe Pro Gln Thr Thr Thr Thr Val Gly Glu Phe Pho <	Tyr			Phe	Asp	Pro		Thr	Asn	Thr	Asn		Ile	Thr	Ala
2090 2095 2100 Lys Arg Val Pro Val Thr Val Asn Val Tyr Gln Phe Glu Phe Pro Gln Thr Thr Thr Thr Thr Thr Thr Thr Thr Ala Ser Gly Gln Thr Ala Ser Gly Tyr Ala Ser Gly Thr Gln Ala Ser Gly Tyr Ala Ser Gly Thr Gln Ala Ser Gly Tyr Ala Ser Gly Lyr Ala Ser Gly Lyr Ala Ser Gly Lyr Ala Ser Gly Lyr Ala Ser Ala Ser Ala Ser Arr Arr <t< td=""><td>Ala</td><td></td><td>Ala</td><td>Asn</td><td>Arg</td><td>Gln</td><td></td><td>Pro</td><td>Asn</td><td>Asn</td><td>Gln</td><td></td><td>Ala</td><td>Gly</td><td>Val</td></t<>	Ala		Ala	Asn	Arg	Gln		Pro	Asn	Asn	Gln		Ala	Gly	Val
210521102115GlnThrThrTyrThrThrThr2125ValGlyGlyThrLeuAlaSerGlyThrGlnAlaSerGlyTyrAlaClyThrCluAlaSerGlyLeuThrGlnAlaSerGlyTyrAlaMisMetGlnAsnAlaSerGlyLeuProThrAspGlyPheThrTyrAlaMetGlnAsnAlaSerGlyLeuThrAspAspAlaAsnTrpSerAlaMetAsnLysProAsnAlaAsnAlaLysValAspAlaAsnTrpSerAlaMetAsnLysProAsnValAlaLysValValAsnAlaLysTyrAspValAsnAsnAspAspValAsnAspLysValValAsnAsnLysSerValIleTyrAsnAspAspIleTyrAspAspValAspValAspAspValAspAspValAspAspValAspAspValAsp <t< td=""><td>Gln</td><td></td><td>Leu</td><td>Asn</td><td>Val</td><td>Asp</td><td></td><td>Thr</td><td>Tyr</td><td>Pro</td><td>Gly</td><td></td><td>Ser</td><td>Ala</td><td>Ala</td></t<>	Gln		Leu	Asn	Val	Asp		Thr	Tyr	Pro	Gly		Ser	Ala	Ala
212021252130ThrGlnAlaSerGlyTyrAlaHisMetGlnAsnAlaThrGlyLeuProThrAspGlyPheThrTyrLysTrpAsnAspAspThrGlyLeuThrAsnAspAlaAsnTrpSerAlaMetAsnLysProAsnAlaLysValAspAlaAsnTrpSerAlaMetAsnLysProAsnAlaLysValValAsnAlaLysTyrAsnLysProAsnValAlaLysValValAsnAlaLysProAsnAsnAsnProAsnAsnLysValValAsnAsnLysProAsnAsnProAsnAsnProAlaSerLysProValAsnLysProAsnAsnAsnProAlaSerLysProValIleTyrAsnAsnAsnProProAlaLysProThrValAsnCluValAsnAsnAsnAsnProAlaLysProThrAlaAsnCluThrAlaAsnAsnProProAlaLysProThrAlaAsnCluAlaAsnPro <td< td=""><td>Lys</td><td></td><td>Val</td><td>Pro</td><td>Val</td><td>Thr</td><td></td><td>Asn</td><td>Val</td><td>Tyr</td><td>Gln</td><td></td><td>Glu</td><td>Phe</td><td>Pro</td></td<>	Lys		Val	Pro	Val	Thr		Asn	Val	Tyr	Gln		Glu	Phe	Pro
213521402145ProThrAspGlyPheThrTyrLysTrpAsnArgAspThrThrGlyThrAsnAspAlaAsnTrpSerAlaMetAsnLysProAsnAlaLysValAsnAsnAsnTyrSerValMetAsnLysPro2170AsnValAlaLysValValAsnAlaLysTyrAsnLysProSerValAlaPheAlaValAsnAsnLysTyrAspValIleTyrAsnGlyHisThrPhoAlaValAsnAsnLysTyrAspValIleTyrAspGlyHisThrPhoAlaSerValIleTyrAsnLysAspValGlyAspIlePhoAlaSerValIleTyrAspClyAspIleThrPhoAlaSerFroThrValAspIleTyrAspIleThrPhoAlaSerFroThrValAspIleTyrAspIleThrPhoAlaSerFroThrValAspIleAspIleThrIleAspPhoAlaSerFroThrValAspIle <t< td=""><td>Gln</td><td></td><td>Thr</td><td>Tyr</td><td>Thr</td><td>Thr</td><td></td><td>Val</td><td>Gly</td><td>Gly</td><td>Thr</td><td></td><td>Ala</td><td>Ser</td><td>Gly</td></t<>	Gln		Thr	Tyr	Thr	Thr		Val	Gly	Gly	Thr		Ala	Ser	Gly
215021552160ThrAsnAspAlaAsnTrpSer 2170AlaMetAsnLysPro 2175AsnValAlaLysVal 2180ValAsnAlaLysTyr 2185AspValIleTyr 2195AsnGlyHisThrPheAla 2195ThrSerLeuPro 2200AlaLysProIleTyr 2195AspValGlyPheAla 2195ThrSerLusPheValValLys 2205AspValGlnPro 22195Ala 22195LysPro 22195ThrValAlaAlaGlyAlaIleThrPhe 22195Ala 22195LysPro 22195ThrValAspIleThrAlaAlaGlyAlaIlePro 22195Ala 22195LysPro 22195Pro 22195ThrCluThrAlaAlaCluAlaIleThrPro 22195Ala 22195Pro 22195Pro 22195ThrValAsn 22195ThrAlaAlaIleThrPro 22195Ala 22195Pro 22195Pro 22195Pro 22195ThrAlaAlaAlaAlaAlaPro 22195Ala 22195Pro 22195Pro 22195Pro 22195Pro 22195AlaAlaAlaAlaAla	Thr		Ala	Ser	Gly	Tyr		His	Met	Gln	Asn		Thr	Gly	Leu
2165 2170 2175 Lys Val Val Asn Ala Lys Tyr Asn I Tyr San I Tyr Asn Asn I San Val I Tyr Asn Asn I San Val I I San Val I I San Val I I San Asn I	Pro		Asp	Gly	Phe	Thr		Lys	Trp	Asn	Arg		Thr	Thr	Gly
218021852190PheAlaThrSerLeuProAlaLysPheValLysAspValGlnProAlaLysProThrValThrAlaAlaGlyAlaIleThrProAlaLysProThrValThrAlaAlaGlyAlaIleThrIleAlaLysProGlyAlaAsnGlyThrValAsnThrLysAlaGlyAsnValThrThrTyrAlaAspLysLeuValIleLysArgAsnGlyAsnValValThrThrPheThrArgArgAsnAsnSerValAsnSerValLysGluAlaSerAlaAlaThrValAsnAsnSerAsnSerValLysGluAlaSerAlaAnnCasoAnnSerAnnSerAnnSerAnnSerLysGluAlaSerAnnAnnAnnAnnAnnSerAnnSerAnnSerAnnSerLysGluAlaSerAnnAnnAnnAnnAnnSerAnnSerAnnSerAnnSerAnnSerAnnSerAnnSerAnnSerAnnSerAnnSer<	Thr			Ala	Asn	Trp		Ala	Met	Asn	ГЛа		Asn	Val	Ala
219522002205ProAlaLysProThrValThrAlaAlaGlyAlaIleThr2210AlaLysProThrValAlaAlaGlyAlaIleThr11eAlaProGlyAlaAsnGlnThrValAsnThrHisAlaGlyAsnValThrThrTyrAlaAspLysLeuValIleLysArgAsnGlyAsnValValValThrThrPheThrArgArgAsnAsnThrYalValValAlaSerAlaAlaThrValAlaGlyThrAsnLysGluAlaSerAlaAlaThrValAlaGlyThrAsn	ГЛа			Asn	Ala	Гла			Val	Ile	Tyr			His	Thr
221022152220IleAlaProGlyAlaAsnGlnThrValAsnThrHisAlaGlyAsn2225ThrThrThrYalAsnLysLeuValIleLysArgAsnGlyAsnValValValThrThrPheThrArgArgAsnAsnThrValValValValThrThrPheThrArgArgAsnThrSerProTrpValLysGluAlaSerAlaAlaThrValAlaGlyThrAsn	Phe			Ser	Leu	Pro		Lys	Phe	Val	Val			Val	Gln
222522302235ValThrThrTyrAlaAspLysLeuValIleLysArgAsnGlyAsnValValThrThrPheThrArgArgAsnAsnThrSerProTrpValLysGluAlaSerAlaAlaThrValAlaGlyIleAlaGlyThrAsn	Pro		-	Pro	Thr	Val			Thr	Ala	Ala	-	Ala	Ile	Thr
2240 2245 2250 Val Val Thr Thr Phe Thr Arg 2260 Arg Asn Asn Thr Ser 2265 Pro Trp Val 2265 Lys Glu Ala Ser Ala Ala Thr Val Ala Gly Ile Ala Gly Thr Asn	Ile		Pro	Gly	Ala	Asn		Thr	Val	Asn	Thr		Ala	Gly	Asn
2255 2260 2265 Lys Glu Ala Ser Ala Ala Thr Val Ala Gly Ile Ala Gly Thr Asn	Val			Tyr	Ala	Asp		Leu	Val	Ile	Lys		Asn	Gly	Asn
	Val			Thr	Phe	Thr	-	-	Asn	Asn	Thr		Pro	Trp	Val
	ГÀа	Glu 2270		Ser	Ala	Ala	Thr 2275		Ala	Gly	Ile	Ala 2280	Gly	Thr	Asn

													1000	~
Asn	Gly 2285	Ile	Thr	Val	Ala	Ala 2290	-	Thr	Phe	Asn	Pro 2295	Ala	Asp	Thr
Ile	Gln 2300	Val	Val	Ala	Thr	Gln 2305		Ser	Gly	Glu	Thr 2310	Val	Ser	Asp
Glu	Gln 2315	Arg	Ser	Asp	Asp	Phe 2320		Val	Val	Ala	Pro 2325	Gln	Pro	Asn
Gln	Ala 2330		Thr	Lys	Ile	Trp 2335		Asn	Gly	His	Ile 2340		Ile	Thr
Pro	Asn 2345	Asn	Pro	Ser	Gly	His 2350		Ile	Asn	Pro	Thr 2355	Gln	Ala	Met
Asp			Tyr	Thr	Glu		Val	Gly	Asn	Gly	Ala 2370	Glu	His	Ser
Lya		Ile	Asn	Val	Val		Gly	Gln	Asn	Asn	Gln 2385	-	Thr	Ile
Ala		Lys	Pro	Asp	Tyr		Thr	Leu	Asp	Ala	Gln 2400		Gly	Lya
Val		Phe	Asn	Ala	Asn		Ile	Lys	Pro	Asn	Ser 2415	Ser	Ile	Thr
Ile	Thr		Lys	Ala	Gly	Thr	Gly	His	Ser	Val	Ser	Ser	Asn	Pro
Ser		Leu	Thr	Ala	Pro		Ala	His	Thr	Val	2430 Asn	Thr	Thr	Glu
Ile			Asp	Tyr	Gly		Asn	Val	Thr	Ala	2445 Ala	Glu	Ile	Asn
Asn	2450 Ala		Gln	Val	Ala	2455 Asn		Arg	Thr	Ala	2460 Thr	Ile	Lys	Asn
Gly	2465 Thr	Ala	Met	Pro	Thr	2470 Asn		Ala	Gly	Gly	2475 Ser	Thr	Thr	Thr
	2480					2485					2490 Thr			
	2495					2500					2505 Glu			
	2510					2515					2520 Glu			
	2525					2530					2535			
	2540					2545					His 2550			
	2555					2560					Gln 2565			
Asn	Glu 2570	Arg	Ala	Thr	Pro	Gln 2575	Gln	Val	Ser	Asp	Ala 2580	Leu	Thr	Lys
Val	Arg 2585	Ala	Ala	Gln	Thr	Lys 2590	Ile	Asp	Gln	Ala	Lys 2595	Ala	Leu	Leu
Gln	Asn 2600	Lys	Glu	Asp	Asn	Ser 2605	Gln	Leu	Val	Thr	Ser 2610	Lys	Asn	Asn
Leu	Gln 2615	Ser	Ser	Val	Asn	Gln 2620	Val	Pro	Ser	Thr	Ala 2625	Gly	Met	Thr
Gln	Gln 2630	Ser	Ile	Asp	Asn	Tyr 2635	Asn	Ala	Lys	Гла	Arg 2640	Glu	Ala	Glu
Thr	Glu 2645	Ile	Thr	Ala	Ala	Gln 2650	Arg	Val	Ile	Asp	Asn 2655	Gly	Asp	Ala
Thr	Ala 2660	Gln	Gln	Ile	Ser	Asp 2665	Glu	Lys	His	Arg	Val 2670	Asp	Asn	Ala
Leu		Ala	Leu	Asn	Gln		Lys	His	Asp	Leu	Thr	Ala	Asp	Thr

	2675					2680					2685			
His	Ala 2690	Leu	Glu	Gln	Ala	Val 2695	Gln	Gln	Leu	Asn	Arg 2700	Thr	Gly	Thr
Thr	Thr 2705	Gly	Lys	Lys	Pro	Ala 2710	Ser	Ile	Thr	Ala	Tyr 2715	Asn	Asn	Ser
Ile	Arg 2720	Ala	Leu	Gln	Ser	Asp 2725	Leu	Thr	Ser	Ala	Lys 2730	Asn	Ser	Ala
Asn	Ala 2735	Ile	Ile	Gln	Lys	Pro 2740	Ile	Arg	Thr	Val	Gln 2745	Glu	Val	Gln
Ser	Ala 2750	Leu	Thr	Asn	Val	Asn 2755	Arg	Val	Asn	Glu	Arg 2760	Leu	Thr	Gln
Ala	Ile 2765	Asn	Gln	Leu	Val	Pro 2770	Leu	Ala	Aap	Asn	Ser 2775	Ala	Leu	Lys
Thr	Ala 2780	Lys	Thr	Lys	Leu	Asp 2785	Glu	Glu	Ile	Asn	Lys 2790	Ser	Val	Thr
Thr	Asp 2795	Gly	Met	Thr	Gln	Ser 2800	Ser	Ile	Gln	Ala	Tyr 2805	Glu	Asn	Ala
Lys	Arg 2810	Ala	Gly	Gln	Thr	Glu 2815	Ser	Thr	Asn	Ala	Gln 2820	Asn	Val	Ile
Asn	Asn 2825	Gly	Asp	Ala	Thr	Asp 2830	Gln	Gln	Ile	Ala	Ala 2835	Glu	Lys	Thr
Lys	Val 2840	Glu	Glu	Lys	Tyr	Asn 2845	Ser	Leu	Lys	Gln	Ala 2850	Ile	Ala	Gly
Leu	Thr 2855	Pro	Asp	Leu	Ala	Pro 2860	Leu	Gln	Thr	Ala	Lys 2865	Thr	Gln	Leu
Gln	Asn 2870	Asp	Ile	Asp	Gln	Pro 2875	Thr	Ser	Thr	Thr	Gly 2880	Met	Thr	Ser
Ala	Ser 2885	Ile	Ala	Ala	Phe	Asn 2890	Glu	Lys	Leu	Ser	Ala 2895	Ala	Arg	Thr
Lys	Ile 2900	Gln	Glu	Ile	Asp	Arg 2905	Val	Leu	Ala	Ser	His 2910	Pro	Asp	Val
Ala	Thr 2915	Ile	Arg	Gln	Asn	Val 2920	Thr	Ala	Ala	Asn	Ala 2925	Ala	Lys	Ser
Ala	Leu 2930	Asp	Gln	Ala	Arg	Asn 2935	Gly	Leu	Thr	Val	Asp 2940	Lys	Ala	Pro
Leu	Glu 2945	Asn	Ala	Lys	Asn	Gln 2950	Leu	Gln	His	Ser	Ile 2955	Asp	Thr	Gln
Thr	Ser 2960	Thr	Thr	Gly	Met	Thr 2965	Gln	Asp	Ser	Ile	Asn 2970	Ala	Tyr	Asn
Ala	Lys 2975	Leu	Thr	Ala	Ala	Arg 2980	Asn	Lys	Ile	Gln	Gln 2985	Ile	Asn	Gln
Val	Leu 2990	Ala	Gly	Ser	Pro	Thr 2995	Val	Glu	Gln	Ile	Asn 3000	Thr	Asn	Thr
Ser	Thr 3005	Ala	Asn	Gln	Ala	Lys 3010	Ser	Asp	Leu	Asp	His 3015	Ala	Arg	Gln
Ala	Leu 3020	Thr	Pro	Asp	Гла	Ala 3025	Pro	Leu	Gln	Thr	Ala 3030	ГЛа	Thr	Gln
	Glu	Gln	Ser	Ile	Asn	Gln	Pro	Thr	Asp	Thr	Thr 3045	Gly	Met	Thr
Leu	3035					3040					5015			
	3035	Ser	Leu	Asn	Ala	3040 Tyr 3055	Asn	Gln	Lys	Leu		Ala	Ala	Arg

Val	Gln 3080	Asn	Ile	Asn	Asp	Lys 3085		Thr	Glu	Ala	Asn 3090	Gln	Ala	Lys
Asp	Gln 3095	Leu	Asn	Thr	Ala	Arg 3100		Gly	Leu	Thr	Leu 3105	Asp	Arg	Gln
Pro	Ala 3110	Leu	Thr	Thr	Leu	His 3115		Ala	Ser	Asn	Leu 3120	Asn	Gln	Ala
Gln	Gln 3125	Asn	Asn	Phe	Thr	Gln 3130		Ile	Asn	Ala	Ala 3135	Gln	Asn	His
Ala	Ala 3140	Leu	Glu	Thr	Ile	Lys 3145		Asn	Ile	Thr	Ala 3150	Leu	Asn	Thr
Ala	Met 3155	Thr	Lys	Leu	Lys	Asp 3160		Val	Ala	Asp	Asn 3165	Asn	Thr	Ile
Lys	Ser 3170	Asp	Gln	Asn	Tyr	Thr 3175		Ala	Thr	Pro	Ala 3180	Asn	Lys	Gln
Ala	Tyr 3185	Asp	Asn	Ala	Val	Asn 3190		Ala	ГÀа	Gly	Val 3195	Ile	Gly	Glu
Thr	Thr 3200	Asn	Pro	Thr	Met	Asp 3205		Asn	Thr	Val	Asn 3210	Gln	Lys	Ala
Ala	Ser 3215	Val	Lys	Ser	Thr	Lys 3220		Ala	Leu	Asp	Gly 3225	Gln	Gln	Asn
Leu	Gln 3230	Arg	Ala	Lys	Thr	Glu 3235		Thr	Asn	Ala	Ile 3240	Thr	His	Ala
Ser	Asp 3245	Leu	Asn	Gln	Ala	Gln 3250		Asn	Ala	Leu	Thr 3255	Gln	Gln	Val
Asn	Ser 3260	Ala	Gln	Asn	Val	Gln 3265		Val	Asn	Asp	Ile 3270	Lys	Gln	Thr
Thr	Gln 3275	Ser	Leu	Asn	Thr	Ala 3280	Met	Thr	Gly	Leu	Lys 3285	Arg	Gly	Val
Ala	Asn 3290	His	Asn	Gln	Val	Val 3295	Gln	Ser	Asp	Asn	Tyr 3300	Val	Asn	Ala
Asp	Thr 3305	Asn	Lys	Lys	Asn	Asp 3310		Asn	Asn	Ala	Tyr 3315	Asn	His	Ala
Asn	Asp 3320	Ile	Ile	Asn	Gly	Asn 3325		Gln	His	Pro	Val 3330	Ile	Thr	Pro
Ser	Asp 3335	Val	Asn	Asn	Ala	Leu 3340	Ser	Asn	Val	Thr	Ser 3345	Lys	Glu	His
Ala	Leu 3350	Asn	Gly	Glu	Ala	Lys 3355	Leu	Asn	Ala	Ala	Lys 3360	Gln	Glu	Ala
Asn	Thr 3365	Ala	Leu	Gly	His	Leu 3370	Asn	Asn	Leu	Asn	Asn 3375	Ala	Gln	Arg
Gln	Asn 3380	Leu	Gln	Ser	Gln	Ile 3385	Asn	Gly	Ala	His	Gln 3390	Ile	Asp	Ala
Val	Asn 3395	Thr	Ile	Гла	Gln	Asn 3400	Ala	Thr	Asn	Leu	Asn 3405	Ser	Ala	Met
Gly	Asn 3410	Leu	Arg	Gln	Ala	Val 3415		Asp	Lys	Asp	Gln 3420	Val	Lys	Arg
Thr	Glu 3425	Asp	Tyr	Ala	Asp	Ala 3430		Thr	Ala	Lys	Gln 3435	Asn	Ala	Tyr
Asn	Ser 3440	Ala	Val	Ser	Ser	Ala 3445	Glu	Thr	Ile	Ile	Asn 3450	Gln	Thr	Thr
Asn	Pro 3455	Thr	Met	Ser	Val	Asp 3460	Asp	Val	Asn	Arg	Ala 3465	Thr	Ser	Ala

Val	Thr 3470	Ser	Asn	Lys	Asn	Ala 3475		Asn	Gly	Tyr	Glu 3480		Leu	Ala
Gln	Ser 3485	Lys	Thr	Asp	Ala	Ala 3490		Ala	Ile	Asp	Ala 3495		Pro	His
Leu	Asn 3500	Asn	Ala	Gln	Lys	Ala 3505		Val	Lys	Ser	Lys 3510		Asn	Ala
Ala	Ser 3515	Asn	Ile	Ala	Gly	Val 3520		Thr	Val	Lys	Gln 3525		Gly	Thr
Asp	Leu 3530	Asn	Thr	Ala	Met	Gly 3535		Leu	Gln	Gly	Ala 3540		Asn	Asp
Glu	Gln 3545	Thr	Thr	Leu	Asn	Ser 3550		Asn	Tyr	Gln	Asp 3555		Thr	Pro
Ser	Lys 3560	Lys	Thr	Ala	Tyr	Thr 3565		Ala	Val	Gln	Ala 3570		Lys	Asp
Ile	Leu 3575	Asn	Lys	Ser	Asn	Gly 3580		Asn	Lys	Thr	Lуя 3585		Gln	Val
Thr	Glu 3590	Ala	Met	Asn	Gln	Val 3595		Ser	Ala	Lys	Asn 3600		Leu	Asp
Gly	Thr 3605	Arg	Leu	Leu	Asp	Gln 3610		Гла	Gln	Thr	Ala 3615		Gln	Gln
Leu	Asn 3620	Asn	Met	Thr	His	Leu 3625		Thr	Ala	Gln	Lуя 3630		Asn	Leu
Thr	Asn 3635	Gln	Ile	Asn	Ser	Gly 3640		Thr	Val	Ala	Gly 3645		Gln	Thr
Val	Gln 3650	Ser	Asn	Ala	Asn	Thr 3655		Asp	Gln	Ala	Met 3660		Thr	Leu
Arg	Gln 3665	Ser	Ile	Ala	Asn	Lys 3670		Ala	Thr	Lys	Ala 3675		Glu	Asp
Tyr	Val 3680	Asp	Ala	Asn	Asn	Asp 3685		Gln	Thr	Ala	Tyr 3690		Asn	Ala
Val	Ala 3695	Ala	Ala	Glu	Thr	Ile 3700		Asn	Ala	Asn	Ser 3705		Pro	Glu
Met	Asn 3710	Pro	Ser	Thr	Ile	Thr 3715	Gln	Lys	Ala	Glu	Gln 3720		Asn	Ser
Ser	Lys 3725	Thr	Ala	Leu	Asn	Gly 3730	Asp	Glu	Asn	Leu	Ala 3735		Ala	Lys
Gln	Asn 3740	Ala	Lys	Thr	Tyr	Leu 3745	Asn	Thr	Leu	Thr	Ser 3750	Ile	Thr	Asp
Ala	Gln 3755	Lys	Asn	Asn	Leu	Ile 3760		Gln	Ile	Thr	Ser 3765	Ala	Thr	Arg
Val	Ser 3770	Gly	Val	Asp	Thr	Val 3775	Lys	Gln	Asn	Ala	Gln 3780	His	Leu	Aap
Gln	Ala 3785	Met	Ala	Ser	Leu	Gln 3790	Asn	Gly	Ile	Asn	Asn 3795		Ser	Gln
Val	Lys 3800	Ser	Ser	Glu	Lys	Tyr 3805	Arg	Asp	Ala	Asp	Thr 3810	Asn	Lys	Gln
Gln	Glu 3815	Tyr	Asp	Asn	Ala	Ile 3820	Thr	Ala	Ala	Lys	Ala 3825	Ile	Leu	Asn
Lys	Ser 3830	Thr	Gly	Pro	Asn	Thr 3835	Ala	Gln	Asn	Ala	Val 3840	Glu	Ala	Ala
Leu	Gln 3845	Arg	Val	Asn	Asn	Ala 3850	Lys	Asp	Ala	Leu	Asn 3855	Gly	Asp	Ala
Гла	Leu	Ile	Ala	Ala	Gln	Asn	Ala	Ala	Lys	Gln	His	Leu	Gly	Thr

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	3860					3865					3870					
Leu	Thr 3875		Ile	Thr	Thr	Ala 3880		Arg	Asn	Asp	Leu 3885	Thr	Asn	Gln		
Ile	Ser 3890		Ala	Thr	Asn	Leu 3895	Ala	Gly	Val	Glu	Ser 3900	Val	Lys	Gln		
Asn	Ala 3905		Ser	Leu	Asp	Gly 3910	Ala	Met	Gly	Asn	Leu 3915	Gln	Thr	Ala		
Ile	Asn 3920	-	Гла	Ser	Gly	Thr 3925	Leu	Ala	Ser	Gln	Asn 3930	Phe	Leu	Asp		
Ala	Aap 3935		Gln	Lys	Arg	Asn 3940		Tyr	Asn	Gln	Ala 3945	Val	Ser	Ala		
Ala	Glu 3950		Ile	Leu	Asn	Lys 3955	Gln	Thr	Gly	Pro	Asn 3960	Thr	Ala	Lys		
Thr	Ala 3965		Glu	Gln	Ala	Leu 3970		Asn	Val	Asn	Asn 3975	Ala	Lys	His		
Ala	Leu 3980		Gly	Thr	Gln	Asn 3985	Leu	Asn	Asn	Ala	Lys 3990	Gln	Ala	Ala		
Ile	Thr 3995		Ile	Asn	Gly	Ala 4000		Asp	Leu	Asn	Gln 4005	Lya	Gln	Гла		
Asp	Ala 4010		Гла	Ala	Gln	Ala 4015	Asn	Gly	Ala	Gln	Arg 4020	Val	Ser	Asn		
Ala	Gln 4025	Asp	Val	Gln	His	Asn 4030	Ala	Thr	Glu	Leu	Asn 4035	Thr	Ala	Met		
Gly	Thr 4040		Lys	His	Ala	Ile 4045	Ala	Asp	Lys	Thr	Asn 4050	Thr	Leu	Ala		
Ser	Ser 4055	-	Tyr	Val	Asn	Ala 4060	_	Ser	Thr	Гла	Gln 4065	Asn	Ala	Tyr		
Thr	Thr 4070	-	Val	Thr	Asn	Ala 4075	Glu	His	Ile	Ile	Ser 4080	Gly	Thr	Pro		
Thr	Val 4085	Val	Thr	Thr	Pro	Ser 4090	Glu	Val	Thr	Ala	Ala 4095	Ala	Asn	Gln		
Val	Asn 4100	Ser	Ala	Lys	Gln	Glu 4105	Leu	Asn	Gly	Asp	Glu 4110	Arg	Leu	Arg		
Glu	Ala 4115	Гла	Gln	Asn	Ala	Asn 4120	Thr	Ala	Ile	Asp	Ala 4125	Leu	Thr	Gln		
Leu	Asn 4130	Thr	Pro	Gln	Lys	Ala 4135	Lys	Leu	Lys	Glu	Gln 4140	Val	Gly	Gln		
Ala		-	Leu	Glu	Asp			Thr	Val	Gln	Thr 4155	Asn	Gly	Gln		
Ala		Asn	Asn	Ala	Met			Leu	Arg	Asp	Ser 4170	Ile	Ala	Asn		
Glu		Thr	Val	Lys	Thr	Ser 4180		Asn	Tyr	Thr	Asp 4185	Ala	Ser	Pro		
Asn		Gln	Ser	Thr	Tyr		Ser	Ala	Val	Ser	Asn 4200	Ala	Гла	Gly		
Ile	Ile	Asn	Gln	Thr	Asn	Asn		Thr	Met	Asp	Thr	Ser	Ala	Ile		
Thr			Thr	Thr	Gln		Asn	Asn	Ala	Lys	4215 Asn	Gly	Leu	Asn		
	4220					4225					4230					

Gly Ala Glu Asn Leu Arg Asn Ala Gln Asn Thr Ala Lys Gln Asn 4235 4240 4245

Leu Asn Thr Leu Ser His Leu Thr Asn Asn Gln Lys Ser Ala Ile 4250 4255 4260

Ser	Ser 4265	Gln	Ile	Asp	Arg	Ala 4270	-	His	Val	Ser	Glu 4275	Val	Thr	Ala
Thr	Lys 4280		Ala	Ala	Thr	Glu 4285	Leu	Asn	Thr	Gln	Met 4290	Gly	Asn	Leu
Glu	Gln 4295	Ala	Ile	His	Asp	Gln 4300	Asn	Thr	Val	ГЛЗ	Gln 4305	Ser	Val	Lys
Phe	Thr 4310	Asp	Ala	Asp	Lys	Ala 4315	Lys	Arg	Asp	Ala	Tyr 4320	Thr	Asn	Ala
Val	Ser 4325	Arg	Ala	Glu	Ala	Ile 4330		Asn	Lys	Thr	Gln 4335	Gly	Ala	Asn
Thr	Ser 4340	Lys	Gln	Asp	Val	Glu 4345	Ala	Ala	Ile	Gln	Asn 4350	Val	Ser	Ser
Ala	Lys 4355		Ala	Leu	Asn	Gly 4360		Gln	Asn	Val	Thr 4365	Asn	Ala	ГЛа
Asn	Ala 4370		ГЛа	Asn	Ala	Leu 4375	Asn	Asn	Leu	Thr	Ser 4380	Ile	Asn	Asn
Ala	Gln 4385	-	Arg	Asp	Leu	Thr 4390		ГÀа	Ile	Asp	Gln 4395	Ala	Thr	Thr
Val	Ala 4400	Gly	Val	Glu	Ala	Val 4405	Ser	Asn	Thr	Ser	Thr 4410	Gln	Leu	Asn
Thr	Ala 4415	Met	Ala	Asn	Leu	Gln 4420	Asn	Gly	Ile	Asn	Asp 4425	Гла	Thr	Asn
Thr	Leu 4430		Ser	Glu	Asn	Tyr 4435		Asp	Ala	Asp	Ser 4440	Asp	Lys	Lys
Thr	Ala 4445	-	Thr	Gln	Ala	Val 4450		Asn	Ala	Glu	Asn 4455	Ile	Leu	Asn
Lys	Asn 4460		Gly	Ser	Asn	Leu 4465	Asp	Lys	Thr	Ala	Val 4470	Glu	Asn	Ala
Leu	Ser 4475		Val	Ala	Asn	Ala 4480		Gly	Ala	Leu	Asn 4485	Gly	Asn	His
Asn	Leu 4490		Gln	Ala	Lys	Ser 4495	Asn	Ala	Asn	Thr	Thr 4500	Ile	Asn	Gly
Leu	Gln 4505		Leu	Thr	Thr	Ala 4510	Gln	Lys	Asp	ГЛа	Leu 4515	Lya	Gln	Gln
Val	Gln 4520	Gln	Ala	Gln	Asn	Val 4525	Ala	Gly	Val	Asp	Thr 4530	Val	Lys	Ser
Ser	Ala 4535	Asn	Thr	Leu	Asn	Gly 4540	Ala	Met	Gly	Thr	Leu 4545	Arg	Asn	Ser
Ile	Gln 4550	Asp	Asn	Thr	Ala	Thr 4555	Lys	Asn	Gly	Gln	Asn 4560	-	Leu	Asp
Ala	Thr 4565	Glu	Arg	Asn	ГЛа	Thr 4570	Asn	Tyr	Asn	Asn	Ala 4575	Val	Asp	Ser
Ala	Asn 4580	Gly	Val	Ile	Asn	Ala 4585		Ser	Asn	Pro	Asn 4590	Met	Asp	Ala
Asn	Ala 4595		Asn	Gln	Ile	Ala 4600		Gln	Val	Thr	Ser 4605	Thr	Lys	Asn
Ala	Leu 4610	Asp	Gly	Thr	His	Asn 4615	Leu	Thr	Gln	Ala	Lys 4620	Gln	Thr	Ala
Thr	Asn 4625	Ala	Ile	Asp	Gly	Ala 4630	Thr	Asn	Leu	Asn	Lys 4635	Ala	Gln	Lys
Asp	Ala 4640		Гла	Ala	Gln	Val 4645		Ser	Ala	Gln	Arg 4650	Val	Ala	Asn

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Val	Thr 4655	Ser	Ile	Gln	Gln	Thr 4660	Ala	Asn	Glu	Leu	Asn 4665		Ala	Met
Gly	Gln 4670	Leu	Gln	His	Gly	Ile 4675		Asp	Glu	Asn	Ala 4680		Lys	Gln
Thr	Gln 4685	Lys	Tyr	Arg	Asp	Ala 4690		Gln	Ser	Lys	Lys 4695		Ala	Tyr
Asp	Gln 4700	Ala	Val	Ala	Ala	Ala 4705		Ala	Ile	Leu	Asn 4710		Gln	Thr
Gly	Ser 4715	Asn	Ser	Asp	Lys	Ala 4720		Val	Asp	Arg	Ala 4725	Leu	Gln	Gln
Val	Thr 4730	Ser	Thr	Lys	Asp	Ala 4735		Asn	Gly	Asp	Ala 4740		Leu	Ala
Glu	Ala 4745	Lys	Ala	Ala	Ala	Lys 4750		Asn	Leu	Gly	Thr 4755	Leu	Asn	His
Ile	Thr 4760	Asn	Ala	Gln	Arg	Thr 4765		Leu	Glu	Gly	Gln 4770	Ile	Asn	Gln
Ala	Thr 4775	Thr	Val	Asp	Gly	Val 4780		Thr	Val	Lys	Thr 4785	Asn	Ala	Asn
Thr	Leu 4790	Asp	Gly	Ala	Met	Asn 4795		Leu	Gln	Gly	Ser 4800	Ile	Asn	Asp
Гла	Asp 4805	Ala	Thr	Leu	Arg	Asn 4810		Asn	Tyr	Leu	Asp 4815	Ala	Asp	Glu
Ser	Lys 4820		Asn	Ala	Tyr	Thr 4825	Gln	Ala	Val	Thr	Ala 4830	Ala	Glu	Gly
Ile	Leu 4835	Asn	Lys	Gln	Thr	Gly 4840		Asn	Thr	Ser	Lys 4845	Ala	Asp	Val
Asp	Asn 4850	Ala	Leu	Asn	Ala	Val 4855		Arg	Ala	Lys	Ala 4860	Ala	Leu	Asn
Gly	Ala 4865		Asn	Leu	Arg	Asn 4870		Lys	Thr	Ser	Ala 4875	Thr	Asn	Thr
Ile	Asp 4880	Gly	Leu	Pro	Asn	Leu 4885		Gln	Leu	Gln	Lys 4890	Asp	Asn	Leu
Lys	His 4895	Gln	Val	Glu	Gln	Ala 4900		Asn	Val	Ala	Gly 4905	Val	Asn	Gly
Val	Lys 4910	Asp	ГЛа	Gly	Asn	Thr 4915	Leu	Asn	Thr	Ala	Met 4920	Gly	Ala	Leu
Arg	Thr 4925	Ser	Ile	Gln	Asn	Asp 4930	Asn	Thr	Thr	Lys	Thr 4935	Ser	Gln	Asn
Tyr	Leu 4940	Asp	Ala	Ser	Asp	Ser 4945	Asn	Lys	Asn	Asn	Tyr 4950	Asn	Thr	Ala
Val	Asn 4955	Asn	Ala	Asn	Gly	Val 4960		Asn	Ala	Thr	Asn 4965	Asn	Pro	Asn
Met	Asp 4970	Ala	Asn	Ala	Ile	Asn 4975	Gly	Met	Ala	Asn	Gln 4980	Val	Asn	Thr
Thr	Lys 4985	Ala	Ala	Leu	Asn	Gly 4990		Gln	Asn	Leu	Ala 4995		Ala	Lys
Thr	Asn 5000	Ala	Thr	Asn	Thr	Ile 5005	Asn	Asn	Ala	His	Asp 5010	Leu	Asn	Gln
Lys	Gln 5015	Lys	Asp	Ala	Leu	Lys 5020		Gln	Val	Asn	Asn 5025	Ala	Gln	Arg
Val	Ser 5030	Asp	Ala	Asn	Asn	Val 5035		His	Thr	Ala	Thr 5040	Glu	Leu	Asn
Ser	Ala	Met	Thr	Ala	Leu	Lys	Ala	Ala	Ile	Ala	Asp	Гла	Glu	Arg

	5045					5050					5055			
Thr	Lys 5060		Ser	Gly	Asn	Tyr 5065		Asn	Ala	Asp	Gln 5070	Glu	Lys	Arg
Gln	Ala 5075	-	Asp	Ser	Lys	Val 5080		Asn	Ala	Glu	Asn 5085	Ile	Ile	Ser
Gly	Thr 5090		Asn	Ala	Thr	Leu 5095		Val	Asn	Asp	Val 5100	Asn	Ser	Ala
Ala	Ser 5105	Gln	Val	Asn	Ala	Ala 5110		Thr	Ala	Leu	Asn 5115	Gly	Asp	Asn
Asn	Leu 5120		Val	Ala	Lys	Glu 5125		Ala	Asn	Asn	Thr 5130	Ile	Asp	Gly
Leu	Ala 5135		Leu	Asn	Asn	Ala 5140	Gln	Lys	Ala	Lys	Leu 5145		Glu	Gln
Val	Gln 5150		Ala	Thr	Thr	Leu 5155				Gln	Thr 5160	Val	Lys	Asn
Ser	Ser 5165		Thr	Leu	Asn	Thr 5170		Met		Gly	Leu 5175	Arg	Asp	Ser
Ile	Ala 5180	Asn	Glu	Ala	Thr	Ile 5185		Ala		Gln	Asn 5190	-	Thr	Asp
Ala	Ser 5195	Pro	Asn	Asn	Arg	Asn 5200		-	Asp		Ala 5205	Val	Thr	Ala
Ala	Lys 5210	Ala	Ile	Ile	Asn	Gln 5215		Ser	Asn	Pro	Thr 5220	Met	Glu	Pro
Asn	Thr 5225		Thr	Gln	Val	Thr 5230		Gln	Val	Thr	Thr 5235		Glu	Gln
Ala	Leu 5240	Asn	Gly	Ala	Arg	Asn 5245				Ala	Lys 5250	Thr	Thr	Ala
Lys	Asn 5255		Leu	Asn	Asn	Leu 5260		Ser	Ile	Asn	Asn 5265	Ala	Gln	Lys
Asp	Ala 5270	Leu	Thr	Arg	Ser	Ile 5275				Thr	Thr 5280	Val	Ala	Gly
Val	Asn 5285	Gln	Glu	Thr	Ala	Lys 5290		Thr	Glu	Leu	Asn 5295	Asn	Ala	Met
His	Ser 5300		Gln	Asn	Gly	Ile 5305		Asp	Glu	Thr	Gln 5310	Thr	Lys	Gln
Thr	Gln 5315			Leu		Ala 5320		Pro			Lys 5325	Ser	Ala	Tyr
Asp	Gln 5330	Ala	Val	Asn	Ala	Ala 5335	Гла	Ala	Ile	Leu	Thr 5340	Гла	Ala	Ser
Gly	Gln 5345	Asn	Val	Asp	Lys	Ala 5350	Ala	Val	Glu	Gln	Ala 5355	Leu	Gln	Asn
Val	Asn 5360	Ser	Thr	Lys	Thr	Ala 5365	Leu	Asn	Gly	Asp	Ala 5370	ГЛа	Leu	Asn
Glu	Ala 5375	Lys	Ala	Ala	Ala	Lys 5380	Gln	Thr	Leu	Gly	Thr 5385	Leu	Thr	His
Ile	Asn 5390	Asn	Ala	Gln	Arg	Thr 5395	Ala	Leu	Asp	Asn	Glu 5400	Ile	Thr	Gln
Ala	Thr 5405	Asn	Val	Glu	Gly	Val 5410	Asn	Thr	Val	Гла	Ala 5415	Гла	Ala	Gln
Gln	Leu	Asp	Gly	Ala	Met	Gly	Gln	Leu	Glu	Thr	Ser	Ile	Arg	Asp
Lys	5420 Asp	Thr	Thr	Leu	Gln		Gln	Asn	Tyr	Gln		Ala	Asp	Asp
	5435					5440					5445			

Ala	Lys 5450	Arg	Thr	Ala	Tyr	Ser 5455	Gln	Ala	Val	Asn	Ala 5460	Ala	Ala	Thr
Ile	Leu 5465	Asn	Гла	Thr	Ala	Gly 5470	Gly	Asn	Thr	Pro	Lys 5475	Ala	Asp	Val
Glu	Arg 5480	Ala	Met	Gln	Ala	Val 5485	Thr	Gln	Ala	Asn	Thr 5490	Ala	Leu	Asn
Gly	Ile 5495	Gln	Asn	Leu	Asp	Arg 5500	Ala	Lys	Gln	Ala	Ala 5505	Asn	Thr	Ala
Ile	Thr 5510	Asn	Ala	Ser	Asp	Leu 5515	Asn	Thr	Lys	Gln	Lys 5520	Glu	Ala	Leu
Lys	Ala 5525	Gln	Val	Thr	Ser	Ala 5530	Gly	Arg	Val	Ser	Ala 5535	Ala	Asn	Gly
Val	Glu 5540	His	Thr	Ala	Thr	Glu 5545	Leu	Asn	Thr	Ala	Met 5550	Thr	Ala	Leu
ГЛа	Arg 5555	Ala	Ile	Ala	Asp	Lys 5560	Ala	Glu	Thr	ГÀа	Ala 5565	Ser	Gly	Asn
Tyr	Val 5570	Asn	Ala	Asp	Ala	Asn 5575	Гла	Arg	Gln	Ala	Tyr 5580	Asp	Glu	ГЛа
Val	Thr 5585	Ala	Ala	Glu	Asn	Ile 5590	Val	Ser	Gly	Thr	Pro 5595	Thr	Pro	Thr
Leu	Thr 5600	Pro	Ala	Asp	Val	Thr 5605	Asn	Ala	Ala	Thr	Gln 5610	Val	Thr	Asn
Ala	Lys 5615	Thr	Gln	Leu	Asn	Gly 5620	Asn	His	Asn	Leu	Glu 5625	Val	Ala	Lya
Gln	Asn 5630	Ala	Asn	Thr	Ala	Ile 5635	Asp	Gly	Leu	Thr	Ser 5640	Leu	Asn	Gly
Pro	Gln 5645	Lys	Ala	Гла	Leu	Lys 5650	Glu	Gln	Val	Gly	Gln 5655	Ala	Thr	Thr
Leu	Pro 5660	Asn	Val	Gln	Thr	Val 5665	Arg	Asp	Asn	Ala	Gln 5670	Thr	Leu	Asn
Thr	Ala 5675	Met	Lys	Gly	Leu	Arg 5680	Asp	Ser	Ile	Ala	Asn 5685	Glu	Ala	Thr
Ile	Lys 5690	Ala	Gly	Gln	Asn	Tyr 5695	Thr	Asp	Ala	Ser	Gln 5700	Asn	Lys	Gln
Thr	Asp 5705	Tyr	Asn	Ser	Ala	Val 5710	Thr	Ala	Ala	Lys	Ala 5715	Ile	Ile	Gly
Gln	Thr 5720	Thr	Ser	Pro	Ser	Met 5725	Asn	Ala	Gln	Glu	Ile 5730	Asn	Gln	Ala
ГЛа	Asp 5735	Gln	Val	Thr	Ala	Lys 5740	Gln	Gln	Ala	Leu	Asn 5745	Gly	Gln	Glu
Asn	Leu 5750	Arg	Thr	Ala	Gln	Thr 5755	Asn	Ala	Lys	Gln	His 5760	Leu	Asn	Gly
Leu	Ser 5765	Asp	Leu	Thr	Asp	Ala 5770	Gln	Lys	Asp	Ala	Val 5775	Lys	Arg	Gln
Ile	Glu 5780	Gly	Ala	Thr	His	Val 5785	Asn	Glu	Val	Thr	Gln 5790	Ala	Gln	Asn
Asn	Ala 5795	Asp	Ala	Leu	Asn	Thr 5800	Ala	Met	Thr	Asn	Leu 5805	Lys	Asn	Gly
Ile	Gln 5810	Asp	Gln	Asn	Thr	Ile 5815	Lys	Gln	Gly	Val	Asn 5820	Phe	Thr	Asp
Ala	Asp 5825	Glu	Ala	Lys	Arg	Asn 5830	Ala	Tyr	Thr	Asn	Ala 5835	Val	Thr	Gln

Ala	Glu 5840	Gln	Ile	Leu	Asn	Lys 5845		Gln	Gly	Pro	Asn 5850	Thr	Ser	LYa
Aap	Gly 5855	Val	Glu	Thr	Ala	Leu 5860		Asn	Val	Gln	Arg 5865	Ala	ГЛа	Asn
Glu	Leu 5870	Asn	Gly	Asn	Gln	Asn 5875		Ala	Asn	Ala	Lys 5880	Thr	Thr	Ala
Lys	Asn 5885	Ala	Leu	Asn	Asn	Leu 5890		Ser	Ile	Asn	Asn 5895	Ala	Gln	Lys
Glu	Ala 5900	Leu	Lys	Ser	Gln	Ile 5905		Gly	Ala	Thr	Thr 5910	Val	Ala	Gly
Val	Asn 5915	Gln	Val	Ser	Thr	Thr 5920		Ser	Glu	Leu	Asn 5925	Thr	Ala	Met
Ser	Asn 5930	Leu	Gln	Asn	Gly	Ile 5935		Asp	Glu	Ala	Ala 5940	Thr	Lys	Ala
Ala	Gln 5945	Lys	Tyr	Thr	Aab	Ala 5950		Arg	Glu	Гла	Gln 5955	Thr	Ala	Tyr
Asn	Asp 5960	Ala	Val	Thr	Ala	Ala 5965		Thr	Leu	Leu	Asp 5970	Lys	Thr	Ala
Gly	Ser 5975	Asn	Asp	Asn	Lys	Ala 5980	Ala	Val	Glu	Gln	Ala 5985	Leu	Gln	Arg
Val	Asn 5990	Thr	Ala	Lys	Thr	Ala 5995	Leu	Asn	Gly	Asp	Glu 6000	Arg	Leu	Asn
Glu	Ala 6005	Lys	Asn	Thr	Ala	Lys 6010		Gln	Val	Ala	Thr 6015	Met	Ser	His
Leu	Thr 6020	Asp	Ala	Gln	Lys	Ala 6025		Leu	Thr	Ser	Gln 6030	Ile	Glu	Ser
Gly	Thr 6035	Thr	Val	Ala	Gly	Val 6040		Gly	Ile	Gln	Ala 6045	Asn	Ala	Gly
Thr	Leu 6050	Asp	Gln	Ala	Met	Asn 6055	Gln	Leu	Arg	Gln	Ser 6060	Ile	Ala	Ser
Lys	Asp 6065	Ala	Thr	Lys	Ser	Ser 6070		Asp	Tyr	Gln	Asp 6075	Ala	Asn	Ala
Aab	Leu 6080	Gln	Asn	Ala	Tyr	Asn 6085		Ala	Val	Thr	Asn 6090	Ala	Glu	Gly
Ile	Ile 6095	Ser	Ala	Thr	Asn	Asn 6100	Pro	Glu	Met	Asn	Pro 6105	Asp	Thr	Ile
Asn	Gln 6110	Lys	Ala	Ser	Gln	Val 6115	Asn	Ser	Ala	ГЛа	Ser 6120	Ala	Leu	Asn
Gly	Asp 6125	Glu	Lys	Leu	Ala	Ala 6130		Lys	Gln	Thr	Ala 6135	Lys	Ser	Asp
Ile	Gly 6140	Arg	Leu	Thr	Aab	Leu 6145		Asn	Ala	Gln	Arg 6150	Thr	Ala	Ala
Asn	Ala 6155	Glu	Val	Asp	Gln	Ala 6160		Asn	Leu	Ala	Ala 6165	Val	Thr	Ala
Ala	Lys 6170	Asn	Lys	Ala	Thr	Ser 6175	Leu	Asn	Thr	Ala	Met 6180	Gly	Asn	Leu
Lys	His 6185	Ala	Leu	Ala	Glu	Lys 6190		Asn	Thr	Lys	Arg 6195	Ser	Val	Asn
Tyr	Thr 6200	Asp	Ala	Asp	Gln	Pro 6205	-	Gln	Gln	Ala	Tyr 6210	Asp	Thr	Ala
Val	Thr 6215	Gln	Ala	Glu	Ala	Ile 6220		Asn	Ala	Asn	Gly 6225	Ser	Asn	Ala
Asn	Glu	Thr	Gln	Val	Gln	Ala	Ala	Leu	Asn	Gln	Leu	Asn	Gln	Ala

	6230					6235					6240				
Lys	Asn 6245		Leu	Asn		Asp 6250		Lys	Val		Gln 6255	Ala	Lys	Glu	
Ser	Ala 6260	-	Arg	Ala	Leu	Ala 6265		-			Leu 6270	Asn	Asn	Ala	
Gln	Ser 6275		Ala	Ala	Ile	Ser 6280		Ile	Asp		Ala 6285	Thr	Thr	Val	
Ala	Gly 6290		Thr	Ala	Ala	Gln 6295					Glu 6300	Leu	Asn	Thr	
Ala	Met 6305	_	Gln	Leu	Gln	Asn 6310	_			_	Gln 6315	Asn	Thr	Val	
Lys	Gln 6320		Val	Asn	Phe	Thr 6325					Gly 6330		Lys	Asp	
Ala	Tyr 6335		Asn	Ala	Val	Thr 6340					Ile 6345	Leu	Asp	ГЛа	
Ala	His 6350			Asn	Met	Thr 6355	-				Glu 6360	Ala	Ala	Leu	
Asn	Gln 6365		Thr	Thr	Ala	Lys 6370		Ala	Leu	Asn	Gly 6375	Asp	Ala	Asn	
Val	Arg 6380		Ala	Lys	Ser	Asp 6385				Asn	Leu 6390	Gly	Thr	Leu	
Thr	His 6395		Asn	Asn	Ala	Gln 6400					Thr 6405	Ser	Gln	Ile	
Glu	Gly 6410		Thr	Thr	Val	Asn 6415					Val 6420	Lys	Thr	Lys	
Ala						Ala 6430		Gln	Arg		Gln 6435	Ser	Ala	Ile	
Ala	Asn 6440		Asp	Gln	Thr	Lys 6445		Ser	Glu		Tyr 6450	Ile	Asp	Ala	
Asp	Pro 6455		Гла	Гла	Thr	Ala 6460	Phe	Asp	Asn		Ile 6465	Thr	Gln	Ala	
Glu	Ser 6470			Asn	Lys	Asp 6475					Lys 6480	Asp	Lys	Gln	
Ala	Val 6485		Gln	Ala	Ile	Gln 6490			Thr		Thr 6495	Glu	Asn	Ala	
Leu	Asn 6500					Leu 6505					Thr 6510	Glu	Ala	Ile	
Gln	Ala 6515	Ile	Asp	Asn	Leu	Thr 6520		Leu	Asn	Thr	Pro 6525	Gln	ГЛа	Thr	
Ala	Leu 6530	Гла	Gln	Gln	Val	Asn 6535	Ala	Ala	Gln	Arg	Val 6540	Ser	Gly	Val	
Thr	Asp 6545	Leu	ГЛа	Asn	Ser	Ala 6550	Thr	Ser	Leu	Asn	Asn 6555	Ala	Met	Asp	
Gln	Leu 6560	Гла	Gln	Ala	Ile	Ala 6565	Asp	His	Asp	Thr	Ile 6570	Val	Ala	Ser	
Gly	Asn 6575	Tyr	Thr	Asn	Ala	Ser 6580	Pro	Asp	Lys	Gln	Gly 6585	Ala	Tyr	Thr	
Asp	Ala 6590	Tyr	Asn	Ala	Ala	Lys 6595	Asn	Ile	Val	Asn	Gly 6600	Ser	Pro	Asn	
Val	Ile 6605	Thr	Asn	Ala	Ala	Asp 6610	Val	Thr	Ala	Ala	Thr 6615	Gln	Arg	Val	
Asn		Ala	Glu	Thr	Gly	Leu 6625	Asn	Gly	Asp	Thr		Leu	Ala	Thr	
						20									

		d]	a 1		T	3			3	G]	M - +-	m 1		*
AIA	Lys 6635	GIN	GIN	AIA	гуз	Asp 6640	AIA	Leu	Arg	GIN	Met 6645	Inr	HIS	Leu
Ser	Asp 6650	Ala	Gln	ГЛЗ	Gln	Ser 6655	Ile	Thr	Gly	Gln	Ile 6660	Asp	Ser	Ala
Thr	Gln 6665	Val	Thr	Gly	Val	Gln 6670	Ser	Val	Lys	Asp	Asn 6675	Ala	Thr	Asn
Leu	Asp 6680	Asn	Ala	Met	Asn	Gln 6685	Leu	Arg	Asn	Ser	Ile 6690	Ala	Asn	Lys
Asp	Asp 6695	Val	Гла	Ala	Ser	Gln 6700	Pro	Tyr	Val	Asp	Ala 6705	Asp	Arg	Asp
Lys	Gln 6710	Asn	Ala	Tyr	Asn	Thr 6715	Ala	Val	Thr	Asn	Ala 6720	Glu	Asn	Ile
Ile	Asn 6725	Ala	Thr	Ser	Gln	Pro 6730	Thr	Leu	Asp	Pro	Ser 6735	Ala	Val	Thr
Gln	Ala 6740	Ala	Asn	Gln	Val	Ser 6745	Thr	Asn	Lys	Thr	Ala 6750	Leu	Asn	Gly
Ala	Gln 6755	Asn	Leu	Ala	Asn	Lys 6760	Lys	Gln	Glu	Thr	Thr 6765	Ala	Asn	Ile
Asn	Gln 6770	Leu	Ser	His	Leu	Asn 6775	Asn	Ala	Gln	Lys	Gln 6780	Asp	Leu	Asn
Thr	Gln 6785	Val	Thr	Asn	Ala	Pro 6790	Asn	Ile	Ser	Thr	Val 6795	Asn	Gln	Val
Lys	Thr 6800	Lys	Ala	Glu	Gln	Leu 6805	Aab	Gln	Ala	Met	Glu 6810	Arg	Leu	Ile
Asn	Gly 6815	Ile	Gln	Asp	Lys	Asp 6820	Gln	Val	Lys	Gln	Ser 6825	Val	Asn	Phe
Thr	Asp 6830	Ala	Asp	Pro	Glu	Lys 6835	Gln	Thr	Ala	Tyr	Asn 6840	Asn	Ala	Val
Thr	Ala 6845	Ala	Glu	Asn	Ile	Ile 6850	Asn	Gln	Ala	Asn	Gly 6855	Thr	Asn	Ala
Asn	Gln 6860	Ser	Gln	Val	Glu	Ala 6865	Ala	Leu	Ser	Thr	Val 6870	Thr	Thr	Thr
Lys	Gln 6875	Ala	Leu	Asn	Gly	Asp 6880	Arg	Lys	Val	Thr	Asp 6885	Ala	Lys	Asn
Asn	Ala 6890	Asn	Gln	Thr	Leu	Ser 6895	Thr	Leu	Asp	Asn	Leu 6900	Asn	Asn	Ala
Gln	Lys 6905	Gly	Ala	Val	Thr	Gly 6910	Asn	Ile	Asn	Gln	Ala 6915	His	Thr	Val
Ala	Glu 6920	Val	Thr	Gln	Ala	Ile 6925	Gln	Thr	Ala	Gln	Glu 6930	Leu	Asn	Thr
Ala	Met 6935	Gly	Asn	Leu	Lys	Asn 6940	Ser	Leu	Asn	Asp	Lys 6945	Asp	Thr	Thr
Leu	Gly 6950	Ser	Gln	Asn	Phe	Ala 6955	Asp	Ala	Asp	Pro	Glu 6960	Гла	Lys	Asn
Ala	Tyr 6965	Asn	Glu	Ala	Val	His 6970	Asn	Ala	Glu	Asn	Ile 6975	Leu	Asn	Lys
Ser	Thr 6980	Gly	Thr	Asn	Val	Pro 6985	Lys	Asp	Gln	Val	Glu 6990	Ala	Ala	Met
Asn	Gln 6995	Val	Asn	Ala	Thr	Lys 7000	Ala	Ala	Leu	Asn	Gly 7005	Thr	Gln	Asn
Leu	Glu 7010	Гла	Ala	Гла	Gln	His 7015	Ala	Asn	Thr	Ala	Ile 7020	Asp	Gly	Leu

Ser	His 7025	Leu	Thr	Asn	Ala	Gln 7030		Glu	Ala	Leu	Lys 7035	Gln	Leu	Val
Gln	Gln 7040		Thr	Thr	Val	Ala 7045		Ala	Gln	Gly	Asn 7050	Glu	Gln	Lys
Ala	Asn 7055	Asn	Val	Asp	Ala	Ala 7060		Asp	Lys	Leu	Arg 7065	Gln	Ser	Ile
Ala	Asp 7070		Ala	Thr	Thr	Lys 7075		Asn	Gln	Asn	Tyr 7080	Thr	Asp	Ala
Ser	Gln 7085	Asn	Lys	Lys	Asp	Ala 7090		Asn	Asn	Ala	Val 7095	Thr	Thr	Ala
Gln	Gly 7100		Ile	Asp	Gln	Thr 7105		Ser	Pro	Thr	Leu 7110	Asp	Pro	Thr
Val	Ile 7115	Asn	Gln	Ala	Ala	Gly 7120		Val	Ser	Thr	Thr 7125	Гла	Asn	Ala
Leu	Asn 7130		Asn	Glu	Asn	Leu 7135		Ala	Ala	Lys	Gln 7140	Gln	Ala	Ser
Gln	Ser 7145	Leu	Gly	Ser	Leu	Asp 7150		Leu	Asn	Asn	Ala 7155	Gln	Lys	Gln
Thr	Val 7160		Asp	Gln	Ile	Asn 7165	-	Ala	His	Thr	Val 7170	Asp	Glu	Ala
Asn	Gln 7175	Ile	Lys	Gln	Asn	Ala 7180		Asn	Leu	Asn	Thr 7185	Ala	Met	Gly
Asn	Leu 7190		Gln	Ala	Ile	Ala 7195		Lys	Asp	Ala	Thr 7200	Lys	Ala	Thr
Val	Asn 7205		Thr	Asp	Ala	Asp 7210		Ala	Lys	Gln	Gln 7215	Ala	Tyr	Asn
Thr	Ala 7220	Val	Thr	Asn	Ala	Glu 7225		Ile	Ser	Lys	Ala 7230	Asn	Gly	Asn
Ala	Thr 7235		Ala	Glu	Val	Glu 7240		Ala	Ile	Lys	Gln 7245	Val	Asn	Ala
Ala	Lys 7250		Ala	Leu	Asn	Gly 7255		Ala	Asn	Val	Gln 7260	His	Ala	Lys
Aab	Glu 7265	Ala	Thr	Ala	Leu	Ile 7270		Ser	Ser	Asn	Asp 7275	Leu	Asn	Gln
Ala	Gln 7280	Lys	Asp	Ala	Leu	Lys 7285		Gln	Val	Gln	Asn 7290	Ala	Thr	Thr
Val	Ala 7295	Gly	Val	Asn	Asn	Val 7300	Lys	Gln	Thr	Ala	Gln 7305	Glu	Leu	Asn
Asn	Ala 7310	Met	Thr	Gln	Leu	Lys 7315	Gln	Gly	Ile	Ala	Asp 7320	Гла	Glu	Gln
Thr	Lys 7325	Ala	Asp	Gly	Asn	Phe 7330	Val	Asn	Ala	Asp	Pro 7335	Asp	Lys	Gln
Asn	Ala 7340	Tyr	Asn	Gln	Ala	Val 7345	Ala	Lys	Ala	Glu	Ala 7350	Leu	Ile	Ser
Ala	Thr 7355	Pro	Asp	Val	Val	Val 7360		Pro	Ser	Glu	Ile 7365	Thr	Ala	Ala
Leu	Asn 7370	Lys	Val	Thr	Gln	Ala 7375	-	Asn	Asp	Leu	Asn 7380	Gly	Asn	Thr
Asn	Leu 7385	Ala	Thr	Ala	Lys	Gln 7390		Val	Gln	His	Ala 7395	Ile	Asp	Gln
Leu	Pro 7400	Asn	Leu	Asn	Gln	Ala 7405	Gln	Arg	Asp	Glu	Tyr 7410	Ser	Lys	Gln
Ile	Thr	Gln	Ala	Thr	Leu	Val	Pro	Asn	Val	Asn	Ala	Ile	Gln	Gln

	7415					7420					7425				
Ala	Ala 7430		Thr	Leu	Asn	Asp 7435		Met	Thr	Gln	Leu 7440	Lys	Gln	Gly	
Ile	Ala 7445		Гла	Ala	Gln	Ile 7450		Gly	Ser	Glu	Asn 7455	Tyr	His	Asp	
Ala	Asp 7460	Thr	Asp	Lys	Gln	Thr 7465		Tyr	Asp	Asn	Ala 7470	Val	Thr	Lys	
Ala	Glu 7475	Glu	Leu	Leu	Lys	Gln 7480		Thr	Asn	Pro	Thr 7485	Met	Asp	Pro	
Asn	Thr 7490	Ile	Gln	Gln	Ala	Leu 7495		ГЛа	Val	Asn	Asp 7500	Thr	Asn	Gln	
Ala	Leu 7505	Asn	Gly	Asn	Gln	Lys 7510		Ala	Asp	Ala	Lys 7515	Gln	Asp	Ala	
Lys	Thr 7520	Thr	Leu	Gly	Thr	Leu 7525		His	Leu	Asn	Asp 7530	Ala	Gln	ГЛа	
Gln	Ala 7535	Leu	Thr	Thr	Gln	Val 7540		Gln	Ala	Pro	Asp 7545	Ile	Ala	Thr	
Val	Asn 7550	Asn	Val	Lys	Gln	Asn 7555		Gln	Asn	Leu	Asn 7560	Asn	Ala	Met	
Thr	Asn 7565	Leu	Asn	Asn	Ala	Leu 7570	Gln	Asp	Lys	Thr	Glu 7575	Thr	Leu	Asn	
Ser	Ile 7580	Asn	Phe	Thr	Asp	Ala 7585		Gln	Ala	Lys	Lys 7590	Asp	Ala	Tyr	
Thr	Asn 7595		Val	Ser	His	Ala 7600	Glu	Gly	Ile	Leu	Ser 7605		Ala	Asn	
Gly	Ser 7610		Ala	Ser	Gln	Thr 7615	Glu	Val	Glu	Gln	Ala 7620	Met	Gln	Arg	
Val	Asn 7625		Ala	Гла	Gln	Ala 7630	Leu	Asn	Gly	Asn	Asp 7635	Asn	Val	Gln	
Arg	Ala 7640		Asp	Ala	Ala	Lys 7645		Val	Ile	Thr	Asn 7650	Ala	Asn	Asp	
Leu	Asn 7655		Ala	Gln	Lys	Asp 7660		Leu	Lys	Gln	Gln 7665	Val	Asp	Ala	
Ala	Gln 7670		Val	Ala	Asn	Val 7675		Thr	Ile	Lys	Gln 7680	Thr	Ala	Gln	
Asp	Leu 7685		Gln	Ala		Thr 7690		Leu	Lys	Gln	Gly 7695	Ile	Ala	Asp	
Lys	Asp 7700	Gln	Thr	Гла	Ala	Asn 7705		Asn	Phe	Val	Asn 7710	Ala	Asp	Thr	
Asp	Lys 7715	Gln	Asn	Ala	Tyr	Asn 7720		Ala	Val	Ala	His 7725	Ala	Glu	Gln	
Ile	Ile 7730	Ser	Gly	Thr	Pro	Asn 7735		Asn	Val	Asp	Pro 7740	Gln	Gln	Val	
Ala	Gln 7745	Ala	Leu	Gln	Gln	Val 7750	Asn	Gln	Ala	Гла	Gly 7755	Asp	Leu	Asn	
Gly	Asn 7760	His	Asn	Leu	Gln	Val 7765	Ala	Lys	Asp	Asn	Ala 7770	Asn	Thr	Ala	
Ile	Asp 7775	Gln	Leu	Pro	Asn		Asn	Gln	Pro	Gln		Thr	Ala	Leu	
Lys	Asp	Gln	Val	Ser	His	Ala	Glu	Leu	Val	Thr	Gly	Val	Asn	Ala	
Ile	7790 Lys	Gln	Asn	Ala	Asp	7795 Ala	Leu	Asn	Asn	Ala	7800 Met	Gly	Thr	Leu	
	7805					7810					7815				

Lys	Gln 7820	Gln	Ile	Gln	Ala	Asn 7825	Ser	Gln	Val	Pro	Gln 7830	Ser	Val	Asp
Phe	Thr 7835	Gln	Ala	Asp	Gln	Asp 7840	Lys	Gln	Gln	Ala	Tyr 7845	Asn	Asn	Ala
Ala	Asn 7850	Gln	Ala	Gln	Gln	Ile 7855	Ala	Asn	Gly	Ile	Pro 7860	Thr	Pro	Val
Leu	Thr 7865	Pro	Asp	Thr	Val	Thr 7870	Gln	Ala	Val	Thr	Thr 7875	Met	Asn	Gln
Ala	Lys 7880	Asp	Ala	Leu	Asn	Gly 7885	Asp	Glu	Lys	Leu	Ala 7890	Gln	Ala	Lys
Gln	Glu 7895	Ala	Leu	Ala	Asn	Leu 7900	Asp	Thr	Leu	Arg	Asp 7905	Leu	Asn	Gln
Pro	Gln 7910	Arg	Asp	Ala	Leu	Arg 7915	Asn	Gln	Ile	Asn	Gln 7920	Ala	Gln	Ala
Leu	Ala 7925	Thr	Val	Glu	Gln	Thr 7930	Lys	Gln	Asn	Ala	Gln 7935	Asn	Val	Asn
Thr	Ala 7940	Met	Ser	Asn	Leu	Lys 7945	Gln	Gly	Ile	Ala	Asn 7950	Lys	Asp	Thr
Val	Lys 7955	Ala	Ser	Glu	Asn	Tyr 7960	His	Asp	Ala	Asp	Ala 7965	Asp	Lys	Gln
Thr	Ala 7970	Tyr	Thr	Asn	Ala	Val 7975	Ser	Gln	Ala	Glu	Gly 7980	Ile	Ile	Asn
Gln	Thr 7985	Thr	Asn	Pro	Thr	Leu 7990	Asn	Pro	Asp	Glu	Ile 7995	Thr	Arg	Ala
Leu	Thr 8000	Gln	Val	Thr	Asp	Ala 8005	Lys	Asn	Gly	Leu	Asn 8010	Gly	Glu	Ala
Гла	Leu 8015	Ala	Thr	Glu	Lys	Gln 8020	Asn	Ala	Lys	Asp	Ala 8025	Val	Ser	Gly
Met	Thr 8030	His	Leu	Asn	Asp	Ala 8035	Gln	Lys	Gln	Ala	Leu 8040	Lys	Gly	Gln
Ile	Asp 8045	Gln	Ser	Pro	Glu	Ile 8050	Ala	Thr	Val	Asn	Gln 8055	Val	Lys	Gln
Thr	Ala 8060	Thr	Ser	Leu	Asp	Gln 8065	Ala	Met	Asp	Gln	Leu 8070	Ser	Gln	Ala
Ile	Asn 8075	Asp	Lys	Ala	Gln	Thr 8080	Leu	Ala	Asp	Gly	Asn 8085	Tyr	Leu	Asn
Ala	Aap 8090	Pro	Asp	ГЛа	Gln	Asn 8095	Ala	Tyr	Lys	Gln	Ala 8100	Val	Ala	Гла
Ala	Glu 8105	Ala	Leu	Leu	Asn	Lys 8110	Gln	Ser	Gly	Thr	Asn 8115	Glu	Val	Gln
Ala	Gln 8120	Val	Glu	Ser	Ile	Thr 8125	Asn	Glu	Val	Asn	Ala 8130	Ala	Lys	Gln
Ala	Leu 8135	Asn	Gly	Asn	Aab	Asn 8140	Leu	Ala	Asn	Ala	Lys 8145	Gln	Gln	Ala
ГЛа	Gln 8150	Gln	Leu	Ala	Asn	Leu 8155	Thr	His	Leu	Asn	Asp 8160	Ala	Gln	Lya
Gln	Ser 8165	Phe	Glu	Ser	Gln	Ile 8170	Thr	Gln	Ala	Pro	Leu 8175	Val	Thr	Aap
Val	Thr 8180	Thr	Ile	Asn	Gln	Lys 8185	Ala	Gln	Thr	Leu	Asp 8190	His	Ala	Met
Glu	Leu 8195	Leu	Arg	Asn	Ser	Val 8200	Ala	Asp	Asn	Gln	Thr 8205	Thr	Leu	Ala

												10 11	1000	
Ser	Glu 8210	Asp	Tyr	His	Asp	Ala 8215	Thr	Ala	Gln	Arg	Gln 8220	Asn	Asp	Tyr
Asn	Gln 8225	Ala	Val	Thr	Ala	Ala 8230	Asn	Asn	Ile	Ile	Asn 8235	Gln	Thr	Thr
Ser	Pro 8240	Thr	Met	Asn	Pro	Asp 8245	Asp	Val	Asn	Gly	Ala 8250	Thr	Thr	Gln
Val	Asn 8255	Asn	Thr	Lys	Val	Ala 8260	Leu	Asp	Gly	Asp	Glu 8265	Asn	Leu	Ala
Ala	Ala 8270	Lys	Gln	Gln	Ala	Asn 8275	Asn	Arg	Leu	Asp	Gln 8280	Leu	Asp	His
Leu	Asn 8285	Asn	Ala	Gln	Lys	Gln 8290	Gln	Leu	Gln	Ser	Gln 8295	Ile	Thr	Gln
Ser	Ser 8300	Asp	Ile	Ala	Ala	Val 8305	Asn	Gly	His	Lys	Gln 8310	Thr	Ala	Glu
Ser	Leu 8315	Asn	Thr	Ala	Met	Gly 8320	Asn	Leu	Ile	Asn	Ala 8325	Ile	Ala	Asp
His	Gln 8330	Ala	Val	Glu	Gln	Arg 8335	Gly	Asn	Phe	Ile	Asn 8340	Ala	Asp	Thr
Aap	Lys 8345	Gln	Thr	Ala	Tyr	Asn 8350		Ala	Val	Asn	Glu 8355	Ala	Ala	Ala
Met	Ile 8360	Asn	Lys	Gln	Thr	Gly 8365	Gln	Asn	Ala	Asn	Gln 8370	Thr	Glu	Val
Glu	Gln 8375	Ala	Ile	Thr	Lys	Val 8380	Gln	Thr	Thr	Leu	Gln 8385	Ala	Leu	Asn
Gly	Aap 8390		Asn	Leu	Gln	Val 8395	Ala	Lys	Thr		Ala 8400	Thr	Gln	Ala
Ile	Asp 8405	Ala	Leu	Thr	Ser	Leu 8410	Asn	Asp	Pro	Gln	Lys 8415	Thr	Ala	Leu
Lys	Asp 8420	Gln	Val	Thr	Ala	Ala 8425	Thr	Leu	Val	Thr	Ala 8430	Val	His	Gln
Ile	Glu 8435	Gln	Asn	Ala	Asn	Thr 8440	Leu	Asn	Gln	Ala	Met 8445	His	Gly	Leu
Arg	Gln 8450	Ser	Ile	Gln	Asp	Asn 8455	Ala	Ala	Thr	Lys	Ala 8460	Asn	Ser	Гуз
Tyr	Ile 8465	Asn	Glu	Asp	Gln	Pro 8470	Glu	Gln	Gln	Asn	Tyr 8475	Asp	Gln	Ala
Val	Gln 8480	Ala	Ala	Asn	Asn	Ile 8485	Ile	Asn	Glu	Gln	Thr 8490	Ala	Thr	Leu
Aap	Asn 8495	Asn	Ala	Ile	Asn	Gln 8500	Ala	Ala	Thr	Thr	Val 8505	Asn	Thr	Thr
Lys	Ala 8510	Ala	Leu	His	Gly	Asp 8515	Val	Lys	Leu	Gln	Asn 8520	Asp	Lys	Asp
His	Ala 8525	Lys	Gln	Thr	Val	Ser 8530	Gln	Leu	Ala	His	Leu 8535	Asn	Asn	Ala
Gln	Lys 8540	His	Met	Glu	Asp	Thr 8545	Leu	Ile	Asp	Ser	Glu 8550	Thr	Thr	Arg
Thr	Ala 8555	Val	Lys	Gln	Asp	Leu 8560	Thr	Glu	Ala	Gln	Ala 8565	Leu	Asp	Gln
Leu	Met 8570	Asp	Ala	Leu	Gln	Gln 8575	Ser	Ile	Ala	Asp	Lys 8580	Asp	Ala	Thr
Arg	Ala 8585	Ser	Ser	Ala	Tyr	Val 8590	Asn	Ala	Glu	Pro	Asn 8595	Гла	Гла	Gln

Ser Tyr Asp Glu Ala Val Gln Asn Ala Glu Ser Ile Ile Ala Gly

_	8600	_	_	_	_	8605	_	_	_	_	8610	_	_	_
Leu	Asn 8615		Pro	Thr	Ile	Asn 8620	-	Gly	Asn		Ser 8625		Ala	Thr
Gln	Ala 8630		Ile	Ser	Ser	Lys 8635		Ala	Leu		Gly 8640	Val	Glu	Arg
Leu	Ala 8645		Asp	Lys	Gln	Thr 8650		Gly	Asn		Leu 8655		His	Leu
Asp	Gln 8660		Thr	Pro	Ala	Gln 8665		Gln	Ala		Glu 8670	Asn	Gln	Ile
Asn	Asn 8675		Thr	Thr	Arg	Gly 8680		Val	Ala		Lys 8685	Leu	Thr	Glu
Ala	Gln 8690		Leu	Asn	Gln	Ala 8695		Glu	Ala		Arg 8700	Asn	Ser	Ile
Gln	Asp 8705		Gln	Gln	Thr	Glu 8710		Gly	Ser		Phe 8715		Asn	Glu
Asp	Lys 8720		Gln	Lys		Ala 8725					Val 8730	Gln	Asn	Ala
Lys	Asp 8735		Ile	Asn	Gln	Thr 8740		Asn	Pro		Leu 8745	-	Lys	Ala
Gln	Val 8750		Gln	Leu	Thr	Gln 8755		Val	Asn		Ala 8760	Lys	Asp	Asn
Leu	His 8765					Leu 8770		Asp	Asp		Gln 8775	His	Ala	Val
Thr	Asp 8780		Asn	Gln	Leu	Asn 8785		Leu	Asn		Pro 8790	Gln	Arg	Gln
Ala	Leu 8795		Ser	Gln	Ile	Asn 8800		Ala	Ala		Arg 8805	Gly	Glu	Val
Ala	Gln 8810	-	Leu	Ala		Ala 8815					Gln 8820	Ala	Met	Gln
Ala	Leu 8825		Asn	Ser	Ile	Gln 8830					Thr 8835	Glu	Ser	Gly
Ser	Lys 8840		Ile	Asn	Glu	Asp 8845		Pro	Gln		Asp 8850	Ala	Tyr	Gln
Ala	Ala 8855		Gln	Asn	Ala	Lys 8860			Ile		Gln 8865	Thr	Gly	Asn
Pro	Thr 8870		Asp			Gln 8875		Glu			Thr 8880	Gln	Ala	Val
Thr	Thr 8885	Ala	Lys	Asp	Asn	Leu 8890		Gly	Asp	Gln	Lys 8895		Ala	Arg
Asp	Gln 8900	Gln	Gln	Ala	Val	Thr 8905	Thr	Val	Asn	Ala	Leu 8910	Pro	Asn	Leu
Asn	His 8915	Ala	Gln	Gln	Gln	Ala 8920	Leu	Thr	Asp	Ala	Ile 8925	Asn	Ala	Ala
Pro	Thr 8930	Arg	Thr	Glu	Val	Ala 8935	Gln	His	Val	Gln	Thr 8940	Ala	Thr	Glu
Leu	Asp 8945	His	Ala	Met	Glu	Thr 8950	Leu	Lys	Asn	Гла	Val 8955	Asp	Gln	Val
Asn	Thr 8960	Asp	Гла	Ala	Gln	Pro 8965	Asn	Tyr	Thr	Glu	Ala 8970	Ser	Thr	Asp
Lys	Lys 8975	Glu	Ala	Val	Asp	Gln 8980	Ala	Leu	Gln	Ala	Ala 8985	Glu	Ser	Ile
Thr		Pro	Thr	Asn	Gly	Ser 8995	Asn	Ala	Asn	Lys		Ala	Val	Asp

Gln	Val 9005	Leu	Thr	Lys	Leu	Gln 9010		Lys	Glu	Asn	Glu 9015	Leu	Asn	Gly
Asn	Glu 9020	Arg	Val	Ala	Glu	Ala 9025		Thr	Gln	Ala	Lys 9030	Gln	Thr	Ile
Asp	Gln 9035	Leu	Thr	His	Leu	Asn 9040		Asp	Gln	Ile	Ala 9045	Thr	Ala	Lys
Gln	Asn 9050	Ile	Asp	Gln	Ala	Thr 9055		Leu	Gln	Pro	Ile 9060	Ala	Glu	Leu
Val	Asp 9065	Gln	Ala	Thr	Gln	Leu 9070		Gln	Ser	Met	Asp 9075	Gln	Leu	Gln
Gln	Ala 9080	Val	Asn	Glu	His	Ala 9085		Val	Glu	Gln	Thr 9090	Val	Asp	Tyr
Thr	Gln 9095	Ala	Asp	Ser	Asp	Lys 9100		Asn	Ala	Tyr	Lys 9105	Gln	Ala	Ile
Ala	Asp 9110	Ala	Glu	Asn	Val	Leu 9115		Gln	Asn	Ala	Asn 9120	Lys	Gln	Gln
Val	Asp 9125	Gln	Ala	Leu	Gln	Asn 9130		Leu	Asn	Ala	Lys 9135	Gln	Ala	Leu
Asn	Gly 9140	Asp	Glu	Arg	Val	Ala 9145		Ala	Lys	Thr	Asn 9150	Gly	Lys	His
Asp	Ile 9155	Asp	Gln	Leu	Asn	Ala 9160	Leu	Asn	Asn	Ala	Gln 9165	Gln	Asp	Gly
Phe	Lys 9170	Gly	Arg	Ile	Asp	Gln 9175		Asn	Asp	Leu	Asn 9180	Gln	Ile	Gln
Gln	Ile 9185	Val	Asp	Glu	Ala	Lys 9190	Ala	Leu	Asn	Arg	Ala 9195	Met	Asp	Gln
Leu	Ser 9200	Gln	Glu	Ile	Thr	Asp 9205		Glu	Gly	Arg	Thr 9210	Lys	Gly	Ser
Thr	Asn 9215	Tyr	Val	Asn	Ala	Asp 9220		Gln	Val	Lys	Gln 9225	Val	Tyr	Asp
Glu	Thr 9230	Val	Asp	Lys	Ala	Lys 9235		Ala	Leu	Asp	Lys 9240	Ser	Thr	Gly
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Arg	Lys 9275	Ala	Glu	Ala	Leu	Gln 9280	Arg	Leu	Asp	Gln	Leu 9285	Thr	His	Leu
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Glu	Thr 9305	Leu	Asn	Lys	Ala	Ser 9310	Arg	Ala	Ile	Asn	Arg 9315	Ala	Thr	Lya
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His	Leu 9335	Gly	Val	Ile	Ser	Ser 9340		Asn	Tyr	Ile	Asn 9345	Ala	Asp	Asp
Asn	Leu 9350	Гла	Ala	Asn	Tyr	Asp 9355		Ala	Ile	Ala	Asn 9360	Ala	Ala	His
Glu	Leu 9365	Asp	Lys	Val	Gln	Gly 9370	Asn	Ala	Ile	Ala	Lys 9375	Ala	Glu	Ala
Glu	Gln 9380	Leu	Lys	Gln	Asn	Ile 9385	Ile	Asp	Ala	Gln	Asn 9390	Ala	Leu	Asn

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Val	Asn 9410	Ser	Leu	Asn	Gly	Leu 9415		Gln	Gln	Gln	Gln 9420	Asp	Leu	Ala
His	Lys 9425	Ala	Ile	Asn	Asn	Ala 9430		Thr	Val	Ser	Asp 9435		Thr	Asp
Ile	Val 9440	Asn	Asn	Gln	Ile	Asp 9445		Asn	Asp	Ala	Met 9450	Glu	Thr	Leu
Lys	His 9455	Leu	Val	Asp	Asn	Glu 9460		Pro	Asn	Ala	Glu 9465	Gln	Thr	Val
Asn	Tyr 9470	Gln	Asn	Ala	Asp	Asp 9475		Ala	Lys	Thr	Asn 9480		Asp	Asp
Ala	Lys 9485		Leu	Ala	Asn	Thr 9490		Leu	Asn	Ser	Asp 9495	Asn	Thr	Asn
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His	Asn 9515	Leu	Asn	Gly	Asp	Gln 9520		Leu	Gln	Asp	Ala 9525	Lys	Asp	ГЛа
Ala	Ile 9530	Gln	Ser	Ile	Asn	Gln 9535		Leu	Ala	Asn	Lys 9540	Leu	Гла	Glu
Ile	Glu 9545	Ala	Ser	Asn	Ala	Thr 9550		Gln	Asp	Lys	Leu 9555	Ile	Ala	Lys
Asn	Lys 9560		Glu	Glu	Leu	Ala 9565		Ser	Ile	Ile	Asn 9570	Asn	Ile	Asn
Гла	Ala 9575		Ser	Asn	Gln	Ala 9580		Ser	Gln	Val	Gln 9585	Thr	Ala	Gly
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ГÀа	Ile 9605		Ala	Asn	Lys	Asp 9610		Asp	Lys	Gln	Val 9615		Ala	Leu
Ile	Asp 9620	Glu	Ile	Asp	Arg	Asn 9625		Asn	Leu	Thr	Asp 9630		Glu	ГЛа
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	Ala 9665					Ala 9670		Gln	Asp		Lys 9675		Leu	Val
LYs	Ala 9680	Lys	Glu	Asp	Ala	Lys 9685		Asp	Val	Asp	Lys 9690		Val	Gln
Ala	Leu 9695		Asp	Glu	Ile	Asp 9700		Asn	Pro	Asn	Leu 9705		Aab	ГЛа
Glu	Lys 9710	Gln	Ala	Leu	Lys	Tyr 9715		Ile	Asn	Gln	Ile 9720	Leu	Gln	Gln
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Leu	Val 9755	Lys	Ala	Lys	Glu	Asp 9760	Ala	ГЛа	Asn	Ala	Ile 9765	Lys	Ala	Leu
Ala	Asn 9770	Ala	Гла	Arg	Asp	Gln 9775		Asn	Ser	Asn	Pro 9780	Asp	Leu	Thr
Pro	Glu	Gln	Lys	Ala	Lys	Ala	Leu	Lys	Glu	Ile	Asp	Glu	Ala	Glu

	9785					9790					97	95					
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Thr	Ala 9890	Thr	Ile	Ser	Asp	Ser 9895	Leu	Thr	Ala	ь Цуя	99		lu	Val	Thr	-	
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Ile	Glu 9935	Asn	Ala	Ala	Gln	Gln 9940	Lys	Ile	Asn	ı Glı	ı Il 99		sn	Asn	Sei	£	
Val	Thr 9950	Leu	Thr	Leu	Glu	Gln 9955	Lys	Glu	Ala	Ala	a Il 99		la	Glu	Val	L	
Asn	Lys 9965	Leu	Lys	Gln	Gln	Ala 9970	Ile	Asp	His	Va]	l As 99		sn	Ala	Pro	>	
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Ile	Glu 9995	Gln	Phe	Asn	Pro	Glu 10000		ı Ph	e Th	r Il		lu 0005	Gl	n A	la I	Ъа	
Ser	Asn 10010		a Ile	ь Гла	Ser	Ile 1001		lu A	sp A	la 1		Gln 1002)		lis 1	Met	Ile	
) Ile		-			5 As		-		/ap		0 G			Ile Gln	
Asp	10010 Glu) Ile Ile	e Lys	; Ala	. Arg	1001 g Thr	5 0 As G]	sp L	eu T	'hr A	Asp 1	1002) Lys 1003!	0 5 7	3lu i	Lys		
Asp Glu	10010 Glu 10025 Ala) Ile Ile) Glr	e Lys e Ala	a Lys	Arg	1001 g Thr 1003 L Asn	5 0 5 1]	sp L	eu T eu L	'hr A	Asp : Glu (1002) Lys 1003! Gln	0 5 0 0	lu i	Lys Ile	Gln	
Asp Glu Ala	10010 Glu 10025 Ala 10040 Ile) Ile , , , , , , , , , , , , , , , , , , ,	e Lys e Ala n Arg	; Ala Lys ; Ala	Arg Leu Glr	1001 3 Thr 1003 1 Asn 1004 1 Ser 1006	5 0 5 0 1 1 0 Ly	sp L In L Le A	eu T eu L sp G	hr A ys (Asp : Glu (Ile) Asn :	1002 Lys 1003 Gln 1005 Ser 1006	0 5 0 5 5 7 6 5	lu i la i	Lys Ile Gln	Gln Gln Leu	
Asp Glu Ala Glu	10010 Glu 10025 Ala 10040 Ile 10055 Gln) Ile ; Ile ; Glr ; Phe Ale	e Lys e Ala n Arg e Lys	; Ala Lys ; Ala ; Ala	Arg Leu Glr Glr	1001 3 Thr 1003 1 Asn 1004 1 Ser 1006 1 Met 1007	5 0 5 0 1 1 0 5 5 6	sp L In L Ie A 75 A	eu T eu L sp G la A	hr A ys (lu] la A	Asp : Glu ([le : Asn : Ger :	1002) Lys 1003! Gln 1005) Ser 1006! Pro 1008)		lu i la i lu i	Lys Ile Gln Ala	Gln Gln Leu Lys	
Asp Glu Ala Glu Glu	10010 Glu 10029 Ala 10040 Ile 10059 Gln 10070 Leu) Ile) Glr ; Phe ; Ala ;	e Lys e Als n Arg e Lys a Lys	s Ala Lys g Ala s Ala s Arg	Arg Leu Glr Glr	1001 3 Thr 1003 1 Asn 1004 1 Ser 1006 1 Met 1007 3 Gln 1009	5 0 As 5 G] 5 I] 5 Ly 6 G] 0 Se	sp L In L Ie A Vs A Iu A	eu T eu L sp G la A la I	hr A ys (lu] la A	Asp : Glu (Asn : Ger :	1002) Lys 1003! Gln 1005) Ser 1006! Pro 1008) Arg 1009!		Glu : Ala : Chr :	Lys Ile Gln Ala Lys	Gln Gln Leu Lys Asp	
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Asp Glu Ala Glu Glu Phe Thr	10010 Glu 10025 Ala 10040 Ile 10055 Gln 10070 Leu 10085 Ser 10100 Ala 10115 Leu) Ile (Ile) (Ile) (Ile) (Ile) (Ile) (Ile) (Ile) (Ile	 Lys Als Arg Lys Lys Glu 	Ala Lys Ala Ala Lys Lys	: Arg : Leu : Glr : Glr : Lys : Ile	1001 Thr 1003 Asn 1004 Ser 1006 Met 1007 Gln 1009 Asn 1010 Asn 1012 (Asp	5 0 5 3 5 5 5 5 5 6 11 5 6 13 5 6 13 13 13 13 13 14 15 13 14 15 15 15 15 15 15 15 15 15 15	3p L ln L le A vs A lu A er I la M	eu T eu L sp G la A la I le A et A	hr / ys (lu] le s .sn (Asp : Slu (Ile : Asn : Sln : Sln : Ala :	1002: Lys 1003: Gln 1005: Ser 1008: Arg 1009: Ser 1011: Lle 1012:		Slu : Ala : Slu : Slu : Slu :	Lys Ile Gln Ala Lys Ile Glu	Gln Gln Leu Lys Gly Ile	
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Asp Glu Ala Glu Glu Phe Thr Val Gln	10010 Glu 10025 Ala 10040 Ile 10055 Gln 10070 Leu 10105 Ser 10100 Ala 10115 Leu 10130 Val 10145 Gln)	 Lys Als Arco Lys Lys Lys Glu Glu Thr Als 	Ala Lys Ala Ala Arg Lys Lys Lys I Lys	: Arg : Lev : Glr : Glr : Ile : Glr : Clr : Arg	1001 Thr 1003 Asn 1004 Ser 1006 Met 1007 Gln 1009 Asn 1010 Ala 1012 Asp 1013 Asn 1015 Asp	5 0 3 5 11 5 12 5 6 11 5 11 5 11 5 11 5 11 5 11 5 11 5 11 11	sp L ln L le A vs A lu A le A le A sn G	eu T sp G la A la I le A sn A	Thr 2 Nys (lu] le s .sn (.sn 2 le 2	Asp : Slu (Ile : Asn : Ser . Asn : Sln Ala : Ala :	1002: Lys 1003: Gln 1005: Ser 1008: Arg 1009: Ser 1011: Ile 1012: His 1014: Arg 1015:		Glu : Glu : Glu : Glu : Glu : Chr : Chr : Chr :	Lys Ile Gln Ala Lys Ile Glu Leu Ser	Gln Gln Leu Lys Gly Ile Gln	
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	Asn 1022		ne G	ly A	sn Va		Ile 10225		Asn	Ala	Ile	Gly 10230		Val	Gly
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	Asn 1038		ln L	ys A	ab ya		Gln 10390		Lys	Asp		Lys 10395		Ala	Ser
	Asn 1040		nr Se	er Lj	ys Lj		Val 10405		Ala	Lys		Lys 10410		Lys	Lys
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Asp	Lys	Lys 35	Phe	Val	Val	Pr	o Glu 40	Ser	Gly	Ile	Asn	Lys I 45	le I	le P:	ro
Ala	Tyr 50	Asp	Glu	Phe	Гла	As 55	n Ser	Pro	Lys	Val	Asn 60	Val S	er A	sn L	eu
Thr 65	Asp	Asn	Гла	Asn	Phe 70	Va	l Ala	Ser	Glu	Asp 75	Lys	Leu A	sn L	ys I 8	
Ala	Asp	Ser	Ser	Ala 85	Ala	Se	r Lys	Ile	Val 90	Asp	Lys	Asn P	he V 9		al
Pro	Glu	Ser	Lys 100	Leu	Gly	As	n Ile	Val 105	Pro	Glu	Tyr	-	lu I 10	le A	sn
Asn	Arg	Val	Asn	Val	Ala	Th	r Asn	Asn	Pro	Ala	Ser	Gln G	ln V	al A	ap

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Lys	His 130	Phe	Val	Ala	Lys	Gly 135	Pro	Glu	Val	Asn	Arg 140	Phe	Ile	Thr	Gln
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Pro	Arg	Tyr 195		His	Pro	Ser	Gln 200	Ser	Leu	Ile	Ile	Lys 205	His	His	Phe
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Pro	Asn	Thr	Leu	Tyr 85	Ile	Glu	Гла	Arg	Asn 90	Leu	Met	Lys	Gln	Lys 95	Leu
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n Lys Tyr Glu Tyr Gly Asp Asn Ile 657070
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Gly T	hr Gl 43		Thr	Leu	Lys	Gly 440	Thr	Gln	Gly	Glu	Ser 445	Ser	Asp	Ile
Glu Va 4	al Ly 50	s Pro	Gln	Ala	Thr 455	Glu	Thr	Thr	Glu	Ala 460	Ser	Gln	Tyr	Gly
Pro A: 465	rg Pr	o Gln	Phe	Asn 470	Lys	Thr	Pro	Lys	Tyr 475	Val	Lys	Tyr	Arg	Asp 480
Ala G	ly Th	r Gly	Ile 485	Arg	Glu	Tyr	Asn	Asp 490	Gly	Thr	Phe	Gly	Tyr 495	Glu
Ala A:	rg Pr	o Arg 500	Phe	Asn	Lys	Pro	Ser 505	Glu	Thr	Asn	Ala	Tyr 510	Asn	Val
Thr T	hr Hi 51		Asn	Gly	Gln	Val 520	Ser	Tyr	Gly	Ala	Arg 525	Pro	Thr	Tyr
Lуа Lj 5:	ys Pr 30	o Ser	Glu	Thr	Asn 535	Ala	Tyr	Asn	Val	Thr 540	Thr	His	Ala	Asn
Gly G 545	ln Va	l Ser	Tyr	Gly 550	Ala	Arg	Pro	Thr	Gln 555	Asn	Lys	Pro	Ser	Lys 560
Thr A	sn Al	a Tyr	Asn 565	Val	Thr	Thr	His	Gly 570	Asn	Gly	Gln	Val	Ser 575	Tyr
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Val T	hr Th 59		Ala	Asn	Gly	Gln 600	Val	Ser	Tyr	Gly	Ala 605	Arg	Pro	Thr
Tyr L 6	ys Ly 10	s Pro	Ser	Гла	Thr 615	Asn	Ala	Tyr	Asn	Val 620	Thr	Thr	His	Ala
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Lys A	la Th	r Thr 20	Aap	Гла	Gln	Gln	Val 25	Pro	Pro	Thr	Гла	Glu 30	Ala	Ala
His H	is Se 35	r Gly	ГЛа	Glu	Ala	Ala 40	Thr	Asn	Val	Ser	Ala 45	Ser	Ala	Gln
Gly T 5		a Asp	Asp	Thr	Asn 55	Ser	Lys	Val	Thr	Ser 60	Asn	Ala	Pro	Ser
Asn Ly 65	ys Pr	o Ser	Thr	Val 70	Val	Ser	Thr	Lys	Val 75	Asn	Glu	Thr	Arg	Asp 80
Val A	sp Th	r Gln	Gln 85	Ala	Ser	Thr	Gln	Lys 90	Pro	Thr	His	Thr	Ala 95	Thr
Phe L	ys Le	u Ser 100	Asn	Ala	Гла	Thr	Ala 105	Ser	Leu	Ser	Pro	Arg 110	Met	Phe
Ala A	la As	n Ala	Pro	Gln	Thr	Thr	Thr	His	Lys	Ile	Leu	His	Thr	Asn

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Asp	Ala	Gly	Asp	Ala 165	Phe	Gln	Gly	Leu	Pro 170	Leu	Ser	Asn	Gln	Ser 175	Lys
Gly	Glu	Glu	Met 180	Ala	Гла	Ala	Met	Asn 185	Ala	Val	Gly	Tyr	Asp 190	Ala	Met
Ala	Val	Gly 195	Asn	His	Glu	Phe	Asp 200	Phe	Gly	Tyr	Asp	Gln 205	Leu	Lys	Lys
Leu	Glu 210	Gly	Met	Leu	Asp	Phe 215	Pro	Met	Leu	Ser	Thr 220	Asn	Val	Tyr	Lys
Asp 225	Gly	Lys	Arg	Ala	Phe 230	Lys	Pro	Ser	Thr	Ile 235	Val	Thr	Lys	Asn	Gly 240
Ile	Arg	Tyr	Gly	Ile 245	Ile	Gly	Val	Thr	Thr 250	Pro	Glu	Thr	Lys	Thr 255	Lys
Thr	Arg	Pro	Glu 260	Gly	Ile	Lys	Gly	Val 265	Glu	Phe	Arg	Asp	Pro 270	Leu	Gln
Ser	Val	Thr 275	Ala	Glu	Met	Met	Arg 280	Ile	Tyr	ГЛа	Asp	Val 285	Asp	Thr	Phe
Val	Val 290	Ile	Ser	His	Leu	Gly 295	Ile	Asp	Pro	Ser	Thr 300	Gln	Glu	Thr	Trp
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Arg		515 Tyr	Tyr	Asp	Ile		520 Lys	Pro	Ser	Gly		525 Arg	Ile	Asn	Ala
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Lys	Arg	Val	Tyr	His 565	Val	Thr	Met	Asn	Asp 570	Phe	Thr	Ala	Ser	Gly 575	Gly
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Asp	Gln	Val 595	Leu	Ala	Ser	Tyr	Leu 600	Lys	Thr	Ala	Asn	Leu 605	Ala	Lys	Tyr
Asp	Thr 610	Thr	Glu	Pro	Gln	Arg 615	Met	Leu	Leu	Gly	Lys 620	Pro	Ala	Val	Ser
3lu 525	Gln	Pro	Ala	Lys	Gly 630	Gln	Gln	Gly	Ser	Lys 635	Gly	Ser	Lys	Ser	Gly 640
JAa	Asp	Thr	Gln	Pro 645	Ile	Gly	Asp	Asp	Lys 650	Val	Met	Asp	Pro	Ala 655	Lys
JÀa	Pro	Ala	Pro 660	Gly	Lys	Val	Val	Leu 665	Leu	Leu	Ala	His	Arg 670	Gly	Thr
Val	Ser	Ser 675	Gly	Thr	Glu	Gly	Ser 680	Gly	Arg	Thr	Ile	Glu 685	Gly	Ala	Thr
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				165					170					175	
Ile	His	Ser	Asp 180		Asp	Asp	Ile	Leu 185	Val	Asn	Met	Phe	Leu 190	Tyr	Leu
Pro	Asn	Phe 195	Phe	Gln	Asn	Gln	Asn 200	Ser	Glu	Asp	Asn	Met 205	Tyr	Leu	Ala
Gln	Arg 210		Met	Tyr	Gln	Val 215	Asp	Asp	Ile	Leu	Lys 220	Glu	Asp	Met	Leu
Asn 225	Glu	Tyr	Tyr	Tyr	Leu 230		Гла	Thr	Leu	Tyr 235	Asn	Thr	Leu	Ala	Ser 240
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Asp	Gln	Tyr	Lys 420	Leu	Phe	Tyr	Lys	Lys 425	Gln	Asp	Leu	Ser	Lys 430	Ser	Phe
Asp	Ala	Thr 435	Phe	Thr	Leu	Leu	Ile 440	Asp	Ala	Ser	Ala	Ser 445	Met	His	Asp
Lys	Met 450	Ala	Glu		Lys					Leu		His	Glu	Thr	Leu
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Phe	Aab	Ser	Asp	Glu 485	His	Ala	Gln	Pro	Asn 490	Ile	Ile	Asn	Glu	Ile 495	Ile
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Leu	Glu	Pro 515	Gln	Asp	Asp	Asn	Arg 520	Asp	Gly	Val	Ala	Ile 525	Arg	Val	Ala
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75 80Asp Ala Ala Thr Thr Asn Ala Gln Val Glu Ala Ile Lys Thr Lys Ala Ile Asn Asp Ile Asn Gln Thr Thr Pro Ala Thr Thr Ala Lys Ala Ala Ala Leu Glu Glu Phe Asp Glu Val Val Gln Ala Gln Ile Asp Gln Ala Pro Leu Asn Pro Asp Thr Thr Asn Glu Glu Val Ala Glu Ala Ile Glu 130 135 Arg Ile Asn Ala Ala Lys Val Ser Gly Val <210> SEQ ID NO 31 <211> LENGTH: 584 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 31 Met Lys Phe Lys Ser Leu Ile Thr Thr Thr Leu Ala Leu Gly Val Leu Ala Ser Thr Gly Ala Asn Phe Asn Asn Asn Glu Ala Ser Ala Ala Ala Lys Pro Leu Asp Lys Ser Ser Ser Ser Leu His His Gly Tyr Ser Lys Val His Val Pro Tyr Ala Ile Thr Val Asn Gly Thr Ser Gln Asn Ile Leu Ser Ser Leu Thr Phe Asn Lys Asn Gln Asn Ile Ser Tyr Lys Asp Leu Glu Asp Arg Val Lys Ser Val Leu Lys Ser Asp Arg Gly Ile Ser Asp Ile Asp Leu Arg Leu Ser Lys Gln Ala Lys Tyr Thr Val Tyr Phe Lys Asn Gly Thr Lys Lys Val Ile Asp Leu Lys Ala Gly Ile Tyr Thr

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Asp 145	Thr	Lys	Lys	Gln	Val 150	Glu	Asp	Lys	Lys	Lys 155	Asp	Lys	Ala	Asn	Tyr 160
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Thr	Lys	Гла	His 260	Ile	Glu	Asn	Гла	Ala 265	Lys	Arg	Asn	Tyr	Gln 270	Val	Pro
Tyr	Ser	Ile 275	Asn	Leu	Asn	Gly	Thr 280	Ser	Thr	Asn	Ile	Leu 285	Ser	Asn	Leu
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Ile 305	Lys	Ser	Val	Leu	Lys 310	His	Aab	Arg	Gly	Ile 315	Ser	Glu	Gln	Aab	Leu 320
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Asp	Leu 530	Lys	Phe	Ala	Lys	Gln 535	Ala	Lys	Tyr	Thr	Val 540	Tyr	Phe	Lys	Asn

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Asn	Pro	Tyr 35	Val	Ser	Glu	Ser	Leu 40	Lys	Leu	Thr	Asn	Asn 45	Lys	Asn	Lys	
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Asp	Asn			Tyr	Leu	Gly			His	Glu	Arg	-		Ser	Val	
Phe		115 Thr	Leu	Гла	Гла		120 Ser	Glu	Glu	Phe	Leu	125 Lys	Glu	Ile	Glu	
Asp	130 Ile	Lys	Lys	Asp	Asn	135 Pro	Glu	Leu	Lys	Asp	140 Phe	Asn	Glu	Glu	Glu	
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Met	Leu	Gly	Lys	165 Thr	Phe	Tyr	Gln	Asn	170 Tyr	Arq	Asp	Asp	Val	175 Glu	Ser	
		-	180			-	_	185		-	Lys	_	190	_		
	-	195	-		_		200		-	-	Glu	205			-	
	210	-	-			215	-	-			220		-	-		
225					230	-				235	Aap		-	-	240	
Arg	Pro	Asn	Asn	Ile 245	Pro	Val	Leu	Glu	Asp 250	Glu	Lys	Gln	Glu	Glu 255	ГЛА	
Asn	His	Lys	Asn 260	Met	Ala	Gln	Leu	Lys 265	Ser	Asp	Thr	Glu	Ala 270	Ala	Lys	
Ser	Asp	Glu 275	Ser	Lys	Arg	Ser	Lys 280	Arg	Ser	ГÀа	Arg	Ser 285	Leu	Asn	Thr	
Gln	Asn 290	His	Lys	Pro	Ala	Ser 295	Gln	Glu	Val	Ser	Glu 300	Gln	Gln	Lys	Ala	
Glu 305	Tyr	Asp	Lys	Arg	Ala 310	Glu	Glu	Arg	Lys	Ala 315	Arg	Phe	Leu	Asp	Asn 320	
Gln	Lys	Ile	Lys	Lys 325	Thr	Pro	Val	Val	Ser 330	Leu	Glu	Tyr	Asp	Phe 335	Glu	

His	Lys	Gln	Arg 340	Ile	Asp	Asn	Glu	Asn 345	Asp	Lys	Lys	Leu	Val 350	Val	Ser
Ala	Pro	Thr 355	Lys	Гла	Pro	Thr	Ser 360	Pro	Thr	Thr	Tyr	Thr 365	Glu	Thr	Thr
Thr	Gln 370	Val	Pro	Met	Pro	Thr 375	Val	Glu	Arg	Gln	Thr 380	Gln	Gln	Gln	Ile
Ile 385	Tyr	Asn	Ala	Pro	Lys 390	Gln	Leu	Ala	Gly	Leu 395	Asn	Gly	Glu	Ser	His 400
Asp	Phe	Thr	Thr	Thr 405	His	Gln	Ser	Pro	Thr 410	Thr	Ser	Asn	His	Thr 415	His
Asn	Asn	Val	Val 420	Glu	Phe	Glu	Glu	Thr 425	Ser	Ala	Leu	Pro	Gly 430	Arg	Lya
Ser	Gly	Ser 435	Leu	Val	Gly	Ile	Ser 440	Gln	Ile	Asp	Ser	Ser 445	His	Leu	Thr
Glu	Arg 450	Glu	Lys	Arg	Val	Ile 455	Lys	Arg	Glu	His	Val 460	Arg	Glu	Ala	Gln
Lys 465	Leu	Val	Asp	Asn	Tyr 470	Lys	Asp	Thr	His	Ser 475	Tyr	Lys	Asp	Arg	Ile 480
Asn	Ala	Gln	Gln	Lys 485	Val	Asn	Thr	Leu	Ser 490	Glu	Gly	His	Gln	Lys 495	Arg
Phe	Asn	Lys	Gln 500	Ile	Asn	Lys	Val	Tyr 505	Asn	Gly	Lys				
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20/	

Leu Leu Ser Glu Ala Lys Lys Leu Asn Glu Ser Gln Ala Pro Lys AlaApp Aan Lys Phe Aan Lys Glu Gln Gln Ann Ala Phe Tyr Glu Ile LeuAlas Pan Lys Phe Aan Lys Glu Gln Gln Ann Ala Phe Tyr Glu Ile LeuHis Leu Pro Asn Leu Asn Glu Glu Gln Arg Asn Gly Phe Ile Gln Ser245Leu Lys Asp Asp Pro Ser Gln Ser Ala Asn Leu Leu Ala Glu Ala LysLys Leu Aan Asp Ala Gln Ala Pro Lys Ala Asp Asn Lys Phe Asn Lys290Glu Gln Gln Asn Ala Phe Tyr Glu Ile Leu His Leu Pro Asn Leu Thr290301Glu Gln Gln Asn Ala Phe Tyr Glu Ile Leu His Lys Asp Asp Pro Ser310311212213214215214215215215216216217218219219219210211211211212212213213214215215215216216217218218219219219219219219219211219211219211211121112112212213213213214215214215215215216216217				195					200					205			
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Asp Thr Val Asn Asp Ile Ala Lys Ala Asn Gly Thr Thr Ala Asp Lys 435 Asp Thr Val Asn Asp Asn Lys Leu Ala Asp Lys Asn Met Ile Lys Pro Gly 450 Gln Glu Leu Val Val Asp Lys Lys Gln Pro Ala Asn His Ala Asp Ala 465 Asn Lys Ala Gln Ala Leu Pro Glu Thr Gly Glu Glu Asn Pro Phe Ile 485 Gly Thr Thr Val Phe Gly Gly Leu Ser Leu Ala Leu Gly Ala Ala Leu 500 Leu Ala Gly Arg Arg Arg Glu Leu 515 S20 <210> SEQ ID NO 34 <211> LENGTH: 291 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 34 Ala Gln His Asp Glu Ala Lys Lys Asn Ala Phe Tyr Gln Val Leu Asn 1 Met Pro Asn Leu Asn Ala Asp Gln Arg Asn Gly Phe Ile Gln Ser Leu 20 25 30	1	Lys	Pro	Gly	Lys		Asp	Asn	Asn	Lys		Gly	Lys	Glu	Asp	-	Asn
435440445Ile Ala Ala Asp Asn Lys Leu Ala Asp Lys Asn Met Ile Lys Pro Gly 450Gln Glu Leu Val Val Asp Lys Lys Gln Pro Ala Asn His Ala Asp Ala 460Asn Lys Ala Gln Ala Leu Pro Glu Thr Gly Glu Glu Asn Pro Phe Ile 485Asn Lys Ala Gln Ala Leu Pro Glu Thr Gly Glu Glu Asn Pro Phe Ile 485Gly Thr Thr Val Phe Gly Gly Leu Ser Leu Ala Leu Gly Ala Ala Leu 500Leu Ala Gly Arg Arg Arg Glu Leu 515<210> SEQ ID NO 34 <211> LENGTH: 291 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus<400> SEQUENCE: 34Ala Gln His Asp Glu Ala Lys Lys Asn Ala Phe Tyr Gln Val Leu Asn 10Met Pro Asn Leu Asn Ala Asp Gln Arg Asn Gly Phe Ile Gln Ser Leu 2021 <td>1</td> <td>Lys</td> <td>Pro</td> <td>Gly</td> <td>-</td> <td>Glu</td> <td>Asp</td> <td>Gly</td> <td>Asn</td> <td>-</td> <td>Val</td> <td>His</td> <td>Val</td> <td>Val</td> <td>-</td> <td>Pro</td> <td>Gly</td>	1	Lys	Pro	Gly	-	Glu	Asp	Gly	Asn	-	Val	His	Val	Val	-	Pro	Gly
450 455 460 Gln Glu Leu Val Val Asp Lys Lys Gln Pro Ala Asn His Ala Asp Ala 465 Ann Lys Ala Gln Ala Leu Pro Glu Thr Gly Glu Glu Asn Pro Phe Ile 485 470 Gly Leu Ser Leu Ala Leu Gly Ala Ala Leu 500 500 500 500 500 Leu Ala Gly Arg Arg Arg Glu Leu 515 520 <210> SEQ ID NO 34 <211> LENGTH: 291 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 34 Ala Gln His Asp Glu Ala Lys Lys Asn Ala Phe Tyr Gln Val Leu Asn 1 5 10 Met Pro Asn Leu Asn Ala Asp Gln Arg Asn Gly Phe Ile Gln Ser Leu 20 25 30	j	Asp	Thr		Asn	Asp	Ile	Ala	-	Ala	Asn	Gly	Thr		Ala	Asp	Lys
465470475480Asn Lys Ala Gln Ala Leu Pro Glu Thr Gly Glu Glu Asn Pro Phe Ile 485480Gly Thr Thr Val Phe Gly Gly Leu Ser Leu Ala Leu Gly Ala Ala Leu 505500Leu Ala Gly Arg Arg Arg Glu Leu 515520<210> SEQ ID NO 34 <211> LENGTH: 291 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus<400> SEQUENCE: 34Ala Gln His Asp Glu Ala Lys Lys Asn Ala Phe Tyr Gln Val Leu Asn 1Met Pro Asn Leu Asn Ala Asp Gln Arg Asn Gly Phe Ile Gln Ser Leu 20		Ile		Ala	Asp	Asn	ГЛЗ		Ala	Asp	Lys	Asn		Ile	Гла	Pro	Gly
485490495Gly Thr Thr Val Phe Gly Gly Leu Ser Leu Ala Leu Gly Ala Ala LeuAla Cly Ala Cly Ala Ala LeuAla LeuLeu Ala Gly Arg Arg Arg Arg Glu Leu SloSEQ ID NO 34Ser LeuSAR<210> SEQ ID NO 34Staphylococcus aureusSer Seq ID NO 34<212> TYPE: PRTStaphylococcus aureusSeq ID NO 34<213> ORGANISM: Staphylococcus aureusSeq ID NO 34<400> SEQUENCE: 34In His Asp Glu Ala Lys Lys Asn Ala Phe Tyr Gln Val 15Met Pro Asn Leu Asn Ala Asp Gln Arg Asn Gly Phe Ile Gln Ser Leu 30			Glu	Leu	Val	Val		ГЛЗ	Гла	Gln	Pro		Asn	His	Ala	Asp	
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Ala Gln His Asp Glu Ala Lys Lys Asn Ala Phe Tyr Gln Val Leu Asn 1 5 10 15 Met Pro Asn Leu Asn Ala Asp Gln Arg Asn Gly Phe Ile Gln Ser Leu 20 25 30		<211 <212	L> LE 2> TY	ENGTH 7PE :	H: 29 PRT	91	phylo	0000	cus a	aureu	15						
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20 25 30			Gln	His	Asp		Ala	ГЛа	Lys	Asn		Phe	Tyr	Gln	Val		Asn
	J	Met	Pro	Asn		Asn	Ala	Asp	Gln		Asn	Gly	Phe	Ile		Ser	Leu
Lys Ala Ala Pro Ser Gln Ser Ala Asn Val Leu Gly Glu Ala Gln Lys 35 40 45	1	Lys	Ala		Pro	Ser	Gln	Ser		Asn	Val	Leu	Gly		Ala	Gln	Lys

Leu	Asn 50	Asp	Ser	Gln	Ala	Pro 55	Lys	Ala	Asb	Ala	Gln 60	Gln	Asn	Asn	Phe
Asn 65	Lys	Asp	Lys	Lys	Ser 70	Ala	Phe	Tyr	Glu	Ile 75	Leu	Asn	Met	Pro	Asn 80
Leu	Asn	Glu	Ala	Gln 85	Arg	Asn	Gly	Phe	Ile 90	Gln	Ser	Leu	Lys	Ala 95	Ala
Pro	Ser	Gln	Ser 100	Thr	Asn	Val	Leu	Gly 105	Glu	Ala	Lys	Lys	Leu 110	Asn	Glu
Ser	Gln	Ala 115	Pro	Lys	Ala	Asp	Asn 120	Asn	Phe	Asn	Lys	Glu 125	Lys	Lys	Asn
Ala	Phe 130	Tyr	Glu	Ile	Leu	Asn 135	Met	Pro	Asn	Leu	Asn 140	Glu	Glu	Gln	Arg
Asn 145	Gly	Phe	Ile	Gln	Ser 150	Leu	Lys	Ala	Ala	Pro 155	Ser	Gln	Ser	Ala	Asn 160
Leu	Leu	Ser	Glu	Ala 165	Lys	Lys	Leu	Asn	Glu 170	Ser	Gln	Ala	Pro	Lys 175	Ala
Asp	Asn	Lys	Phe 180	Asn	Гла	Glu	Lys	Lys 185	Asn	Ala	Phe	Tyr	Glu 190	Ile	Leu
TT-2	T	Dece	7	T	7	a 1	a 1	a 1	7	7	a1	D 1	T 1 -	a 1	a

Asn Gly Phe Ile Gln Ser Leu Lys Ala Ala Pro Ser Leu Leu Ser Glu Ala Lys Lys Leu Asn Glu Ser Gln Asp Asn Lys Phe Asn Lys Glu Lys Lys Asn Ala Phe His Leu Pro Asn Leu Asn Glu Glu Gln Arg Asn Gly Phe Ile Gln Ser Leu Lys Ala Ala Pro Ser Gln Ser Ala Asn Leu Leu Ala Glu Ala Lys Lys Leu Asn Asp Ala Gln Ala Pro Lys Ala Asp Asn Lys Phe Asn Lys Glu Lys Lys Asn Ala Phe Tyr Glu Ile Leu His Leu Pro Asn Leu Thr Glu Glu Gln Arg Asn Gly Phe Ile Gln Ser Leu Lys Ala Ala Pro Ser Val Ser Lys Glu Ile Leu Ala Glu Ala Lys Lys Leu Asn Asp Ala Gln Ala Pro Lys <210> SEQ ID NO 35 <211> LENGTH: 772 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 35 Met Lys Ala Leu Leu Leu Lys Thr Ser Val Trp Leu Val Leu Leu Phe

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Ala	Lys 130	Thr	Ala	Ser	Leu	Ser 135	Pro	Arg	Met	Phe	Ala 140	Ala	Asn	Ala	Pro
Gln 145	Thr	Thr	Thr	His	Lys 150	Ile	Leu	His	Thr	Asn 155	Asp	Ile	His	Gly	Arg 160
Leu	Ala	Glu	Glu	Lys 165	Gly	Arg	Val	Ile	Gly 170	Met	Ala	Lys	Leu	Lys 175	Thr
Val	Lys	Glu	Gln 180	Glu	Гла	Pro	Asp	Leu 185	Met	Leu	Asp	Ala	Gly 190	Asp	Ala
Phe	Gln	Gly 195	Leu	Pro	Leu	Ser	Asn 200	Gln	Ser	Lys	Gly	Glu 205	Glu	Met	Ala
ГЛа	Ala 210	Met	Asn	Ala	Val	Gly 215	Tyr	Asp	Ala	Met	Ala 220	Val	Gly	Asn	His
Glu 225	Phe	Asp	Phe	Gly	Tyr 230	Asp	Gln	Leu	Lys	Lys 235	Leu	Glu	Gly	Met	Leu 240
Asp	Phe	Pro	Met	Leu 245	Ser	Thr	Asn	Val	Tyr 250	Гла	Asp	Gly	Lys	Arg 255	Ala
Phe	Lys	Pro	Ser 260	Thr	Ile	Val	Thr	Lys 265	Asn	Gly	Ile	Arg	Tyr 270	Gly	Ile
Ile	Gly	Val 275	Thr	Thr	Pro	Glu	Thr 280	Lys	Thr	Lys	Thr	Arg 285	Pro	Glu	Gly
Ile	Lys 290	Gly	Val	Glu	Phe	Arg 295	Asp	Pro	Leu	Gln	Ser 300	Val	Thr	Ala	Glu
Met 305	Met	Arg	Ile	Tyr	Lys 310	Asp	Val	Aab	Thr	Phe 315	Val	Val	Ile	Ser	His 320
Leu	Gly	Ile	Asp	Pro 325	Ser	Thr	Gln	Glu	Thr 330	Trp	Arg	Gly	Asp	Tyr 335	Leu
Val	Lys	Gln	Leu 340	Ser	Gln	Asn	Pro	Gln 345	Leu	Lys	ГЛЗ	Arg	Ile 350	Thr	Val
Ile	Asp	Gly 355	His	Ser	His	Thr	Val 360	Leu	Gln	Asn	Gly	Gln 365	Ile	Tyr	Asn
Asn	Asp 370	Ala	Leu	Ala	Gln	Thr 375	Gly	Thr	Ala	Leu	Ala 380	Asn	Ile	Gly	Lys
Ile 385	Thr	Phe	Asn	Tyr	Arg 390	Asn	Gly	Glu	Val	Ser 395	Asn	Ile	Lys	Pro	Ser 400
Leu	Ile	Asn	Val	Lys 405	Asp	Val	Glu	Asn	Val 410	Thr	Pro	Asn	Lys	Ala 415	Leu
Ala	Glu	Gln	Ile 420	Asn	Gln	Ala	Asp	Gln 425	Thr	Phe	Arg	Ala	Gln 430	Thr	Ala
Glu	Val	Ile 435	Ile	Pro	Asn	Asn	Thr 440	Ile	Asp	Phe	ГЛа	Gly 445	Glu	Arg	Aap
Asp	Val 450	Arg	Thr	Arg	Glu	Thr 455	Asn	Leu	Gly	Asn	Ala 460	Ile	Ala	Asp	Ala
Met 465	Glu	Ala	Tyr	Gly	Val 470	Гла	Asn	Phe	Ser	Lys 475	Lys	Thr	Asp	Phe	Ala 480
Val	Thr	Asn	Gly	Gly 485	Gly	Leu	Arg	Ala	Ser 490	Ile	Ala	Lys	Gly	Lys 495	Val
Thr	Arg	Tyr	Asp 500	Leu	Ile	Ser	Val	Leu 505	Pro	Phe	Gly	Asn	Thr 510	Ile	Ala
Gln	Ile	Asp 515	Val	Lys	Gly	Ser	Asp 520	Val	Trp	Thr	Ala	Phe 525	Glu	His	Ser
Leu	Gly 530	Ala	Pro	Thr	Thr	Gln 535	Lys	Asp	Gly	Lys	Thr 540	Val	Leu	Thr	Ala

Asn 545	Gly	Gly	Leu	Leu	His 550	Ile	Ser	Asb	Ser	Ile 555	Arg	Val	Tyr	Tyr	Asp 560
Ile	Asn	Lys	Pro	Ser 565	Gly	Lys	Arg	Ile	Asn 570	Ala	Ile	Gln	Ile	Leu 575	Asn
Lys	Glu	Thr	Gly 580	Lys	Phe	Glu	Asn	Ile 585	Asp	Leu	Lys	Arg	Val 590	Tyr	His
Val	Thr	Met 595	Asn	Asp	Phe	Thr	Ala 600	Ser	Gly	Gly	Asp	Gly 605	Tyr	Ser	Met
Phe	Gly 610	Gly	Pro	Arg	Glu	Glu 615	Gly	Ile	Ser	Leu	Asp 620	Gln	Val	Leu	Ala
Ser 625	Tyr	Leu	Гла	Thr	Ala 630	Asn	Leu	Ala	Lys	Tyr 635	Asp	Thr	Thr	Glu	Pro 640
Gln	Arg	Met	Leu	Leu 645	Gly	Lys	Pro	Ala	Val 650	Ser	Glu	Gln	Pro	Ala 655	Lys
Gly	Gln	Gln	Gly 660	Ser	Lys	Gly	Ser	Lys 665	Ser	Gly	Lys	Asp	Thr 670	Gln	Pro
Ile	Gly	Asp 675	Asp	Lys	Val	Met	Asp 680	Pro	Ala	Lys	Lys	Pro 685	Ala	Pro	Gly
ГЛа	Val 690	Val	Leu	Leu	Leu	Ala 695	His	Arg	Gly	Thr	Val 700	Ser	Ser	Gly	Thr
Glu 705	Gly	Ser	Gly	Arg	Thr 710	Ile	Glu	Gly	Ala	Thr 715	Val	Ser	Ser	Lys	Ser 720
Gly	Lys	Gln	Leu	Ala 725	Arg	Met	Ser	Val	Pro 730	Lys	Gly	Ser	Ala	His 735	Glu
Lys	Gln	Leu	Pro 740	Lys	Thr	Gly	Thr	Asn 745	Gln	Ser	Ser	Ser	Pro 750	Glu	Ala
Met	Phe	Val 755	Leu	Leu	Ala	Gly	Ile 760	Gly	Leu	Ile	Ala	Thr 765	Val	Arg	Arg
Arg	Lys 770	Ala	Ser												
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	3> OF			-	phylo	0000	cus a	aureu	15						
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1	-		-	5					10					15	
Thr	Ala	Суз	Gly 20	Asn	Asp	Thr	Pro	Lys 25	Aab	Glu	Thr	Lys	Ser 30	Thr	Glu
Ser	Asn	Thr 35	Asn	Gln	Asp	Thr	Asn 40	Thr	Thr	Lys	Asp	Val 45	Ile	Ala	Leu
ГÀа	Asp 50	Val	Lys	Thr	Ser	Pro 55	Glu	Aab	Ala	Val	Lys 60	Lys	Ala	Glu	Glu
Thr 65	Tyr	Lys	Gly	Gln	Lys 70	Leu	Гла	Gly	Ile	Ser 75	Phe	Glu	Asn	Ser	Asn 80
Gly	Glu	Trp	Ala	Tyr 85	Lys	Val	Thr	Gln	Gln 90	Lys	Ser	Gly	Glu	Glu 95	Ser
Glu	Val	Leu	Val 100	Ala	Asp	Lys	Asn	Lys 105	Lys	Val	Ile	Asn	Lys 110	Lys	Thr
Glu	Lys	Glu 115	Asp	Thr	Met	Asn	Glu 120	Asn	Aap	Asn	Phe	Lys 125	Tyr	Ser	Aab
Ala	Ile 130	Asp	Tyr	Lys	Lys	Ala 135	Ile	Lys	Glu	Gly	Gln 140	Lys	Glu	Phe	Asp

Gly Asp Ile Lys Glu Trp Ser Leu Glu Lys Asp Asp Gly Lys Leu Val Tyr Asn Ile Asp Leu Lys Lys Gly Asn Lys Lys Gln Glu Val Thr Val Asp Ala Lys Asn Gly Lys Val Leu Lys Ser Glu Gln Asp His <210> SEQ ID NO 37 <211> LENGTH: 502 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 37 Met Arg Glu Asn Phe Lys Leu Arg Lys Met Lys Val Gly Leu Val Ser Val Ala Ile Thr Met Leu Tyr Ile Met Thr Asn Gly Gln Ala Glu Ala Ser Glu Asn Gln Asn Ala Leu Ile Ser Asn Ile Asn Val Asp Asn Gln Glu Lys Gln Asn Asn Val Asn Gln Ala Val Gln Pro Gln Asn Asn Thr Asn Glu Thr Ser Lys Val Pro Ala Asn Phe Val Lys Leu Asn Asp Ile 65 70 75 80 Lys Pro Gly Asp Thr Ser Ile Gln Gly Thr Thr Leu Pro Asn Gln Phe Ile Leu Leu Thr Ile Asp Lys Lys Asp Val Ser Ser Val Glu Asp Ser Asp Ser Ser Phe Val Met Ser Asp Lys Asp Gly Asn Phe Lys Tyr Asp Leu Asn Gly Arg Lys Ile Val His Asn Gln Glu Ile Glu Val Ser Ser Ser Asp Pro Tyr Leu Gly Asp Asp Glu Glu Asp Glu Glu Val Glu Glu Thr Ser Thr Glu Glu Val Gly Ala Glu Glu Glu Ser Thr Glu Ala Lys Ala Thr Tyr Thr Thr Pro Arg Tyr Glu Lys Ala Tyr Glu Ile Pro Lys Glu Gln Leu Lys Glu Lys Asp Gly His His Gln Val Phe Ile Glu Pro Lys Val Ala Leu Ser Ile Asn Asn Lys Phe Ile Asn Phe Glu Thr Asn Ala Asn Gly Gly Pro Asn Lys Glu Glu Ala Lys Ser Gly Ser Glu Gly Ile \mbox{Trp} Met Pro Ile Asp
 Asp Lys Gly \mbox{Tyr} Phe Asn Phe Asp Phe Lys Thr Lys Arg Phe Asp Asp Leu Glu Leu Lys Lys Asn Asp Glu Ile Ser Leu Thr Phe Ala Pro Asp Asp Glu Asp Glu Ala Leu Lys Ser Leu Ile Phe Lys Thr Lys Val Thr Ser Leu Glu Asp Ile Asp Lys Ala Glu Thr Lys Tyr Asp His Thr Lys Val Glu Lys Val Lys Val Leu Lys Asp Val

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				325					330					335	
Lys	Glu	Asp	Leu 340	His	Val	Asp	Glu	Ile 345	Tyr	Gly	Ser	Leu	Tyr 350	His	Thr
Glu	Lys	Gly 355	Lys	Gly	Ile	Leu	Asp 360	Lys	Glu	Gly	Thr	Lys 365	Val	Ile	Lys
Gly	Lys 370	Thr	Lys	Phe	Ala	Asn 375	Ala	Val	Val	Lys	Val 380	Asp	Ser	Glu	Leu
Gly 385	Glu	Gly	Gln	Glu	Phe 390	Pro	Asp	Leu	Gln	Val 395	Asp	Glu	Lys	Gly	Glu 400
Phe	Ser	Phe	Asp	Val 405	Asp	His	Ala	Gly	Phe 410	Arg	Leu	Gln	Asn	Gly 415	Glu
Thr	Leu	Asn	Phe 420	Thr	Val	Val	Asp	Pro 425	Ile	Thr	Gly	Glu	Leu 430	Leu	Ser
Gly	Asn	Phe 435	Val	Ser	Lys	Asn	Ile 440	Asp	Ile	Tyr	Glu	Ser 445	Pro	Glu	Glu
Lys	Ala 450	Asp	Arg	Glu	Phe	Asp 455	Glu	Arg	Met	Glu	Asn 460	Thr	Pro	Ala	Tyr
His 465	Lya	Leu	His	Gly	Asp 470	ГЛа	Ile	Val	Gly	Tyr 475	Asp	Thr	Asn	Gly	Phe 480
Pro	Ile	Thr	Trp	Phe 485	Tyr	Pro	Leu	Gly	Glu 490	ГÀа	ГÀа	Val	Glu	Arg 495	ГЛа
Ala	Pro	Lys	Leu 500	Glu	Гла										
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ГЛа	Gly	Ser 35	Lys	Asp	Thr	Val	Lys 40	Ile	Glu	Asn	Asn	Tyr 45	Гла	Met	Arg
Gly	Glu 50	Lys	Lys	Asp	Gly	Ser 55	Asp	Ala	Lys	Lys	Val 60	Lys	Glu	Thr	Val
Glu 65	Val	Pro	Lys	Asn	Pro 70	Гла	Asn	Ala	Val	Val 75	Leu	Asp	Tyr	Gly	Ala 80
Leu	Asp	Val	Met	Lys 85	Glu	Met	Gly	Leu	Ser 90	Asp	Lys	Val	Гуз	Ala 95	Leu
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Lys	Asp	Asp 115	Lys	Tyr	Thr	Asn	Val 120	Gly	Asn	Leu	Гла	Glu 125	Val	Asn	Phe
Asp	Lys 130	Leu	Ala	Ala	Thr	Lys 135	Pro	Glu	Val	Ile	Phe 140	Ile	Ser	Gly	Arg
Thr 145	Ala	Asn	Gln	Lys	Asn 150	Leu	Asp	Glu	Phe	Lys 155	Lys	Ala	Ala	Pro	Lys 160
Ala	Lys	Ile	Val	Tyr 165	Val	Gly	Ala	Asp	Glu 170	Lys	Asn	Leu	Ile	Gly 175	Ser
Met	Lys	Gln	Asn 180	Thr	Glu	Asn	Ile	Gly 185	Lys	Ile	Tyr	Asp	Lys 190	Glu	Asp

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Lys	Ala	Lys 195	Glu	Leu	Asn	Lys	Asp 200	Leu	Asp	Asn	Lys	Ile 205	Ala	Ser	Met
Lys	Asp 210	Lys	Thr	Lys	Asn	Phe 215	Asn	Lys	Thr	Val	Met 220	Tyr	Leu	Leu	Val
Asn 225	Glu	Gly	Glu	Leu	Ser 230	Thr	Phe	Gly	Pro	Lys 235	Gly	Arg	Phe	Gly	Gly 240
Leu	Val	Tyr	Asp	Thr 245	Leu	Gly	Phe	Asn	Ala 250	Val	Asp	Lys	Lys	Val 255	Ser
Asn	Ser	Asn	His 260	Gly	Gln	Asn	Val	Ser 265	Asn	Glu	Tyr	Val	Asn 270	Lys	Glu
Asn	Pro	Asp 275	Val	Ile	Leu	Ala	Met 280	Asp	Arg	Gly	Gln	Ala 285	Ile	Ser	Gly
ГÀа	Ser 290	Thr	Ala	Lya	Gln	Ala 295	Leu	Asn	Asn	Pro	Val 300	Leu	Lys	Asn	Val
Lys 305	Ala	Ile	Lys	Glu	Asp 310	Lys	Val	Tyr	Asn	Leu 315	Asp	Pro	Lys	Leu	Trp 320
Tyr	Phe	Ala	Ala	Gly 325	Ser	Thr	Thr	Thr	Thr 330	Ile	LYa	Gln	Ile	Glu 335	Glu
Leu	Aab	Lys	Val 340	Val	Lys										
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Ser	Ser	Glu 35	Ala	Lys	Ala	Tyr	Asn 40	Ile	Ser	Glu	Asn	Glu 45	Thr	Asn	Ile
Asn	Glu 50	Leu	Ile	Lys	Tyr	Tyr 55	Thr	Gln	Pro	His	Phe 60	Ser	Leu	Ser	Gly
Lys 65	Trp	Leu	Trp	Gln	Lys 70	Pro	Asn	Gly	Ser	Ile 75	His	Ala	Thr	Leu	Gln 80
Thr	Trp	Val	Trp	Tyr 85	Ser	His	Ile	Gln	Val 90	Phe	Gly	Ser	Glu	Ser 95	Trp
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Lys	Aab	Glu 115	Asp	Thr	Val	Glu	Gly 120	Tyr	Trp	Thr	Tyr	Asp 125	Glu	Thr	Phe
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Leu 145	Phe	Leu	ГЛа	Tyr	Ser 150	Asp	Lys	Gln	Gln	Thr 155	Ile	Ile	Gly	Gly	His 160
Glu	Phe	Tyr	Lys	Gly 165	Asn	ГЛа	Pro	Val	Leu 170	Thr	Leu	Lys	Glu	Leu 175	Aap
Phe	Arg	Ile	Arg 180	Gln	Thr	Leu	Ile	Lys 185	Asn	Lys	Lys	Leu	Tyr 190	Asn	Gly
Glu	Phe	Asn 195	ГЛа	Gly	Gln	Ile	Lys 200	Ile	Thr	Ala	Asp	Gly 205	Asn	Asn	Tyr
Thr	Ile 210	Asp	Leu	Ser	Lys	Lys 215	Leu	Lys	Leu	Thr	Asp 220	Thr	Asn	Arg	Tyr

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284

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Tyr	Gly	Tyr 35	Asn	Pro	Asn	Asp	Pro 40	Thr	Ser	Tyr	Ser	Tyr 45	Thr	Tyr	Thr
Ile	Asp 50	Ala	Gln	Gly	Asn	Tyr 55	His	Tyr	Thr	Trp	Lys 60	Gly	Asn	Trp	His
Pro 65	Ser	Gln	Leu	Asn	Gln 70	Asp	Asn	Gly	Tyr	Tyr 75	Ser	Tyr	Tyr	Tyr	Tyr 80
Asn	Gly	Tyr	Asn	Asn 85	Tyr	Asn	Asn	Tyr	Asn 90	Asn	Gly	Tyr	Ser	Tyr 95	Asn
Asn	Tyr	Ser	Arg 100	Tyr	Asn	Asn	Tyr	Ser 105	Asn	Asn	Asn	Gln	Ser 110	Tyr	Asn
Tyr	Asn	Asn 115	Tyr	Asn	Ser	Tyr	Asn 120	Thr	Asn	Ser	Tyr	Arg 125	Thr	Gly	Gly
Leu	Gly 130	Ala	Ser	Tyr	Ser	Thr 135	Ser	Ser	Asn	Asn	Val 140	Gln	Val	Thr	Thr
Thr 145	Met	Ala	Pro	Ser	Ser 150	Asn	Gly	Arg	Ser	Ile 155	Ser	Ser	Gly	Tyr	Thr 160
Ser	Gly	Arg	Asn	Leu 165	Tyr	Thr	Ser	Gly	Gln 170	Cys	Thr	Tyr	Tyr	Val 175	Phe
Asp	Arg	Val	Gly 180	Gly	Lys	Ile	Gly	Ser 185	Thr	Trp	Gly	Asn	Ala 190	Ser	Asn
Trp	Ala	Asn 195	Ala	Ala	Ala	Arg	Ala 200	Gly	Tyr	Thr	Val	Asn 205	Asn	Thr	Pro
Lys	Ala 210	Gly	Ala	Ile	Met	Gln 215	Thr	Thr	Gln	Gly	Ala 220	Tyr	Gly	His	Val
Ala 225	Tyr	Val	Glu	Ser	Val 230	Asn	Ser	Asn	Gly	Ser 235	Val	Arg	Val	Ser	Glu 240
Met	Asn	Tyr	Gly	Tyr 245	Gly	Pro	Gly	Val	Val 250	Thr	Ser	Arg	Thr	Ile 255	Ser
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Ala	Cya	Gly	Gln 20	Asp	Ser	Asp	Gln	Gln 25	Lys	Aap	Gly	Asn	Lуз 30	Glu	Lys
Asp	Asp	Lys 35	Ala	Lys	Thr	Glu	Gln 40	Gln	Asp	Lys	Гла	Thr 45	Asn	Asp	Ser
Ser	Lys 50	Aap	Lya	rÀa	Asp	Asn 55	Lys	Asp	Aap	Ser	Lуз 60	Asp	Val	Asn	Lys
Asp 65	Asn	Lys	Asp	Asn	Ser 70	Ala	Asn	Asp	Asn	Gln 75	Gln	Gln	Ser	Asn	Ser 80
Asn	Ala	Thr	Asn	Asn 85	Asp	Gln	Asn	Gln	Thr 90	Asn	Asn	Asn	Gln	Ser 95	Ser
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Leu 145	Asn	Ala	Ala	Asn	Asn 150	Glu	Ala	Asn	Lys	Phe 155	Gly	Ser	Asn	Asn	Lys 160	
Val	Tyr	Asn	Asp	Tyr 165	Ser	Ile	Glu	Glu	His 170	Asn	Gly	Asn	Tyr	Lys 175	Tyr	
Val	Phe	Ser	Phe 180	Lys	Asp	Pro	Asn	Ala 185	Asn	Gly	Lys	Tyr	Ser 190	Ile	Val	
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Thr	Gln	Gln 35	Thr	Ser	Thr	Lys	His 40	Gln	Thr	Thr	Gln	Asn 45	Asn	Tyr	Val	
Thr	Asp 50	Gln	Gln	Гла	Ala	Phe 55	Tyr	Gln	Val	Leu	His 60	Leu	Гла	Gly	Ile	
Thr 65	Glu	Glu	Gln	Arg	Asn 70	Gln	Tyr	Ile	Lys	Thr 75	Leu	Arg	Glu	His	Pro 80	
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Pro	Asp	Arg	Arg 100	Val	Ala	Gln	Gln	Asn 105	Ala	Phe	Tyr	Asn	Val 110	Leu	Lys	
Asn	Asp	Asn 115	Leu	Thr	Glu	Gln	Glu 120	Lys	Asn	Asn	Tyr	Ile 125	Ala	Gln	Ile	
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Ser 145	Ser	Lys	Ala	Lys	Glu 150	Arg	Gln	Asn	Ile	Glu 155	Asn	Ala	Asp	Lys	Ala 160	
Ile	Lys	Asp	Phe	Gln 165	Asp	Asn	Lys	Ala	Pro 170	His	Asp	Lys	Ser	Ala 175	Ala	
Tyr	Glu	Ala	Asn 180	Ser	Lys	Leu	Pro	Lys 185	Asp	Leu	Arg	Asp	Lys 190	Asn	Asn	
Arg	Phe	Val 195	Glu	Гла	Val	Ser	Ile 200	Glu	Lys	Ala	Ile	Val 205	Arg	His	Asp	
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Pro	Met	Asp	Val	Lys 245	Glu	His	Leu	Gln	Lys 250	Gln	Leu	Asp	Ala	Leu 255	Val	
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Gln															
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Val	Glu 290	Val	Pro	Gln	Ile	Gln 295	Ser	Pro	Lys	Val	Glu 300	Val	Pro	Gln	Ser
Lys 305	Leu	Leu	Gly	Tyr	Tyr 310	Gln	Ser	Leu	Lys	Asp 315	Ser	Phe	Asn	Tyr	Gly 320
Tyr	Lys	Tyr	Leu	Thr 325	Asp	Thr	Tyr	Lys	Ser 330	Tyr	Lys	Glu	Гла	Tyr 335	Asp
Thr	Ala	Lys	Tyr 340	Tyr	Tyr	Asn	Thr	Tyr 345	Tyr	Lys	Tyr	Lys	Gly 350	Ala	Ile
Asp	Gln	Thr 355	Val	Leu	Thr	Val	Leu 360	Gly	Ser	Gly	Ser	Lys 365	Ser	Tyr	Ile
Gln	Pro 370	Leu	ГЛа	Val	Asp	Asp 375	ГЛа	Asn	Gly	Tyr	Leu 380	Ala	Lys	Ser	Tyr
Ala 385	Gln	Val	Arg	Asn	Tyr 390	Val	Thr	Glu	Ser	Ile 395	Asn	Thr	Gly	Гла	Val 400
Leu	Tyr	Thr	Phe	Tyr 405	Gln	Asn	Pro	Thr	Leu 410	Val	Lys	Thr	Ala	Leu 415	Lys
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Pro Ser Gly Ala Ser Gly Leu Phe Gln Thr Met Pro Gly Trp Gly Pro

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Val	Lys	Lуя 35	Ser	Phe	Glu	Lys	Thr 40	Leu	Ser	Met	Tyr	Pro 45	Ile	Lys	Asn
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Ala	Pro 210	ГЛа	Leu	Leu	Leu	Lys 215	Gly	Ser	Gly	Asn	Leu 220	ГÀЗ	Gly	Ser	Ser
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Gln	Pro	Thr	Lys	Gln	Gln	Arg	Thr	Val	Leu	Phe	Asp	Arg	Ser	His	Gly

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Val	Ser	Val	Asn 420	Glu	Pro	Phe	Glu	Met 425	Thr	Ile	His	Leu	Lys 430	Gly	Phe
Glu	Ala	Asn 435	Gln	Thr	Leu	Glu	Asn 440	Leu	Arg	Val	Gly	Ile 445	Tyr	Lys	Glu
Gly	Gly 450	Arg	Gln	Ile	Gly	Gln 455	Phe	Ser	Ser	Lys	Asp 460	Asn	Asp	Tyr	Asn

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 Arg Arg Gl
n Tyr Asp Gln $% \mathbb{C}^{2}$ Ser Phe Lys Ile Asp As
n Gly Asp Phe Leu Gl
n Gly Ser Pro $\ensuremath{\operatorname{Phe}}$ Cys Asn Tyr Leu Ile Ala His Ser Gly Ser Ser Gln Pro Leu Val Asp Phe Tyr Asn Arg Met Ala Phe Asp Phe Gly Thr Leu Gly Asn His Glu Phe Asn Tyr Gly Leu Pro Tyr Leu Lys Asp Thr Leu Arg Arg Leu Asn Tyr Pro Val Leu Cys Ala Asn Ile Tyr Glu Asn Asp Ser Thr Leu Thr Asp Asn Gly Val Lys Tyr Phe Gln Val Gly Asp Gln Thr Val Gly Val Ile Gly Leu Thr Thr Gln Phe Ile Pro His Trp Glu Gln Pro Glu His Ile Gln Ser Leu Thr Phe His Ser Ala Phe Glu Ile Leu Gln Gln Tyr Leu Pro Glu Met Lys Arg His Ala Asp Ile Ile Val Val Cys Tyr His Gly Gly Phe Glu Lys Asp Leu Glu Ser Gly Thr Pro Thr Glu Val Leu Thr Gly Glu Asn Glu Gly Tyr Ala Met Leu Glu Ala Phe Ser Lys Asp Ile Asp Ile Phe Ile Thr Gly His Gln His Arg Gln Ile Ala Glu Arg Phe Lys Gln Thr Ala Val Ile Gln Pro Gly Thr Arg Gly Thr Thr Val Gly Arg Val Val Leu Ser Thr Asp Glu Tyr Glu Asn Leu Ser Val Glu Ser Cys Glu Leu Leu Pro Val Ile Asp Asp Ser Thr Phe Thr Ile Asp Glu Asp Asp Gln His Leu Arg Lys Gln Leu Glu Asp Trp Leu Asp Tyr Glu Ile Thr Thr Leu Pro Tyr Asp Met Thr Ile Asn His Ala Phe Glu Ala

Arg Val Ala Pro His Pro Phe Thr Asn Phe Met Asn Tyr Ala Leu Leu Glu Lys Ser Asp Ala Asp Val Ala Cys Thr Ala Leu Phe Asp Ser Ala Ser Gly Phe Lys Gln Val Val Thr Met Arg Asp Val Ile Asn Asn Tyr Pro Phe Pro Asn Thr Phe Lys Val Leu Ala Val Ser Gly Ala Lys Leu Lys Glu Ala Ile Glu Arg Ser Ala Glu Tyr Phe Asp Val Lys Asn Asp Glu Val Ser Val Ser Ala Asp Phe Leu Glu Pro Lys Pro Gln His Phe Asn Tyr Asp Ile Tyr Gly Gly Val Ser Tyr Thr Ile His Val Gly Arg Pro Lys Gly Gln Arg Val Ser Asn Met Met Ile Gln Gly His Ala Val Asp Leu Lys Gln Thr Tyr Thr Ile Cys Val Asn Asn Tyr Arg Ala Val Gly Gly Gln Tyr Asp Met Tyr Ile Asp Ala Pro Val Val Lys Asp Ile Gln Val Glu Gly Ala Gln Leu Leu Ile Asp Phe Leu Ser Asn Asn Asn Leu Met Arg Ile Pro Gln Val Val Asp Phe Lys Val Glu Lys <210> SEQ ID NO 48 <211> LENGTH: 324 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 48 Met Lys Arg Leu Ser Ile Ile Val Ile Ile Gly Ile Phe Ile Ile Thr Gly Cys Asp Trp Gln Arg Thr Ser Lys Glu Arg Ser Lys Asn Ala Gln Asn Gln Gln Val Ile Lys Ile Gly Tyr Leu Pro Ile Thr His Ser Ala Asn Leu Met Met Thr Lys Lys Leu Leu Ser Gln Tyr Asn His Pro Lys Tyr Lys Leu Glu Leu Val Lys Phe Asn Asn Trp Pro Asp Leu Met Asp Ala Leu Asn Ser Gly Arg Ile Asp Gly Ala Ser Thr Leu Ile Glu Leu Ala Met Lys Ser Lys Gln Lys Gly Ser Asn Leu Lys Ala Val Ala Leu Gly His His Glu Gly Asn Val Ile Met Gly Gln Lys Gly Met His Leu Asn Glu Phe Asn Asn Asn Gly Asp Asp Tyr His Phe Gly Ile Pro His Arg Tyr Ser Thr His Tyr Leu Leu Leu Glu Glu Leu Arg Lys Gln Leu Lys Ile Lys Pro Gly His Phe Ser Tyr His Glu Met Ser Pro Ala Glu Met Pro Ala Ala Leu Ser Glu His Arg Ile Thr Gly Tyr Ser Val Ala

													CIII		
			180					185					190		
Glu	Pro	Phe 195	Gly	Ala	Leu	Gly	Glu 200	Lys	Leu	Gly	Lys	Gly 205	ГЛа	Thr	Leu
Lys	His 210	Gly	Asp	Asp	Val	Ile 215	Pro	Asp	Ala	Tyr	Cys 220	Суз	Val	Leu	Val
Leu 225	Arg	Gly	Glu	Leu	Leu 230	Asp	Gln	His	Lys	Asp 235	Val	Ala	Gln	Ala	Phe 240
Val	Gln	Asp	Tyr	Lys 245	Lys	Ser	Gly	Phe	Lys 250	Met	Asn	Asp	Arg	Lys 255	Gln
Ser	Val	Asp	Ile 260	Met	Thr	His	His	Phe 265	Lys	Gln	Ser	Arg	Asp 270	Val	Leu
Thr	Gln	Ser 275	Ala	Ala	Trp	Thr	Ser 280	Tyr	Gly	Asp	Leu	Thr 285	Ile	ГЛа	Pro
Ser	Gly 290	Tyr	Gln	Glu	Ile	Thr 295	Thr	Leu	Val	Lya	Gln 300	His	His	Leu	Phe
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Ala	Ser	Arg	Ser												
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Lys	Val	Glu 35	Val	Lys	Gly	Glu	Arg 40	Pro	Thr	Ile	His	Phe 45	Leu	Gly	Gln
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Ser	Thr	Gly 115	Ser	Asn	Ser	Leu	Leu 120	-	Asp	Lys	His	Val 125	Asp	Gln	Leu
Leu	Asn 130	Lys	Ala	Ser	Thr	Gln 135	Asn	Glu	Ala	Asp	Val 140	Lys	Gln	Thr	Tyr
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Phe	Asp	Tyr 195	Asn	Asn	Ser	Arg	Glu 200	Arg	Asp	Thr	Arg	Pro 205	Leu	Val	Met
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Ala		Ser	Val	Tyr	Ser		Asn	Met	Asn	Met	Tyr	Thr	Arg	Leu	Leu

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Leu	Leu	Asp	Glu	Asn 245	Asp	His	Leu	Thr	Thr 250	Lys	Gly	Ser	Leu	Ser 255	His
Asp	Tyr	Ala	Val 260	Asn	ГЛЗ	Asp	Asn	Lys 265	Ala	Phe	Tyr	Phe	Leu 270	Leu	Arg
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Gly	Glu 290	Arg	Val	Ser	Ala	Glu 295	Asp	Val	Lys	Phe	Ser 300	Leu	Asp	Arg	Ala
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His	Ile	Asn	Asp	Ile 325	Гла	Ile	Leu	Lys	Asp 330	Glu	Asp	Ile	Asp	Gln 335	Leu
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Asn	Lys 370	Asp	Gly	Ile	Tyr	Gln 375	Ile	Val	Lys	Ile	Thr 380	Thr	Asp	Gln	Ser
Met 385	Pro	Arg	Glu	Val	Asn 390	Tyr	Leu	Thr	His	Ser 395	Ser	Ala	Gly	Ile	Leu 400
Ser	Lys	Lys	Phe	Val 405	Asn	Gln	Val	Asn	Gln 410	Glu	Tyr	Pro	Lys	Gly 415	Tyr
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Tyr	Ala	Ser 435	Gly	Ala	Tyr	Ile	Met 440	Thr	Gln	Lys	Asn	Ala 445	Tyr	Gln	Ala
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Asp	Val	Asn	Gln 500		His	Phe	Asp	Leu 505		Lys	Ser	Asp	Lys 510	Asn	Leu
Ser	Ile			Lys	Asn	Gly			Ser	Val	Phe			Leu	Asn
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)> SH														
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T				5					10					10	

Arg Gln His Ala Arg Leu Thr Lys Tyr His Glu Thr Ala Gln Tyr Arg Glu Asp Tyr Arg Glu Asp Tyr Arg Glu Asp Tyr Arg Glu Gly Asp Gly Asp Tyr Isp Glu Gly Lys Tyr Arg Glu Gly Asp Isp Gly Asp Isp Glu Asp Isp Gly Asp Isp Gly Isp Gly Asp Isp Gly Isp Tyr Arg Glu Asp Tyr Isp Arg Glu Gly Gly Isp Tyr Isp Glu Isp Tyr Isp Glu Asp Tyr Isp Glu Asp Isp Glu Isp Isp <thi< th=""><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th>_</th><th></th><th></th><th>ucu</th><th></th></thi<>												_			ucu	
35 40 45 Ala Leu Asn Val Val Glu Pro From Phe Ala Ser Gly Tile Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly	Leu	Ile	Ser		Ser	His	Pro	Leu		Ala	LYa	Ile	Gly	-	Asp	Val
50 55 60 60 1 <td>Leu</td> <td>Aap</td> <td></td> <td>Gly</td> <td>Gly</td> <td>Asn</td> <td>Ala</td> <td></td> <td>Asp</td> <td>Ala</td> <td>Val</td> <td>Ile</td> <td></td> <td>Ile</td> <td>Gln</td> <td>Leu</td>	Leu	Aap		Gly	Gly	Asn	Ala		Asp	Ala	Val	Ile		Ile	Gln	Leu
65 70 75 80 Ala Arg Gu Th Ala Pro Gu His Val App For Gu For	Ala		Asn	Val	Val	Glu		Phe	Ala	Ser	Gly		Gly	Gly	Gly	Gly
as 90 1 95 Asp Ser Gly Glu Tyr Lys Ser Phe Phe Asp Met Thr Thr His Gly Lys Tr Val Ala Val Pro Ala Ile Pro Lys Leu Phe Asp Met Thr Thr His Gly Lys Arg Tyr Ala Lys Leu Ser Leu Glu Asp Tr Asp		Leu	Leu	Tyr	Tyr		Gln	Ser	Thr	Gly		Ile	Thr	Ala	Phe	
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115 120 125 Arg Tyr Ala Lys Leu Ser Leu Glu Asp Leu Ile Asp Tr Ala Tr Ala Tr Ala Tr Glu Lys Tyr Ser Ser<	Asp	Ser	Gly		Tyr	Lys	Ser	Phe		Asp	Met	Thr	Thr		Gly	Lys
130 135 140 Leu Ala Ile Glu Gly His Ala Ala Asn Tr Ala Tr Glu Tr Glu Glu Fr Sr Glu Tr Ala Asn Tr Ala Tr Glu Tr Ala Glu Tr Fr Ala Glu Tr Fr	Thr	Val		Val	Pro	Ala	Ile		Гла	Leu	Phe	Asp	-	Ile	His	Lya
145 150 155 160 Arg Gln Gln His Ala Arg Leu Thr Lys Tyr His Glu Glu Thr Ala Gln Val 165 160 Phe Thr His Glu Asn Gln Tyr Trp Arg Glu Gly Asp Trp 11e Val Gln 190 110 Pro Glu Leu Gly Lys Thr Phe Gln I1e Leu Arg Glu Gln Gly Asp Val Val 190 110 Ala Phe Tyr Lys Gly Asp 11e Ala Lys Gln Leu Val Asn Val Val 190 205 Ala Phe Tyr Lys Gly Asp 11e Ala Lys Gln Leu Val Asn Val Val 192 205 Ala Phe Tyr Lys Gly Asp 11e Ser Ala Thr Phe Lys Asp Tyr Asp 11e 240 205 Gln Leu Lys Ala Pro 12e Ser Ser Gly Gly 11e Thr Val 11e Gln 11e Leu 270 11e Leu 275 Ser Met Gly Pro Ser Ser Ser Ser Gly Gly 11e Thr Val 11e Glu 777 285 Arg 220 11s His Leu 11e Glu Ala Met His Leu Ala 77 Ser Asp 300 Arg 31a Gln Tyr Leu Ala Asp Asp Asp Asn Phe His Glu Val Pro Val Gln 305 Ser Leu 11e Asp Asp Asp Tyr Leu Lys Ala Asn 11e Asp 300 215 Ser Asn Lys Ala Asn 11e Asp 11e Glu Asn His Gly Val Val Ser Asp 335 Ser Asn Lys Ala Asn 11e Asp Val Glu Gla Asn His 71r Glu Thr Thr Ser 11e 360 Mar 370 11e Tyr Gly Ser Gly Asp 11e Thr 11e 70 360 11e Tyr Gly Ser Gly Asn 11e Asp 400 11e Ser His Thr Asp Val Glu Gla Asn His Thr Glu Thr Thr Ser 11e 360 361 11e Asp 190 370 11e Asp 190 <t< td=""><td>Arg</td><td></td><td>Ala</td><td>Lys</td><td>Leu</td><td>Ser</td><td></td><td>Glu</td><td>Asp</td><td>Leu</td><td>Ile</td><td></td><td>Pro</td><td>Ala</td><td>Ile</td><td>Glu</td></t<>	Arg		Ala	Lys	Leu	Ser		Glu	Asp	Leu	Ile		Pro	Ala	Ile	Glu
165 170 175 Phe Thr His Glu Asn Gln Tyr Trp Arg Glu Glu Asp Tyr Ite Arg Glu Glu Gly Val Gln Pro Glu Leu Gly Lys Thr Phe Gln Ile Leu Arg Glu Glu Gly Phe Asp Ile Lys Gln Leu Arg Glu Glu Gly Phe Asp Ile Lys Gln Leu Asp Glu Kap Tr Lys Gln Leu Asp Ile Tr Lys Gln Lau Lys Asp Ile Tr Asp Ile Asp Ile Asp Ile Ile Ile Ile Ile Ile Ile Ile		Ala	Ile	Glu	Gly		Ala	Ala	Asn	Trp		Thr	Glu	Lys	Tyr	Ser 160
180 185 190 Pro Glu Leu Gly Lys Thr Phe Gln Ile Leu Arg Glu Gln Gly Phe Aan Ala Phe Tyr Lys Gly Asp Ile Ala Lys Gln Leu Val Asn Val Val Lys Ala Cys Gly Gly Thr Ile Ala Lys Gln Leu Val Asn Val Val Lys Gln Leu Lys Ala Pro Ser Ala Thr Phe Cys Asp Tile Tyr Asp Ile Cys Asp Ile Cys Asp Ile Cys Asp Ile Cys Cys Asp Ile Glu Asp Ile Glu Asp Ile Glu Asp Ile Cys Asp Ile Cys Asp Ile Cys Asp Cys Asp Ser Val Ser Val Cys <td< td=""><td>Arg</td><td>Gln</td><td>Gln</td><td>His</td><td></td><td>Arg</td><td>Leu</td><td>Thr</td><td>ГЛа</td><td></td><td>His</td><td>Glu</td><td>Thr</td><td>Ala</td><td></td><td>Val</td></td<>	Arg	Gln	Gln	His		Arg	Leu	Thr	ГЛа		His	Glu	Thr	Ala		Val
195 200 205 Ala Phe Tyr Lys Gly Asp Ile Ala Lys Gln Leu Val Asn Val Val Lys Ala Phe Tyr Lys Gly Asp Ile Thr Leu Glu Asp Leu Asn Val Val Lys Ala Cys Gly Gly Thr Ile Thr Leu Glu Asp Leu Asp Ile Zato Gln Leu Lys Ala Pro Ser Ala Thr Phe Lys Asp Tyr Asp Ile Zato Ser Met Gly Pro Ser Ser Gly Gly Asp Ile Zato Lys Leu Leu Bits Val Asp Leu Pro Ser Asp Zato Lys Leu His Glu Ala Met His Clu Ala Met Asp Zato Zato	Phe	Thr	His		Asn	Gln	Tyr	Trp		Glu	Gly	Asp	Trp		Val	Gln
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225230235240Gln Leu Lys Ala Pro 260Ile Ser Ala Thr Phe 265Lys Asp Tyr Asp Ile 255Tyr 	Ala		Tyr	Lys	Gly	Asp		Ala	Lys	Gln	Leu		Asn	Val	Val	Lys
245 250 250 255 Ser Met Gly Pro Ser Ser Ser Gly Gly Gly Ile Thr Val Ile Gln Ile Leu 270 Ile Glu His Val Asp Leu Pro Ser Met Gly Pro Arg Ser Val 285 Lys Leu Leu Glu His Val Asp Leu Pro Ser Met Gly Pro Arg Ser Val 275 Ile His His Leu Ile Gln Ala Met His Leu Ala Tyr Ser Asp 300 Arg Ala Gln Tyr Leu Ala Asp Asp Asp Asp Asn Phe His Glu Val Pro Val Gln 310 Ser Leu Ile Asp Asp 325 Asp Tyr Leu Lys Ala Arg Ser Thr Leu Ile Asp 330 Ser Asn Lys Ala Asn Ile Asp Ile Glu Glu Asn His Gly Val Val Ser Asp 350 Ser Asp 355 Thr Asp Val Glu Glu Asn His Thr Glu Thr Thr His Phe 355 Gly Met Ile Tyr Gly Ser Gly Ile Thr Ile Asp 390 Ser Phe 360 Thr Ser Ile 400 Asn Thr Thr Met Asp Asp Gly Phe Asp Val Val Val Asp 300 Ser Asp 300 Ser Ile Asp 300 Glu Ile Ala Pro Tyr Lys Arg Pro Leu Ser Asp Met Ala Pro Thr Ile 430 Ser Ile 430 Ser Ile 430		Суз	Gly	Gly	Thr		Thr	Leu	Glu	Asp		Ala	Lys	Tyr	Asp	Ile 240
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420 425 430	Leu	Asn	Thr	Thr		Asp	Gly	Phe	Asp		Val	Asp	Gly	Gly		Asn
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	Val	Met	Tyr	His	Gly	ГЛа	Pro	Ile	Leu	Thr	Val	Gly	Ala	Pro	Gly	Ala

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		435					440					445			
Ile	Ser 450	Ile	Ile	Ala	Ser	Val 455	Ala	Gln	Thr	Leu	Ile 460	Asn	Val	Leu	Val
Phe 465	Gly	Met	Asp	Ile	Gln 470	Gln	Ala	Ile	Asp	Glu 475	Pro	Arg	Ile	Tyr	Ser 480
Ser	His	Pro	Asn	Arg 485	Ile	Glu	Trp	Glu	Pro 490	Gln	Phe	Ser	Gln	Ser 495	Thr
Ile	Leu	Ala	Leu 500	Ile	Ala	His	Gly	His 505	Ala	Met	Glu	His	Lys 510	Pro	Asp
Ala	Tyr	Ile 515	Gly	Asp	Val	His	Gly 520	Leu	Gln	Val	Asp	Pro 525	Thr	Thr	Tyr
Glu	Ala 530	Ser	Gly	Gly	Ser	Asp 535	Asp	Thr	Arg	Glu	Gly 540	Thr	Val	Met	Gly
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Leu	Leu	Ala	Asp 580	Gln	Val	Arg	Trp	Met 585	His	Asp	ГЛа	Tyr	Trp 590	Val	Asp
Glu	Ser	Val 595	Val	Arg	Ile	Ile	Phe 600	Pro	Glu	Val	Ser	Ala 605	His	Ile	Glu
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Trp 625	Leu	Ala	Arg	Lys	Tyr 630	Ala	Tyr	Gln	Val	Thr 635	Leu	Lys	Asp	Asp	Gly 640
Leu	Tyr	Leu	Thr	Asp 645	Asp	Thr	Tyr	Thr	Ser 650	Val	Lys	Arg	Asn	Thr 655	Asn
Ala	Tyr	Tyr	Arg 660	Tyr	Asp	Arg	Asp	Ser 665	Ile	Thr	Arg				
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Val	Tyr	Ser 35	Pro	Tyr	Gln	Ser	Asn 40	Leu	Ile	Arg	Pro	Ile 45	Leu	Asn	Glu
Phe	Glu 50	Lys	Gln	Glu	His	Val 55	Lys	Ile	Glu	Ile	Lys 60	His	Gly	Ser	Thr
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Asp	Val	Phe	Met	Gly 85	Gly	Val	Leu	Ser	Glu 90	Thr	Ile	Asp	His	Pro 95	Glu
Asp	Phe	Val	Pro 100	Tyr	Gln	Asp	Thr	Ser 105	Val	Thr	Gln	Gln	Leu 110	Glu	Asp
Tyr	Arg	Ser 115	Asn	Asn	Lys	Tyr	Val 120	Thr	Ser	Phe	Leu	Leu 125	Met	Pro	Thr
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Ser	Met	His	His 180	Arg	Val	Ser	Asp	Val 185	His	Gln	Phe	Gln	Asn 190	His	Ala
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Lys	Tyr 210	Tyr	Ala	Gly	Leu	Ser 215	Tyr	Glu	Gln	Asp	Ala 220	Arg	Thr	Trp	Lys
Asn 225	Lys	Gly	Tyr	Pro	Val 230	Ser	Ile	Val	Tyr	Pro 235	Ile	Glu	Gly	Thr	Met 240
Leu	Asn	Val	Asp	Gly 245	Ile	Ala	Leu	Val	Lys 250	Asn	Ala	His	Pro	His 255	Pro
Lys	Arg	Lys	Lys 260	Leu	Val	Gln	Tyr	Leu 265	Thr	Ser	Arg	Ser	Val 270	Gln	Gln
Arg	Leu	Val 275	Ala	Glu	Phe	Asp	Ala 280	ГЛа	Ser	Ile	Arg	Lys 285	Asp	Val	Ser
Glu	Gln 290	Ser	Asp	Gln	Ser	Ile 295	Glu	Asn	Leu	Lys	Asn 300	Ile	Pro	Leu	Ile
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Ala	Glu	Ser	20 Leu	Phe	Lys	Thr	Asn	25 Asp	Gln	Gly	Lys	Ile	30 Glu	Lys	Ala
Leu	Val	35 Lys	Ser	Tyr	His		40 Pro	Asn	Asp	Thr		45 Leu	Asp	Ile	Glu
	50 Lys	Asp	Asn	Ile		55 Phe	Gln	Asn	Gly		60 LYs	Leu	Thr	Ala	
65 Lys	Val	Lys	Ser		70 Leu	Glu	Asn	Ser		75 Lys	Lys	Ser	Asp		80 Val
Lys	Tyr	Ser		85 Pro	Ile	Ser	Ser		90 Thr	Ala	Lys	Gly		95 Lys	Leu
Thr	Ile	-	100 Thr	Asn	Ser	Ala	-	105 Pro	Glu	Leu	Val		110 Glu	Leu	Ala
Asn	Pro	115 Phe	Met	Ala	Ile	Tyr	120 Asp	Thr	Asp	Ala	Lys	125 Ser	Asp	Val	Asn
Gln	130 Thr	Pro	Val	Gly	Thr	135 Gly	Pro	Tyr	Gln	Ile	140 Lys	Asp	Tyr	Lys	Gln
145	Arg				150					155					160
	· - 9	шүр	- <u>-</u>	DGT	LCU	Der	17011	1116	-17.0	Tob.	+ Y +	P	-11	ω±γ	-110
_	Lys	_	_	165					170			_		175	_

Arg	Val	Arg 195	Asn	Leu	Glu	Ser	Gln 200	Lys	Asb	Asp	Leu	Ile 205	Thr	Asp	Val
Pro	Val 210	Asn	Гла	Val	Gln	Asp 215	Ile	Glu	Asn	Asn	Gln 220	Asn	Leu	Lys	Val
Ser 225	Lys	Glu	Ser	Gly	Phe 230	Arg	Thr	Ser	Leu	Leu 235	Met	Tyr	Asn	His	Thr 240
Asn	Lys	Lys	Met	Thr 245	Lys	Ser	Val	Arg	Glu 250	Ala	Leu	Asp	His	Ile 255	Ile
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Ala	Thr	Ser 275	Pro	Phe	Asn	Asp	Lys 280	Ile	Pro	Tyr	Ile	Lys 285	Glu	Pro	Lys
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Gly 305	Tyr	Thr	Lys	Glu	His 310	Pro	Leu	Lys	Ile	Lys 315	Leu	Ile	Thr	Tyr	Asp 320
Gly	Arg	Pro	Glu	Leu 325	Ser	Гла	Ile	Ala	Gln 330	Val	Leu	Gln	Ser	Asp 335	Ala
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Gly	Tyr	Leu 355	Lys	Asp	Arg	Ser	Ala 360	Trp	Asp	Ala	Thr	Met 365	Tyr	Ser	Phe
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His	Asn	Ile	Ser 420	Asn	Asp	Ile	Ile	Lys 425	Leu	Ser	Ser	Arg	Asp 430	Val	Pro
Asn	Ser	Tyr 435	Ile	Ala	Tyr	Asn	Asp 440	Gln	Ile	Val	Ala	Ala 445	Asn	Ser	Lys
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Gln	Ala	His 35	Thr	Gln	Met	Ser	Thr 40	Gln	Ser	Gln	Aap	Val 45	Ser	Tyr	Gly
Thr	Tyr 50	Tyr	Thr	Ile	Asp	Ser 55	Asn	Gly	Asp	Tyr	His 60	His	Thr	Pro	Asp
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	Val	Asp	Ala	Gln 85		His	Thr	His	Tyr 90		Tyr	Asn	Сүз	Tyr 95	
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Tyr 145	Ser	His	Ser	Asn	Asn 150	Asn	Gln	Ala	Tyr	Asn 155	Ser	His	Asp	Gly	Asn 160
Gly	Lys	Val	Asn	Tyr 165	Pro	Asn	Gly	Thr	Ser 170	Asn	Gln	Asn	Gly	Gly 175	Ser
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Ala	His 210	Tyr	Gly	Val	Asp	Tyr 215	Ala	Met	Pro	Glu	Asn 220	Ser	Pro	Val	Tyr
Ser 225	Leu	Thr	Asp	Gly	Thr 230	Val	Val	Gln	Ala	Gly 235	Trp	Ser	Asn	Tyr	Gly 240
Gly	Gly	Asn	Gln	Val 245	Thr	Ile	Lys	Glu	Ala 250	Asn	Ser	Asn	Asn	Tyr 255	Gln
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Pro	Lys	Asn 35	Thr	Tyr	Leu	Гла	Ser 40	Glu	Gln	Gln	Thr	Ala 45	Lys	Met	Tyr
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Ala	Ser	Asp	Glu	Ile 85	Val	ГЛЗ	Gly	Leu	Gly 90	Ile	Pro	Lys	Ser	Val 95	Val
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Lys	Ser	Met 115	Ile	Asn	Leu	Glu	Pro 120	Thr	Ile	Ala	Asp	Ser 125	Ala	Leu	Gly
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													τın	acu	
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Ala	Gln	Gln 195	Ser	Asp	Tyr	Ser	Lys 200	Ile	Ala	Glu	Гла	Tyr 205	Ser	Glu	Leu
Ile	Val 210	Asp	Lys	Leu	Asp	Asp 215	Asp	Asn	Phe	Asp	Lys 220	Gly	Lys	Lys	Glu
Glu 225	Ile	Lys	Val	Asn	Gly 230	Glu	Гла	Tyr	Lys	Val 235	Arg	Pro	Val	Thr	Leu 240
Thr	Leu	Ser	Arg	Ala 245	Asp	Thr	Lys	Lys	Ile 250	Thr	Leu	Ala	Val	Leu 255	Glu
Glu	Ala	Lys	Lys 260	Asp	Гла	Asp	Leu	Lys 265	Lys	Leu	Met	Glu	Glu 270	Gln	Gly
Ala	Thr	Lys 275	Asp	Phe	Glu	Гла	Asp 280	Ile	Lys	Lys	Ala	Ile 285	Asp	Asp	Val
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Thr 305	Glu	Lys	His	Thr	Ile 310	Val	Lys	Arg	Glu	Ile 315	Thr	Ile	Thr	Asp	Lys 320
Glu	Asn	Asn	Lys	Thr 325	Lys	Ile	Lys	Gly	Thr 330	Asn	Thr	Leu	Glu	Asp 335	Asp
Lys	Leu	Lys	Leu 340	Asp	Tyr	Ala	Leu	Asp 345	Phe	Asp	Gln	Asp	Lys 350	Tyr	Thr
Tyr	Ala	Glu 355	Ala	Lys	Tyr	Thr	Ile 360	Lys	Gly	Val	Ser	Ser 365	Lys	Glu	Lys
Asp	Asn 370	Lys	Tyr	Asn	Asp	Lys 375	Tyr	Glu	Phe	Gly	Lys 380	Гла	Thr	Glu	Tyr
Asp 385	Glu	Ser	Lys	Ile	Lys 390	Leu	Asp	Asn	Gln	Glu 395	Lys	Val	Asp	Gly	Thr 400
Lys	Arg	Gln	Asp	Lys 405	Gly	Lys	Ile	Thr	Val 410	Ala	Leu	Asp	Lys	Tyr 415	Ser
Asp	Glu	Asn	Glu 420	Phe	Thr	Phe	Glu	Asn 425	Asn	Ile	Asp	Ser	Asp 430	Val	Lys
Asn	Asn	Thr 435	Gln	Lys	Ser	Thr	Leu 440	Asn	Ile	Gly	Ile	Lys 445	Tyr	Ala	Glu
Glu	Pro 450	Ile	Asn	Phe	Ile	Leu 455	Lys	Ser	Ser	Thr	Lys 460	Leu	Lys	Ala	Asp
Ile 465	Asp	Phe	Asp	Asp	Ser 470	Gly	Ala	Lys	Asp	Phe 475	Asn	Ser	Leu	Ser	Ser 480
Lys	Asp	Arg	Glu	Lys 485	Leu	Glu	Lys	Glu	Ile 490	Glu	Lys	Asn	Gly	Gly 495	Lys
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Glu	Glu	Ala 35	Lys	Гла	Ala	His	Pro 40	Asn	Ala	Gln	Phe	Lys 45	Val	Asn	Lys
Asp	Thr 50	Gly	Ala	Tyr	Thr	Tyr 55	Thr	Tyr	Asp	Lys	Asn 60	Asn	Thr	Pro	Asn
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Thr	Ser	Pro 115	Ser	Asn	Pro	Leu	Thr 120	Pro	Ala	Ile	Pro	Asn 125	Val	Glu	Asp
Asn	Asp 130	Asp	Glu	Leu	Asn	Asn 135	Ala	Phe	Ser	Lya	Asp 140	Asn	Гла	Gly	Leu
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Glu	Phe	Asn	Asp	Lys 165	Ala	ГЛа	Thr	Ala	Asp 170	Gly	ГЛа	Pro	Leu	Ala 175	Leu
Gly	Asn	Gly	Lys 180	Ile	Ile	Asp	Gln	Pro 185	Leu	Ile	Thr	Ser	Lys 190	Asn	Asn
Leu	Tyr	Thr 195	Ala	Gly	Gln	Суз	Thr 200	Trp	Tyr	Val	Phe	Asp 205	Lys	Arg	Ala
Lys	Asp 210	Gly	His	Thr	Ile	Ser 215	Thr	Phe	Trp	Gly	Asp 220	Ala	Lys	Asn	Trp
Ala 225	Gly	Gln	Ala	Ser	Ser 230	Asn	Gly	Phe	Lys	Val 235	Asp	Arg	His	Pro	Thr 240
Arg	Gly	Ser	Ile	Leu 245	Gln	Thr	Val	Asn	Gly 250	Pro	Phe	Gly	His	Val 255	Ala
Tyr	Val	Glu	Lys 260	Val	Asn	Ile	Asp	Gly 265	Ser	Ile	Leu	Ile	Ser 270	Glu	Met
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Tyr	Lys	Glu 35	Gln	Asn	Gln	Met	Asn 40	Lys	Ile	Ala	Ser	Lys 45	Val	Gln	Asn
Thr	Ile 50	Lys	Thr	Asp	Ile	Lys 55	Gln	Glu	Asp	Ser	Asn 60	Thr	His	Val	Tyr
Lys 65	Asp	Gly	Lys	Val	Ile 70	Val	Ile	Gly	Ile	Gln 75	Leu	Tyr	Lys	Asp	Arg 80
Glu	Lys	Met	Tyr	Tyr 85	Phe	Ala	Tyr	Glu	Ile 90	Lys	Asp	Gly	Lys	Ala 95	Glu

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n Trp Glu Pro Gly Lys Lys Val His Leu Val Gly His Ser Met Gly Gly Gln

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Glu	Ser	Tyr 515		Asp	Tyr	Ile	Lys 520	Arg	Val	Ser	Lys	Ser 525	Lys	Ile	Trp	
Thr	Ser 530		Asp	Asn	Ala	Ala 535	Tyr	Asp	Leu	Thr	Leu 540	Asp	Gly	Ser	Ala	
Lys 545	Leu	Asn	Asn	Met	Thr 550	Ser	Met	Asn	Pro	Asn 555	Ile	Thr	Tyr	Thr	Thr 560	
Tyr	Thr	Gly	Val	Ser 565	Ser	His	Thr	Gly	Pro 570	Leu	Gly	Tyr	Glu	Asn 575	Pro	
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Gln	Thr	Lys	Val 100	Thr	Glu	Lys	Gln	Ala 105	Glu	Thr	Leu	Ser	His 110	Leu	Ser
Asn	Leu	Ala 115	Val	Lys	Asn	Asp	Leu 120	His	Phe	Lys	Lys	Phe 125	Val	Thr	Glu
Asn	Asn 130	Ile	Pro	Lys	Glu	Tyr 135	Lys	Lys	Pro	Val	Glu 140	Leu	Met	Met	Asn
Tyr 145	Phe	Lys	Ala	Leu	Asn 150	Ser	Thr	Ile	Ala	Asn 155	Val	Asp	Glu	Asp	Ile 160
Glu	Lys	Leu	Ser	Tyr 165	Gln	Pro	Gln	Asn	Lys 170	Ile	Asn	Val	Val	Asp 175	Val
Pro	Thr	Lys	Tyr 180	Ala	Gly	Asp	Val	Asn 185	Lys	Lys	Gln	Gln	Asp 190	Lys	Ile
Lys	Asp	Phe 195	Leu	ГЛа	Ser	Гла	Gly 200	Ile	Гла	Ser	Asp	Val 205	Ile	Asp	ГЛа
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Ile	Ile	Phe	Val 20	Thr	Ser	Сув	Asp	Gly 25	Asp	Asn	Lys	Ile	Ile 30	Gly	Asp
Ser	Lys	Glu 35	Glu	Gln	Ile	Lys	Lys 40	Ser	Phe	Ala	Lys	Thr 45	Leu	Asp	Ile
Tyr	Pro 50	Ile	Гла	Asn	Leu	Glu 55	Asp	Leu	Tyr	Asp	Lys 60	Glu	Gly	Tyr	Arg
Asp 65	Gly	Glu	Phe	Lys	Lys 70	Asp	Asp	Lys	Gly	Thr 75	Trp	Leu	Ile	Arg	Ser 80
Glu	Met	Lys	Ile	Gln 85	Leu	Lys	Gly	Glu	Asn 90	Leu	Glu	Ser	Arg	Gly 95	Ala
Val	Leu	Glu	Ile 100	Asn	Arg	Asn	Thr	Arg 105	Thr	Ala	Lys	Gly	His 110	Tyr	Ile
Val	Arg	Glu 115	Val	Val	Glu	Asp	Ser 120	Asp	Gly	Met	Thr	His 125	Asn	His	Thr
Lya	Arg 130	Tyr	Pro	Val	Lys	Met 135	Glu	Asn	Asn	Lys	Met 140	Ile	Pro	Leu	Lys
Pro 145	Ile	Asp	Asp	Glu	Lys 150	Val	Lys	Lys	Glu	Ile 155	Glu	Glu	Phe	Asn	Phe 160
Phe	Val	Gln	Tyr	Gly 165	Asn	Phe	Гла	Glu	Leu 170	Glu	Asn	Tyr	Гла	Glu 175	Asp
Glu	Val	Ser	Tyr 180	Asn	Pro	Glu	Val	Pro 185	Ile	Tyr	Ser	Ala	Lys 190	Tyr	Gln
Leu	Lys	Asn 195	Ser	Asp	Tyr	Asn	Val 200	Glu	Gln	Leu	Arg	Lys 205	Arg	Tyr	Asn
Ile	Pro 210	Thr	Gln	Lys	Ala	Pro 215	Lys	Leu	Leu	Leu	Lys 220	Gly	Ser	Gly	Asn
Leu 225	Lys	Gly	Ser	Ser	Val 230	Gly	Tyr	Lys	Asn	Ile 235	Glu	Phe	Thr	Phe	Ile 240
Glu	Asn	Lys	Glu	Glu 245	Asn	Ile	Tyr	Phe	Thr 250	Asp	Ser	Ile	Tyr	Phe 255	Asn

Pro Ser Glu Asp Lys

-continued

260

<210> SEQ ID NO <211> LENGTH: 3 <212> TYPE: PR1 <213> ORGANISM:	47	ccus aureus		
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Met Asn Lys Asp 1	Asn Lys Trp 5	o Thr Met Ile 10	e Thr Ala Leu	Phe Ile Thr 15
Val Ile Ser Val 20	. Leu Leu Ala	a Phe His Leu 25	Lys Gln His	Tyr Asp Gln 30
Ile Thr Asn Glu 35	Asn His Ala	a Asn Lys Asp 40	Lys Ile Asn 45	Ile Lys Asn
Lys Asn Val Arc 50	Ile Tyr Gln 55	n Asn Leu Thr	Tyr Asn Arg 60	Val Phe Pro
Asn Ser Lys Leu 65	Asp Ile Ile 70	e Thr Pro Val	Asp Met Ser 75	Ser Asn Ala 80
Lys Leu Pro Val	Ile Phe Trp 85	Met His Gly 90	Gly Gly Tyr	Ile Ala Gly 95
Asp Lys Gln Tyr 100) Leu Leu Ala 105	Lys Ile Ala	Glu Gln Gly 110
Tyr Ile Val Val 115	Asn Val Asn	n Tyr Ala Leu 120	Ala Pro Gln 125	Tyr Lys Tyr
Pro Thr Pro Leu 130	Ile Gln Met 135		Thr Gln Phe 140	Ile Lys Glu
Asn Lys Met Asr 145	Leu Pro Ile 150	e Asp Phe Asn	Gln Val Ile 155	Ile Gly Gly 160
Asp Ser Ala Gly	Ala Gln Leu 165	ı Ala Ser Gln 170		Ile Gln Thr 175
Asn Asp Arg Leu 180		a Met Lys Phe 185	e Asp Gln Ser	Phe Lys Pro 190
Ser Gln Ile Lys 195	Gly Ala Ile	e Leu Phe Gly 200	Gly Phe Tyr 205	Asn Met Gln
Thr Val Arg Glu 210	Thr Glu Phe 215	-	Gln Leu Phe 220	Met Lys Ser
Tyr Thr Gly Glu 225	Glu Asp Trp 230	o Glu Lys Ser	Phe Lys Asn 235	Ile Ser Gln 240
Met Ser Thr Val	Lys Gln Ser 245	r Thr Lys Asn 250		Thr Phe Leu 255
Ser Val Gly Asp 260		Phe Glu Ser 265	Gln Asn Ile	Glu Phe Ser 270
Lys Lys Leu Glr 275	Glu Leu Asn	n Val Pro Val 280	Asp Thr Leu 285	Phe Tyr Asp
Gly Thr His His 290	Leu His His 295	-	Phe His Leu 300	Asn Lys Pro
Glu Ser Ile Asp 305	Asn Ile Lys 310	s Lys Val Leu	Leu Phe Leu 315	Ser Arg Asn 320
Thr Ser Ser Ser	Gly Ile Gln 325	n Thr Glu Glu 330		Ile Glu Asn 335
Pro Ser Asn Glu 340		ı Asn Pro Leu 345	l Asn	

<210> SEQ ID NO 62 <211> LENGTH: 265

<212> TYPE: PRT															
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Phe	Leu	Thr	His 20	His	Asp	Ala	Gln	Ala 25	Ser	Thr	Gln	His	Thr 30	Val	Gln
Ser	Gly	Glu 35	Ser	Leu	Trp	Ser	Ile 40	Ala	Gln	Lys	Tyr	Asn 45	Thr	Ser	Val
Glu	Ser 50	Ile	Lys	Gln	Asn	Asn 55	Gln	Leu	Asp	Asn	Asn 60	Leu	Val	Phe	Pro
Gly 65	Gln	Val	Ile	Ser	Val 70	Gly	Gly	Ser	Asp	Ala 75	Gln	Asn	Thr	Ser	Asn 80
Thr	Ser	Pro	Gln	Ala 85	Gly	Ser	Ala	Ser	Ser 90	His	Thr	Val	Gln	Ala 95	Gly
Glu	Ser	Leu	Asn 100	Ile	Ile	Ala	Ser	Arg 105	Tyr	Gly	Val	Ser	Val 110	Asp	Gln
Leu	Met	Ala 115	Ala	Asn	Asn	Leu	Arg 120	Gly	Tyr	Leu	Ile	Met 125	Pro	Asn	Gln
Thr	Leu 130	Gln	Ile	Pro	Asn	Gly 135	Gly	Ser	Gly	Gly	Thr 140	Thr	Pro	Thr	Ala
Thr 145	Thr	Gly	Ser	Asn	Gly 150	Asn	Ala	Ser	Ser	Phe 155	Asn	His	Gln	Asn	Leu 160
Tyr	Thr	Ala	Gly	Gln 165	Сүз	Thr	Trp	Tyr	Val 170	Phe	Asp	Arg	Arg	Ala 175	Gln
Ala	Gly	Ser	Pro 180	Ile	Ser	Thr	Tyr	Trp 185	Ser	Asp	Ala	Lys	Tyr 190	Trp	Ala
Gly	Asn	Ala 195	Ala	Asn	Asp	Gly	Tyr 200	Gln	Val	Asn	Asn	Thr 205	Pro	Ser	Val
Gly	Ser 210	Ile	Met	Gln	Ser	Thr 215	Pro	Gly	Pro	Tyr	Gly 220	His	Val	Ala	Tyr
Val 225	Glu	Arg	Val	Asn	Gly 230	Asp	Gly	Ser	Ile	Leu 235	Ile	Ser	Glu	Met	Asn 240
Tyr	Thr	Tyr	Gly	Pro 245	Tyr	Asn	Met	Asn	Tyr 250	Arg	Thr	Ile	Pro	Ala 255	Ser
Glu	Val	Ser	Ser 260	Tyr	Ala	Phe	Ile	His 265							
<213 <213	l> L1 2> T1	EQ II ENGTI YPE :	H: 2 PRT	92	. 1 7										
		EQUEI		-	phylo	5000	cus a	aurei	18						
					T 7	T 7			Ŧ			Ţ	DI		
1		-		5	Ile				10					15	
Ile	Ser	Ala	Суз 20	Gly	Asn	Lys	Glu	Lys 25	Glu	Ala	Gln	His	Gln 30	Phe	Thr
Lys	Gln	Phe 35	Lys	Asp	Val	Glu	Gln 40	Lys	Gln	Lys	Glu	Leu 45	Gln	His	Val
Met	Asp 50	Asn	Ile	His	Leu	Lys 55	Glu	Ile	Asp	His	Leu 60	Ser	Lys	Thr	Aap
Thr 65	Thr	Asp	Lys	Asn	Ser 70	ГЛЗ	Glu	Phe	Lys	Ala 75	Leu	Gln	Glu	Asp	Val 80

Lya															
	Asn	His	Leu	Ile 85	Pro	Lys	Phe	Glu	Ala 90	Tyr	Tyr	Lys	Ser	Ala 95	Lys
Asn	Leu	Pro	Asp 100	Asp	Thr	Met	Lys	Val 105	Lys	Lys	Leu	Lys	Lys 110	Glu	Tyr
Met	Thr	Leu 115	Ala	Asn	Glu	Lys	Lys 120	Asp	Ala	Ile	Tyr	Gln 125	Leu	Гла	Lys
Phe	Ile 130	Gly	Leu	Суз	Asn	Gln 135	Ser	Ile	Lys	Tyr	Asn 140	Glu	Asp	Ile	Leu
Asp 145	Tyr	Thr	Lys	Gln	Phe 150	Glu	Lys	Asn	Arg	Tyr 155	Lys	Val	Glu	Ser	Glu 160
Ile	Lys	Leu	Ala	Asp 165	Asn	Lys	Ser	Glu	Ala 170	Thr	Asn	Leu	Thr	Thr 175	Lys
Leu	Glu	His	Asn 180	Asn	LÀa	Ala	Leu	Arg 185	Asp	Thr	Ala	LÀa	Lys 190	Asn	Leu
Asp	Asb	Ser 195	Lys	Glu	Asn	Glu	Val 200	Lys	Gly	Ala	Ile	Lys 205	Asn	His	Ile
Met	Pro 210	Met	Ile	Glu	Lys	Gln 215	Ile	Thr	Aab	Ile	Asn 220	Gln	Thr	Asn	Ile
Ser 225	Asp	Lys	His	Val	Asn 230	Asn	Ala	Arg	Lys	Asn 235	Ala	Ile	Glu	Met	Tyr 240
Tyr	Ser	Leu	Gln	Asn 245	Tyr	Tyr	Asn	Thr	Arg 250	Ile	Glu	Thr	Ile	Lys 255	Val
Ser	Glu	Lys	Leu 260	Ser	Lys	Val	Asp	Val 265	Asp	Lys	Leu	Pro	Lys 270	Lys	Gly
Ile	Asp	Ile 275	Thr	His	Gly	Asp	Lys 280	Ala	Phe	Glu	Lys	Lys 285	Leu	Glu	Lys
Leu	Glu 290	Glu	Lys												
<211 <212	D> SH L> LH 2> TY	ENGTH	I: 24												
	5 > 01		гсм.	Ctor	by l			uro	10						
~ 100) . CI			Star	phylo	coco	cus a	aureu	15						
)> SI	EQUEN	ICE :	64							m]	T	71-	T	c]
Met 1	Lys	EQUEN Lys	NCE: Val	64 Met 5	Gly	Ile	Leu	Leu	Ala 10					15	
Met 1 Ala	Lys Cys	EQUEN Lys Gly	NCE: Val His 20	64 Met 5 His	Gly Gln	Ile Asp	Leu Ser	Leu Ala 25	Ala 10 Lys	Lys	Glu	Ser	Thr 30	15 Ser	His
Met 1 Ala	Lys	EQUEN Lys Gly	NCE: Val His 20	64 Met 5 His	Gly Gln	Ile Asp	Leu Ser	Leu Ala 25	Ala 10 Lys	Lys	Glu	Ser	Thr 30	15 Ser	His
Met 1 Ala Lys	Lys Cys	EQUEN Lys Gly Lys 35	Val His 20 Glu	64 Met 5 His Asn	Gly Gln Asp	Ile Asp Asn	Leu Ser Glu 40	Leu Ala 25 Glu	Ala 10 Lys Leu	Lys Asn	Glu Glu	Ser Glu 45	Thr 30 Leu	15 Ser Lys	His Glu
Met 1 Ala Lys Phe	ГЛа СЛа ГЛа	EQUEN Lys Gly Lys 35 Ser	VAl His 20 Glu Lys	64 Met 5 His Asn Lys	Gly Gln Asp Asn	Ile Asp Asn Met 55	Leu Ser Glu 40 Asp	Leu Ala 25 Glu Ile	Ala 10 Lys Leu Lys	Lys Asn Ile	Glu Glu Lys 60	Ser Glu 45 Gly	Thr 30 Leu Asp	15 Ser Lys Thr	His Glu Ile
Met 1 Ala Lys Phe Val 65	Lуз Суз Lуз 50	EQUEN Lys Gly Lys 35 Ser Asp	Val His 20 Glu Lys Lys	64 Met 5 His Asn Lys Phe	Gly Gln Asp Asn Glu 70	Ile Asp Asn Met 55 Ala	Leu Ser Glu 40 Asp Lys	Leu Ala 25 Glu Ile Ile	Ala 10 Lys Leu Lys Lys	Lys Asn Ile Glu 75	Glu Glu Lys 60 Pro	Ser Glu 45 Gly Phe	Thr 30 Leu Asp Ile	15 Ser Lys Thr Ile	His Glu Ile Asn 80
Met 1 Ala Lys Phe Val 65 Glu	Lys Cys Lys Lys Ser	GQUEN Lys Gly Lys 35 Ser Asp Asp	VE: Val His 20 Glu Lys Lys Glu	64 Met 5 His Asn Lys Phe Lys 85	Gly Gln Asp Asn Glu 70 Lys	Ile Asp Asn Met 55 Ala Lys	Leu Ser Glu 40 Asp Lys Tyr	Leu Ala 25 Glu Ile Ile	Ala 10 Lys Leu Lys Lys Ala 90	Lys Asn Ile Glu 75 Phe	Glu Glu Lys 60 Pro Lys	Ser Glu 45 Gly Phe Met	Thr 30 Leu Asp Ile Glu	15 Ser Lys Thr Ile 95	His Glu Ile Asn 80 Thr
Met 1 Ala Lys Phe Val 65 Glu Ala	Lys Cys Lys 50 Ser Lys	CQUEN Lys Gly Lys Ser Asp Asp Lys	NCE: Val His 20 Glu Lys Glu Lys Glu Asp 100	64 Met 5 His Asn Lys Phe Lys 85 Asp	Gly Gln Asp Asn Glu 70 Lys Lys	Ile Asp Asn Met 55 Ala Lys Asp	Leu Ser Glu 40 Asp Lys Tyr Leu	Leu Ala 25 Glu Ile Ile Asn 105	Ala 10 Lys Leu Lys Lys Ala 90 Pro	Lys Asn Ile Glu 75 Phe Ser	Glu Glu Lys 60 Pro Lys Ser	Ser Glu 45 Gly Phe Met Ile	Thr 30 Leu Asp Ile Glu Ser 110	15 Ser Lys Thr Ile 95 His	His Glu Ile Asn 80 Thr Asp
Met 1 Ala Lys Phe Val 65 Glu Ala Tyr	Lys Cys Lys 50 Ser Lys Lys	CQUEN Lys Gly Lys 35 Ser Asp Lys Lys Asn 115	VCE: Val Lis Glu Lys Glu Asp 100 Ile	64 Met 5 His Asn Lys Phe Lys 85 Asp Thr	Gly Gln Asp Asn Glu Lys Lys Gln	Ile Asp Asn Met 55 Ala Lys Asp Asp	Leu Ser Glu 40 Asp Lys Tyr Leu Asp 120	Leu Ala 25 Glu Ile Ile Asn 105 Lys	Ala 10 Lys Leu Lys Ala 90 Pro Asn	Lys Asn Ile Glu 75 Phe Ser Thr	Glu Glu Lys 60 Pro Lys Ser Val	Ser Glu 45 Gly Phe Met Ile Asn 125	Thr 30 Leu Asp Ile Glu Ser 110 Lys	15 Ser Lys Thr Ile Jle His Leu	His Glu Ile Asn 80 Thr Asp Arg
Met 1 Ala Lys Phe Val 65 Glu Ala Tyr Asp	Lys Cys Lys Ser Lys Lys Lys Ile	CQUEN Lys Gly Lys 35 Ser Asp Lys Asp Lys Asn 115 Tyr	VCE: Val His 20 Glu Lys Glu Lys Glu Asp 100 Ile Leu	64 Met 5 His Asn Lys Phe Lys 85 Asp Thr Leu	Gly Gln Asp Asn Glu 70 Lys Lys Gln Ser	Ile Asp Asn Met 55 Ala Lys Asp Asp Asp 135	Leu Ser Glu 40 Asp Lys Tyr Leu Asp 120 Lys	Leu Ala 25 Glu Ile Ile Lys Lys	Ala 10 Lys Leu Lys Ala 90 Pro Asn Tyr	Lys Asn Ile Glu 75 Phe Ser Thr Lys	Glu Glu Lys 60 Pro Lys Ser Val Asp 140	Ser Glu 45 Gly Phe Met Ile Asn 125 Trp	Thr 30 Leu Asp Ile Glu Ser 110 Lys Thr	15 Ser Lys Thr Ile Jle 95 His Leu Glu	His Glu Ile Asn 80 Thr Asp Arg His

Tyr Glu Leu Arg Gly Asp Gly Asn Ile Asn Leu Asn Val His Lys Tyr Ser Glu Asp Lys Thr Val Asp Ser Lys Ser Phe Lys Phe Ser Lys Leu Lys Thr Glu Asp Phe Ser His Arg Ala Glu Thr Arg Glu Glu Val Glu Lys Lys Glu Lys Glu Phe Glu Glu Glu Tyr Lys Lys Glu Gln Glu Arg Glu Lys Glu Lys Glu Lys Gln Lys Asp Asp Asp His Ser Gly Leu Asp Glu Val <210> SEQ ID NO 65 <211> LENGTH: 439 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 65 Met Arg Leu Thr Ile Tyr His Thr Asn Asp Ile His Ser His Leu His Glu Tyr Glu Arg Leu Lys Ala Tyr Met Ala Glu His Arg Pro Arg Leu Asn His Pro Ser Leu Tyr Val Asp Leu Gly Asp His Val Asp Leu Ser Ala Pro Ile Thr Glu Ala Thr Leu Gly Lys Lys Asn Val Ala Leu Leu Asn Glu Ala Lys Cys Asp Val Ala Thr Ile Gly Asn Asn Glu Gly Met Thr Ile Ser Tyr Glu Ala Leu Asn His Leu Tyr Asp Glu Ala Lys Phe Ile Val Thr Cys Ser Asn Val Ile Asp Glu Ser Gly His Leu Pro Asn Asn Ile Val Ser Ser Tyr Ile Lys Asp Ile Asp Gly Val Lys Ile Leu Phe Val Ala Ala Thr Ala Pro Phe Thr Pro Phe Tyr Arg Ala Leu Asn Trp Ile Val Thr Asp Pro Leu Glu Ser Ile Lys Glu Glu Ile Glu Leu Gln Arg Gly Lys Phe Asp Val Leu Ile Val Leu Ser His Cys Gly Ile Phe Phe Asp Glu Thr Leu Cys Gln Glu Leu Pro Glu Ile Asp Val Ile Phe Gly Ser His Thr His His Tyr Phe Glu His Gly Glu Ile Asn Asn Gly Val Leu Met Ala Ala Ala Gly Lys Tyr Gly Asn Tyr Leu Gly Glu Val Asn Leu Thr Phe Glu Ala His Lys Val Val His Lys Thr Ala Lys Ile Ile Pro Leu Glu Thr Leu Pro Glu Val Glu Thr Ser Phe Glu Glu Glu Gly Lys Thr Leu Met Ser Asn Ser Val Ile Gln His Pro Val Val Leu Lys Arg Ser Met Asn His Ile Thr Glu Ala Ala Tyr Leu Leu Ala

Ala			
Asp 320			
Leu			
Glu			

Gln Ser Val Cys Glu Tyr Thr His Ala Gln Cys Ala Ile Ile Asn A Gly Leu Leu Val Lys Asp Ile Val Lys Asp Glu Val Thr Glu Tyr λ Ile His Gln Met Leu Pro His Pro Ile Asn Met Val Arg Val Arg I Phe Gly Val Lys Leu Lys Glu Ile Ile Ala Lys Ser Asn Lys Gln G Tyr Met Tyr Glu His Ala Gln Gly Leu Gly Phe Arg Gly Asn Ile Phe Gly Gly Tyr Ile Leu Tyr Asn Leu Gly Tyr Ile His Ser Thr Gly Arg Tyr Tyr Leu Asn Gly Glu Glu Ile Glu Asp Asp Lys Glu Tyr Val Leu Gly Thr Ile Asp Met Tyr Thr Phe Gly Arg Tyr Phe Pro Thr Leu Lys Glu Leu Pro Lys Glu Tyr Leu Met Pro Glu Phe Leu Arg Asp Ile Phe Lys Glu Lys Leu Leu Glu Tyr <210> SEO ID NO 66 <211> LENGTH: 774 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 66 Met Glu Trp Thr Leu Val Asp Ile Gly Lys Lys His Val Ile Pro Lys Ser Gln Tyr Arg Arg Lys Arg Arg Glu Phe Phe His Asn Glu Asp Arg Glu Glu Asn Leu Asn Gln His Gln Asp Lys Gln Asn Ile Asp Asn Thr Thr Ser Lys Lys Ala Asp Lys Gln Ile His Lys Asp Ser Ile Asp Lys His Glu Arg Phe Lys Asn Ser Leu Ser Ser His Leu Glu Gln Arg Asn Arg Asp Val Asn Glu Asn Lys Ala Glu Glu Ser Lys Ser Asn Gln Asp Ser Lys Ser Ala Tyr Asn Arg Asp His Tyr Leu Thr Asp Asp Val Ser Lys Lys Gln Asn Ser Leu Asp Ser Val Asp Gln Asp Thr Glu Lys Ser Lys Tyr Tyr Glu Gln Asn Ser Glu Ala Thr Leu Ser Thr Lys Ser Thr Asp Lys Val Glu Ser Thr Glu Met Arg Lys Leu Ser Ser Asp Lys Asn Lys Val Gly His Glu Glu Gln His Val Leu Ser Lys Pro Ser Glu His Asp Lys Glu Thr Arg Ile Asp Ser Glu Ser Ser Arg Thr Asp Ser Asp Ser Ser Met Gl
n Thr Glu Lys Ile Lys Lys Asp
 Ser Ser Asp Gly As
n $% \left({{\mathbb{F}} {\mathbb{F}} {\mathbb{F}}$ Lys Ser Ser Asn Leu Lys Ser Glu Val Ile Ser Asp Lys Ser Asn Thr

	210					215					220				
Val 225	Pro	Lys	Leu	Ser	Glu 230	Ser	Asp	Asp	Glu	Val 235	Asn	Asn	Gln	Lys	Pro 240
Leu	Thr	Leu	Pro	Glu 245	Glu	Gln	Lys	Leu	Lys 250	Arg	Gln	Gln	Ser	Gln 255	Asn
Glu	Gln	Thr	Lys 260	Thr	Tyr	Thr	Tyr	Gly 265	Asp	Ser	Glu	Gln	Asn 270	Asp	Lys
Ser	Asn	His 275	Glu	Asn	Asp	Leu	Ser 280	His	His	Ile	Pro	Ser 285	Ile	Ser	Asp
Asp	Lys 290	Aap	Asn	Val	Met	Arg 295	Glu	Asn	His	Ile	Val 300	Asp	Asp	Asn	Pro
Asp 305	Asn	Asp	Ile	Asn	Thr 310	Pro	Ser	Leu	Ser	Lys 315	Thr	Asp	Asp	Asp	Arg 320
Lys	Leu	Asp	Glu	Lys 325	Ile	His	Val	Glu	Asp 330	ГЛа	His	Lys	Gln	Asn 335	Ala
Asp	Ser	Ser	Glu 340	Thr	Val	Gly	Tyr	Gln 345	Ser	Gln	Ser	Thr	Ala 350	Ser	His
Arg	Ser	Thr 355	Glu	Lys	Arg	Asn	Ile 360	Ser	Ile	Asn	Asp	His 365	Asp	ГЛЗ	Leu
Asn	Gly 370	Gln	Lys	Thr	Asn	Thr 375	Lys	Thr	Ser	Ala	Asn 380	Asn	Asn	Gln	Lys
Lys 385	Ala	Thr	Ser	Lys	Leu 390	Asn	Lys	Gly	Arg	Ala 395	Thr	Asn	Asn	Asn	Tyr 400
Ser	Asp	Ile	Leu	Lys 405	Lys	Phe	Trp	Met	Met 410	Tyr	Trp	Pro	Lys	Leu 415	Val
Ile	Leu	Met	Gly 420	Ile	Ile	Ile	Leu	Ile 425	Val	Ile	Leu	Asn	Ala 430	Ile	Phe
Asn	Asn	Val 435	Asn	Lys	Asn	Asp	Arg 440	Met	Asn	Asp	Asn	Asn 445	Asp	Ala	Asp
Ala	Gln 450	Lys	Tyr	Thr	Thr	Thr 455	Met	Lys	Asn	Ala	Asn 460	Asn	Thr	Val	Lys
Ser 465	Val	Val	Thr	Val	Glu 470	Asn	Glu	Thr	Ser	Lys 475	Asp	Ser	Ser	Leu	Pro 480
Lys	Asp	Lys	Ala	Ser 485	Gln	Asp	Glu	Val	Gly 490	Ser	Gly	Val	Val	Tyr 495	Lys
Lys	Ser	Gly	Asp 500		Leu	Tyr	Ile	Val 505		Asn	Ala	His	Val 510	Val	Gly
Asp	Lys	Glu 515	Asn	Gln	Lys	Ile	Thr 520	Phe	Ser	Asn	Asn	Lys 525	Ser	Val	Val
Gly	Lys 530	Val	Leu	Gly	Lys	Asp 535	Lys	Trp	Ser	Asp	Leu 540	Ala	Val	Val	Lys
Ala 545	Thr	Ser	Ser	Asp	Ser 550	Ser	Val	Lys	Glu	Ile 555	Ala	Ile	Gly	Asp	Ser 560
Asn	Asn	Leu	Val	Leu 565	Gly	Glu	Pro	Ile	Leu 570	Val	Val	Gly	Asn	Pro 575	Leu
Gly	Val	Aap	Phe 580	Lys	Gly	Thr	Val	Thr 585	Glu	Gly	Ile	Ile	Ser 590	Gly	Leu
Asn	Arg	Asn 595	Val	Pro	Ile	Asp	Phe 600	Asp	Lys	Asp	Asn	Lys 605	Tyr	Asp	Met
Leu	Met 610	Lys	Ala	Phe	Gln	Ile 615	Asp	Ala	Ser	Val	Asn 620	Pro	Gly	Asn	Ser
Gly 625	Gly	Ala	Val	Val	Asn 630	Arg	Glu	Gly	Lys	Leu 635	Ile	Gly	Val	Val	Ala 640

Ala Lys Ile Ser Met Pro Asn Val Glu Asn Met Ser Phe Ala Ile Pro Val Asn Glu Val Gln Lys Ile Val Lys Asp Leu Glu Thr Lys Gly Lys Ile Asp Tyr Pro Asp Val Gly Val Lys Met Lys Asn Ile Val Ser Leu Asn Ser Phe Glu Arg Gln Ala Val Lys Leu Pro Gly Lys Val Lys Asn Gly Val Val Asp Gln Val Asp Asn Asn Gly Leu Ala Asp Gln Ser Gly Leu Lys Lys Gly Asp Val Ile Thr Glu Leu Asp Gly Lys Leu Leu Glu Asp Asp Leu Arg Phe Arg Gln Ile Ile Phe Ser His Lys Asp Asp Leu Lys Ser Ile Thr Ala Lys Ile Tyr Arg Asp Gly Lys Glu Lys Glu Ile Asn Ile Lys Leu Lys <210> SEO ID NO 67 <211> LENGTH: 393 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEOUENCE: 67 Met Asn Ser Ser Cys Lys Ser Arg Val Phe Asn Ile Ile Ser Ile Ile Met Val Ser Met Leu Ile Leu Ser Leu Gly Ala Phe Ala Asn Asn Asn Lys Ala Lys Ala Asp Ser His Ser Lys Gln Leu Glu Ile Asn Val Lys Ser Asp Lys Val Pro Gln Lys Val Lys Asp Leu Ala Gln Gln Gln Phe Ala Gly Tyr Ala Lys Ala Leu Asp Lys Gln Ser Asn Ala Lys Thr Gly Lys Tyr Glu Leu Gly Glu Ala Phe Lys Ile Tyr Lys Phe As
n Gly Glu Glu Asp Asn Ser Tyr Tyr Tyr Pro Val Ile Lys Asp Gly Lys Ile Val Tyr Thr Leu Thr Leu Ser Pro Lys Asn Lys Asp Asp Leu Asn Lys Ser Lys Glu Asp Met Asn Tyr Ser Val Lys Ile Ser Asn Phe Ile Ala Lys Asp Leu Asp Gln Ile Lys Asp Lys Asn Ser Asn Ile Thr Val Leu Thr Asp Glu Lys Gly Phe Tyr Phe Glu Glu Asp Gly Lys Val Arg Leu Val Lys Ala Thr Pro Leu Pro Gly Asn Val Lys Glu Lys Glu Ser Ala Lys Thr Val Ser Ala Lys Leu Lys Gln Glu Leu Lys Asn Thr Val Thr Pro Thr Lys Val Glu Glu Asn Glu Ala Ile Gln Glu Asp Gln Val Gln Tyr

Glu Asn Thr Leu Lys Asn Phe Lys Ile Arg Glu Gln Gln Phe Asp Asn

												con	tin	ued	
225					230					235					240
Ser	Trp	Сув	Ala	Gly 245	Phe	Ser	Met	Ala	Ala 250	Leu	Leu	Asn	Ala	Thr 255	Lys
Asn	Thr	Asp	Thr 260	Tyr	Asn	Ala	His	Asp 265	Ile	Met	Arg	Thr	Leu 270	Tyr	Pro
Glu	Val	Ser 275	Glu	Gln	Asp	Leu	Pro 280	Asn	Суз	Ala	Thr	Phe 285	Pro	Asn	Gln
Met	Ile 290	Glu	Tyr	Gly	Lys	Ser 295	Gln	Gly	Arg	Asp	Ile 300	His	Tyr	Gln	Glu
Gly 305	Val	Pro	Ser	Tyr	Glu 310	Gln	Val	Asp	Gln	Leu 315	Thr	Lya	Asp	Asn	Val 320
Gly	Ile	Met	Ile	Leu 325	Ala	Gln	Ser	Val	Ser 330	Gln	Asn	Pro	Asn	Asp 335	Pro
His	Leu	Gly	His 340	Ala	Leu	Ala	Val	Val 345	Gly	Asn	Ala	LÀa	Ile 350	Asn	Asp
Gln	Glu	Lys 355	Leu	Ile	Tyr	Trp	Asn 360	Pro	Trp	Asp	Thr	Glu 365	Leu	Ser	Ile
Gln	Asp 370	Ala	Asp	Ser	Ser	Leu 375	Leu	His	Leu	Ser	Phe 380	Asn	Arg	Asp	Tyr
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Thr	Leu	Leu 115		Asn	Lys	His	Val 120		Asp	Ala	Thr	His 125		Asp	Pro
His	Ala 130		Lys	Ala	Phe	Pro 135		Ala	Ile	Asn	Gln 140		Asn	Tyr	Pro
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	Leu	Ala	Ile	Val 165	Lys	Phe	Ser	Pro	Asn 170		Gln	Asn	Lys	His 175	
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Val	Asn	Gln	180 Asn	Ile	Thr	Val	Thr	185 Gly	Tyr	Pro	Gly	Asp	190 Lys	Pro	Val
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Ala 225	Met	Gln	Tyr	Asp	Leu 230	Ser	Thr	Thr	Gly	Gly 235	Asn	Ser	Gly	Ser	Pro 240	
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Glu	Lys 50	Tyr	Leu	Val	Asp	Arg 55	Asn	Lys	Glu	Lys	Val 60	Ala	Pro	Ser	Lys	
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Val	Lys	Ala 195	Ile	Gln	Lys	Arg	Gly 200	Ile	Asp	Pro	Lys	Lys 205	Tyr	Lys	Гуз	
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Phe	Leu	Arg 275	Pro	Asn	Ile	Leu	Asp 280	Gln	Tyr	Tyr	Gly	Ala 285	Gly	Asn	Leu
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Val	Tyr	Tyr 355	Asn	Asp	Lys	Tyr	Val 360	Val	Val	Leu	Ala	Leu 365	Asn	Val	Lys
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Thr	Glu	Lvs	Glv	Leu	Asn	Asp	Ile	Pro	Val	Gln	Lvs	Asp	Lvs	Val	Gln

Thr Glu Lys Gly Leu Asn Asp Ile Pro Val Gln Lys Asp Lys Val Gln

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Gln	Asp	Ser	Asn	Lys 245	-	Ile	Glu	Asn	Glu 250	Arg	Pro	Lys	Ala	Ser 255	Gly
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Asn	His	Lys 275	Glu	Gln	Pro	Гла	His 280	Lys	Asp	Glu	Lys	Ser 285	Lys	Lys	Glu
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	Ser 50	Tyr	Lys	Thr	Leu	Pro 55	Asn	Arg	Tyr	Lys	Asp 60	Val	Pro	Glu	Ile
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ГЛа	Ala 130	Gln	Ala	ГЛа	Glu	Leu 135	Asn	Asp	His	Leu	Asn 140	Ser	Val	ГЛа	Gln
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Ile			Asp	Ile	Ile	Leu 215		Leu	Pro	His			Pro	Glu	Glu
Val	210 Lys	Lys	Met	Phe		215 Lys	Glu	Phe	Lys		220 Asn	Asp	Ile	Trp	
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 Glu Lys Ile Asn Lys Asp Ile Val Gly Trp
 Ile Lys Leu Ser Gly Thr

 65
 70
 75
 80
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		35					40					45			
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Lys 65	Trp	Leu	Tyr	Gln	Tyr 70	Asp	Asn	Gly	Asn	Ile 75	Tyr	Val	Glu	Leu	Lys 80
Arg	Tyr	Ser	Trp	Ser 85	Ala	His	Ile	Ser	Leu 90	Trp	Gly	Ala	Glu	Ser 95	Trp
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Lys	Asp	Gln 115	Glu	Thr	Ile	Asp	Ser 120	Phe	Ala	Leu	Ser	Gln 125	Glu	Thr	Phe
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Leu 145	Asn	Val	Thr	Tyr	Lys 150	Asp	ГЛа	Ala	Glu	Thr 155	Phe	Thr	Gly	Gly	Phe 160
	Val	Tyr	Glu	Gly 165		Lys	Pro	Val	Leu 170		Leu	Lys	Glu	Leu 175	
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Phe Arg Ile Arg Gln Thr Leu Ile Lys Ser Lys Lys Leu Tyr Asn Asn Ser Tyr Asn Lys Gly Gln Ile Lys Ile Thr Gly Ala Asp Asn Asn Tyr Thr Ile Asp Leu Ser Lys Arg Leu Pro Ser Thr Asp Ala Asn Arg Tyr Val Lys Lys Pro Gln Asn Ala Lys Ile Glu Val Ile Leu Glu Lys Ser Asn <210> SEQ ID NO 75 <211> LENGTH: 565 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 75 Met Ala Tyr Asp Gly Leu Phe Thr Lys Lys Met Val Glu Ser Leu Gln Phe Leu Thr Thr Gly Arg Val His Lys Ile Asn Gln Pro Asp Asn Asp Thr Ile Leu Met Val Val Arg Gln Asn Arg Gln Asn His Gln Leu Leu Leu Ser Ile His Pro Asn Phe Ser Arg Leu Gln Leu Thr Thr Lys Lys Tyr Asp Asn Pro Phe Asn Pro Pro Met Phe Ala Arg Val Phe Arg Lys His Leu Glu Gly Gly Ile Ile Glu Ser Ile Lys Gln Ile Gly Asn Asp Arg Arg Ile Glu Ile Asp Ile Lys Ser Lys Asp Glu Ile Gly Asp Thr Ile Tyr Arg Thr Val Ile Leu Glu Ile Met Gly Lys His Ser Asn Leu Ile Leu Val Asp Glu Asn Arg Lys Ile Ile Glu Gly Phe Lys His Leu Thr Pro Asn Thr Asn His Tyr Arg Thr Val Met Pro Gly Phe Asn Tyr Glu Ala Pro Pro Thr Gln His Lys Ile Asn Pro Tyr Asp Ile Thr Gly Ala Glu Val Leu Lys Tyr Ile Asp Phe Asn Ala Gly Asn Ile Ala Lys Gln Leu Leu Asn Gln Phe Glu Gly Phe Ser Pro Leu Ile Thr Asn Glu Ile Val Ser Arg Arg Gln Phe Met Thr Ser Ser Thr Leu Pro Glu Ala Phe Asp Glu Val Met Ala Glu Thr Lys Leu Pro Pro Thr Pro Ile Phe His Lys Asn His Glu Thr Gly Lys Glu Asp Phe Tyr Phe Ile Lys Leu Asn Gln Phe Asn Asp Asp Thr Val Thr Tyr Asp Ser Leu Asn Asp Leu Leu Asp Arg Phe Tyr Asp Ala Arg Gly Glu Arg Glu Arg Val Lys Gln Arg Ala Asn Asp Leu Val Arg Phe Val Gln Gln Gln Leu His Lys Tyr

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Asn	Ala 370	Gln	Tyr	Tyr	Tyr	Lys 375	Gln	Tyr	Asn	Arg	Met 380	Lys	Thr	Arg	Glu
Arg 385	Glu	Leu	Gln	His	Gln 390	Ile	Gln	Leu	Thr	Lys 395	Asp	Asn	Ile	Asp	Tyr 400
Phe	Ser	Thr	Ile	Glu	Gln	Gln	Leu	His	His	Ile	Ser	Val	His	Asp	Ile

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Glu Leu Met Gly Lys Val Glu Leu Ala Asp Tyr Arg Phe Thr Lys Asp

Ser Lyo Sir Ser Ser Lie Lyo App Val App Ala Phe Phe Lyo Sir Jie Lyo Ala Lyo Ala Lyo Ala Lyo Ala Lyo Sir Jie Ala The Ris App App Ala Lyo Ala Ser Ser Sir Jie Ala Ser Ser Sir Jie Ala Ser Ser Ser Ala Ser Ser Vie Ala Ser Ser Vie Ala Ser Ser Vie Ala Ser Ser Vie Ala Ser Ser App 200 Ala Ser Ser And Die Ala Ser Ser Vie Ala Ser Ser Vie Ala Ser Ser Vie Ala Ser Ser App 200 Ala Ser App 200 Ala Ser Ser																
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Leu	Asp	Gln	Asn 340	Trp	Asn	Asn	Gly	Gly 345	Trp	Arg	Lys	Ala	Glu 350	Val	Ala
His	Lys	Val 355	Val	His	Asn	Tyr	Glu 360	Asn	Asp	Met	Ile	Phe 365	Ile	Arg	Pro
Phe	Lys 370	Lys	Ala												
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		EQUEI					Sub (aur ci	a b						
Met 1	Leu	Lys	Lys	Ala 5	Lys	Phe	Ile	Leu	Met 10	Ala	Thr	Ile	Leu	Leu 15	Ser
Gly	Cys	Ser	Thr 20	Thr	Asn	Asn	Glu	Ser 25		Lys		Thr	Lys 30	Ser	Val
Pro	Glu	Glu 35	Met	Asp	Ala	Ser	Lys 40	Tyr	Val	Gly	Gln	Gly 45	Phe	Gln	Pro
Pro	Ala 50	Glu	Lys	Asp	Ala	Ile 55	Glu	Phe	Ala	Lya	Lys 60	His	Lys	Asp	ГЛа
Ile 65	Ala	Lys	Arg	Gly	Glu 70	Gln	Phe	Phe	Met	Asp 75	Asn	Phe	Gly	Leu	Lуз 80
Val	Lys	Ala	Thr	Asn 85	Val	Ile	Gly	Ser	Gly 90	Asp	Gly	Val	Glu	Val 95	Phe
Val	His	Сув	Asp 100	Aap	His	Asp	Ile	Val 105	Phe	Asn	Ala	Ser	Ile 110	Pro	Phe
Asp	Lys	Ser 115	Ile	Ile	Asp	Ser	Asp 120	Ser	Ser	Leu	Arg	Ser 125	Lys	Asp	Lys
Gly	Asp 130		Met	Ser	Thr	Leu 135		Gly	Ala	Val	Leu 140		Gly	Phe	Glu
-		Ala	Gln	Lys	Glu 150		Tyr	Asp	Lys			Lys	Phe	Phe	-
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Asn	Lys	Thr	Gln 180	Asn	Ser	Gly	Tyr	Glu 185	Asn	Glu	Tyr	Phe	Tyr 190	Ile	Ser
Ala	Ile	Pro 195	Tyr	Asn	Leu	Ala	Glu 200	Tyr	Arg	Asp	Tyr	Phe 205	Glu	Pro	Leu
Leu	Asn 210	Lys	Ser	Asp	Ser	Glu 215	Phe	Ser	Lys	Glu	Leu 220	Ser	Asn	Val	Lys
Lys 225	Gln	Leu	Lys	Asp	Lys 230	Ser	Lys	Val	Ser	Val 235	Thr	Thr	Thr	Leu	Phe 240
Ser	Lys	Lys	Lys	Asn 245	Tyr	Thr	Lys	Lys	Ser 250	Asn	Ser	Glu	Asn	Val 255	Ile
Lys	Met	Ala	Glu 260		Ile	Гла	Lys	Asp 265		Glu	Ile	Pro	Asn 270		Ile
Glu	Leu	Ser 275		Гла	Phe	Ser	Asp 280		Lys	Ile	Asn	Thr 285		Гла	Pro
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Arg	Glu	Asp 35	Asn	His	Gln	Leu	Lys 40	Leu	Asp	Ile	Gln	Glu 45	Leu	Asn	Gln
Gln	Ile 50	Ser	Asp	Ser	ГЛЗ	Ser 55	Lys	Ile	Lys	Gly	Leu 60	Glu	Lys	Asp	Lys
Glu 65	Asn	Ser	Lys	Lys	Thr 70	Ala	Ser	Asn	Asn	Thr 75	Lys	Ile	Lys	Leu	Met 80
Asn	Val	Thr	Ser	Thr 85	Tyr	Tyr	Asp	Lys	Val 90	Ala	Lys	Ala	Leu	Lys 95	Ser
Tyr	Asn	Asp	Ile 100	Glu	Гла	Asp	Val	Ser 105	Lys	Asn	Lys	Gly	Asp 110	Гла	Asn
Val	Gln	Ser 115	Lys	Leu	Asn	Gln	Ile 120	Ser	Asn	Asp	Ile	Gln 125	Ser	Ala	His
Thr	Ser 130	Tyr	Lys	Asp	Ala	Ile 135	Asp	Gly	Leu	Ser	Leu 140	Ser	Asp	Asp	Asp
Lys 145	Lys	Thr	Ser	Lys	Asn 150	Ile	Asp	Lys	Leu	Asn 155	Ser	Asp	Leu	Asn	His 160
Ala	Phe	Asp	Asp	Ile 165	Гла	Asn	Gly	Tyr	Gln 170	Asn	Lys	Asp	Lys	Lys 175	Gln
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Ser

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Met Leu Lys 35	Gly Cys	Gly Gl	у Суз 40	Leu	Ile	Ser	Phe	Ile 45	Leu	Leu	Ile
Ile Leu Leu 50	Ser Ala	Cys Se 55	r Met	Met	Phe	Ser	Asn 60	Asn	Asp	Asn	Ser
Thr Asn Asn 65	Gln Ser	Ser Ly 70	s Thr	Gln	Leu	Thr 75	Gln	ГЛа	Asp	Glu	Asn 80
Lys Asn Glu	Asp Lys 85	Pro Gl	u Glu	Lys	Ser 90	Glu	Thr	Ala	Thr	Asp 95	Glu
Asp Leu Gln	Ser Thr 100	Glu Gl	u Val	Pro 105	Ala	Asn	Glu	Asn	Thr 110	Glu	Asn
Asn Gln His 115	Glu Ile	Asp Gl	u Ile 120		Thr	Lys	Asp	Gln 125	Ser	Asp	Asp
Asp Ile Asn 130	Thr Pro	Asn Va 13		Glu	Asp	Lys	Ser 140	Gln	Asp	Asp	Leu
Lys Asp Asp 145	Leu Lys	Glu Ly 150	s Gln	Gln	Ser	Ser 155	Asn	His	His	Gln	Ser 160
Thr Gln Pro	Lys Thr 165		o Ser	Thr	Glu 170	Thr	Asn	Thr	Gln	Gln 175	Ser
Phe Ala Asn	Суз Lуз 180	Gln Le	u Arg	Gln 185	Val	Tyr	Pro	Asn	Gly 190	Val	Thr
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Asp Thr Asn 35	Lys Lys	Thr Gl	n Gln 40	Thr	Asp	Asn	Thr	Thr 45	Gln	Ser	Asn
Thr Glu Lys 50	Gln Met	Thr Pr 55	o Gln	Glu	Ala	Glu	Asp 60	Ile	Val	Arg	Asn
Asp Tyr Lys 65	Ala Arg	Gly Va 70	l Asn	Glu	Tyr	Gln 75	Thr	Leu	Asn	Tyr	LYS 80
Thr Asn Leu	Glu Arg 85	Ser As	n Glu	His	Glu 90	Tyr	Tyr	Val	Glu	His 95	Leu
Val Arg Asp	Ala Val 100	Gly Th	r Pro	Leu 105	Lys	Arg	Суа	Ala	Ile 110	Val	Asn
Arg His Asn 115	Gly Thr	Ile Il	e Asn 120		Phe	Asp	Asp	Met 125	Ser	Glu	Lys
Asp Lys Glu 130	Glu Phe	Glu Al 13		Lys	Lys	Arg	Ser 140	Pro	Lys	Tyr	Asn

Gly Met Asn Asn Asn Asn Asn Asn Lys Ala Ile Glu Asn Asn Lys Ala Ile Glu Asn Asn Asn Asn Lys Ala Ile Glu Asn A
165 170 175 Gln Lys Val Asp Asp Lys Asn Asp Lys Asn Asp Lys Asn Ala Val Asn Lys Gl 185 185 Val Asn Val Asn Lys Gl 190 191 195 200 Sen Glu Glu Thr Lys Val Ly 200 > SEQ JE NO 82 200 Sen Glu Glu Thr Lys Val Ly 200 > SEQUENCE: 82 200 Sen Ala Sen Glu Glu Thr Lys Val Ly 200 Lys Hie IIe Lys Arg Ala IIe IIe Ser Leu IIe IIe Leu Ser Leu 200 Sen Glu Glu Ceu Ty 200 Ser Val Glu Tyr Lys Asn Thr Ala Thr Phe Asn Lys Leu Val Ly 40 45 Lys Bet Leu Asn Val Val Tyr Asn IIe Pro Glu Leu His Val Al 50 60 Ser Val Glu Tyr Lys Asn Ala Thr Cys Ser Thr Cys IIe Thr Set 85 71 Asp IIe Lys Tyr IIe Asn Ala Thr Cys Ser Thr Cys IIe Thr Set 85 71 Asp Met Ann Lys IIe Thr Asn Glu Ser Leu Phe Ser Arg Gl 100 110 Asp Met Asn Lys IIe Thr Asn Asn Gly Ala Ser Tyr Asp Asp Lo 115 72 Asp Met Asn Lys IIe Thr Asn Asn Gly Ala Ser Thr Asp Ser Lys Ar 115 71 Asp Met Asn Lys IIe Thr Asn Asn Phe Ser Thr Asp Ser Lys Asp 110 71 Asp Met Asn Lys IIe Thr Asn Asn Phe Ser Thr Asp Ser Lys Asp 125 71 Asp Met Asn Lys IIe Thr Asn Asn Phe Ser Thr Asp Ser Lys Asp 125 71 Asp Met Asn Asn Asp Asp Leu Lys Asn Asn Phe Ser Thr Asp Ser Lys Ar 126 71
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195 200 205 > SEQ ID NO 82 > LEMGTH: 457 > TYPE: PRT >> SEQUENCE: 82 Lys Ile Ile Lys Arg Ala Ile Ile Son Ala Ser Ala Ser Glu Glu Leu Ya 30 10 10 11
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35 40 45 Lys Ser Leu Asn Val Yal Yar Asn Ile Pro Glu Leu His Val Yar Ile Lys Met Thr Lys Met His Ala Asn Ala Asn Ala Asn Ala Asn Ala Asn Asn Asn Tra Kasn Ile Asn Tra Kasn Ala Asn Asn Asn Tra Ser Tra Cus Tra Ser Tra Ser Tra Ser Asn Asn Tra Ser Asn Asn Tra Ser
50 55 60 11e Lys Met Thr Lys Met His Ala Asn Ala Leu Ala Asn Tyr Lys Asp I1e Lys Tyr I1e Asn Ala Thr Cys Ser Thr Cys I1e Asn Tyr Lys Asp I1e Lys Tyr I1e Asn Ala Thr Cys Ser Thr Cys I1e Thr Ser Ser Thr Cys Intr Cys Ser Thr Cys Intr Tys Intr Ser Thr Cys Ser Thr Cys Asn Glu Ser Tyr Intr Ser Tr Intr Ser Tyr Intr Ser Tr Ser Asn Intr Ser Intr Intr Intr Ser Intr Intr <td< td=""></td<>
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290 295 300

Arg Glu Tyr Gln Gly Asn Gly Glu Val LysAsp Val Pro Ala Ser Met305310315

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n Ala Ser Phe \mbox{Thr} Glu Met Leu Asn Lys Ile Leu Ala Asp Lys Tyr Lys Asn Lys Val Asn Asp Lys Lys Ile Asp Glu Gl
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n Lys Gl
n Tyr Gly Gly Lys Asp Lys Phe Glu Lys Ala Leu Gln Gln Gln Gly Leu Thr Ala Asp Lys Tyr Lys Glu As
n Leu Arg Thr Ala Ala Tyr His Lys Glu Leu Leu Ser As
p $% \left({{\mathbb{F}}_{{\mathbb{F}}}} \right)$ Lys Ile Lys Ile Ser Asp Ser Glu Ile Lys Glu Asp Ser Lys Lys Ala Ser His Ile Leu Ile Lys Val Lys Ser Lys Lys Ser Asp Lys Glu Gly Leu Asp
 Asp Lys Glu Ala Lys Gl
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Asp Gly Glu Val Ser Glu Val Val Lys Ser Ser Phe Gly Tyr His Leu

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лтс	T TT	ue	u.

					50.	<i>,</i>								
											con	tin	ued	
225				230					235					240
Leu Lys	a Ala	ı Asp	Lys 245	Pro	Thr	Asp	Phe	Asn 250	Ser	Glu	Lys	Gln	Ser 255	Leu
Lys Glu	ι Буг	: Leu 260	Val	Asp	Gln	Lys	Val 265	Gln	Lys	Asn	Pro	Lys 270	Leu	Leu
Thr Asp		ı Tyr	Lys	Asp	Leu		Lys	Glu	Tyr	Asp			Phe	Lys
a	275			~		280					285		-	a 7
Asp Arg 290) Ile	ГЛЗ	Ser	Val 295	Val	Glu	Asp	Lys	Ile 300	Leu	Asn	Pro	GIU
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		20					25					30		-
Ala Lys	Asp 35) Lys	Lys	His	Val	Gln 40	Val	Asn	Val	Glu	Asp 45	Lys	Ser	Val
Pro Thr 50	. yab	Val	Arg	Asn	Leu 55	Ala	Gln	Lys	Asp	Tyr 60	Leu	Ser	Tyr	Val
Thr Ser 65	Leu	ı Asp	ГЛЗ	Ile 70	Tyr	Asn	Lys	Glu	Lys 75	Ala	Ser	Tyr	Thr	Leu 80
Gly Glu	ı Pro) Phe	Lys 85	Ile	Tyr	Lys	Phe	Asn 90	Lys	Lys	Ser	Asp	Gly 95	Asn
Tyr Tyr	Phe			Leu	Asn	Thr			Asn	Ile	Asp	-		Val
Thr Ile	. Cor	100 Pro	Luc	TIA	Thr	Lare	105 Tvr	Ser	Ser	Ser	Ser	110 Ser	Lare	Ͳ៶៸ຠ
	115	5	-			120	-				125		-	-
Thr Ile 130		ı Val	Ser	Pro	Phe 135	Leu	Ser	ГЛа	Val	Leu 140	Asn	Gln	Tyr	ГЛа
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Asp Lys	s Lya	Leu		Lys	Thr	Glu	Ser		Pro	Thr	Gly	Asn		Val
The Cl	- -	180			۲ .	c	185 Val	m]	M-+	D		190 Com	a 1	Dk -
Thr Gln	195 195	-	GIN	гда	Ala	Ser 200	Val	Thr	Met	Pro	Thr 205	Ser	GIN	гhе
Lys Ser 210		ı Asn	Tyr	Thr	Tyr 215	Asn	Glu	Gln	Tyr	Ile 220	Asn	Lys	Leu	Glu
Asn Phe 225	e Lys	lle	Arg	Glu 230	Thr	Gln	Gly	Asn	Asn 235	Gly	Trp	Сүз	Ala	Gly 240
Tyr Thr	: Met	Ser	Glu		Leu	Asn	Ala	Thr		Asn	Thr	Asn	Lys	
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His Ala	ı Glu	1 Ala 260		Met	Arg	Phe	Leu 265	His	Pro	Asn	Leu	Gln 270	GΤλ	GIN
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Ala	Val	Val	Gly 340	Asn	Ala	Lys	Leu	Asp 345	Asn	Gly	Gln	Glu	Val 350	Ile	Ile
Ile	Trp	Asn 355	Pro	Trp	Asp	Asn	Gly 360	Phe	Met	Thr	Gln	Asp 365	Ala	Lys	Asn
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Ile 385	Tyr	Gly	Tyr												
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1 Thr	Ala	Ala	Thr	5 Ile	Ile	Trp	Phe	Ser	10 Tyr	Asp	Lys	Asn	Lys	15 Tyr	Gly
			20		Lys	-		25	•	-	•		30	-	
	-	35	-	-	Ser		40	-	-	-		45	-		
	50			-		55			-		60	-	-		
65					Asp 70					75					80
Asp	Lys	Thr	Leu	Lуя 85	Ile	Ser	Asp	Lys	Arg 90	Ser	ГЛЗ	Thr	Arg	Gly 95	Tyr
Ala	Ile	Asp	Met 100	Asn	Pro	Phe	His	Glu 105	Asn	Lys	Lys	Thr	Leu 110	Thr	Ile
Glu	Met	Pro 115	Asp	Lys	Met	Ile	Lys 120	Arg	Leu	Asn	Leu	Ser 125	Ser	Gly	Ala
-	Ser 130	Val	Arg	Ile	Ser	Asp 135	Val	Asp	Leu	Glu	Asn 140	Thr	Ser	Ile	Gln
Ser 145	Ile	Asn	Gly	Glu	Val 150	Val	Ile	ГЛа	Asn	Ser 155	Asn	Leu	Asp	Ala	Leu 160
Asp	Ser	Lys	Thr	Asn 165	Asn	Ser	Ser	Thr	Tyr 170	Ile	Ser	ГЛа	Ser	Asn 175	Ile
ГЛа	Asn	Ser	Asn 180	Ile	ГЛа	Val	Val	Ile 185	Gly	Thr	Leu	Gln	Ile 190	Asp	Lys
Ser	Gln	Ile 195	Lys	Gln	Ser	Ile	Phe 200	Leu	Asn	Asp	His	Gly 205	Asp	Ile	Glu
Phe	Lys 210	Asn	Met	Pro	Ser	Lys 215	Val	Asp	Ala	Lys	Ala 220	Ser	Thr	Гла	Gln
Gly 225	Asp	Ile	Arg	Phe	Lys 230	Tyr	Asp	Ser	Lys	Pro 235	Glu	Asp	Thr	Ile	Leu 240
Lys	Leu	Asn	Pro	Gly 245	Thr	Gly	Asp	Ser	Val 250	Val	Гла	Asn	Lys	Thr 255	Phe
Thr	Asn	Gly	Lys 260		Gly	Гла	Ser			Val	Leu	Glu	Phe 270		Thr
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Lys	Asp	Asn 35	Leu	Asn	Gly	Glu	Lys 40	Pro	Thr	Thr	Asn	Leu 45	Asn	His	Asn
Ile	Thr 50	Ser	Pro	Ser	Val	Asn 55	Ser	Glu	Met	Asn	Asn 60	Asn	Glu	Thr	Gly
Thr 65	Pro	His	Glu	Ser	Asn 70	Gln	Thr	Gly	Asn	Glu 75	Gly	Thr	Gly	Ser	Asn 80
Ser	Arg	Asp	Ala	Asn 85	Pro	Asp	Ser	Asn	Asn 90	Val	Lys	Pro	Asp	Ser 95	Asn
Asn	Gln	Asn	Pro 100	Ser	Thr	Asp	Ser	Lys 105	Pro	Asp	Pro	Asn	Asn 110	Gln	Asn
Ser	Ser	Pro 115	Asn	Pro	Lys	Pro	Asp 120	Pro	Asp	Asn	Pro	Lys 125	Pro	Lys	Pro
Asp	Pro 130	Lys	Pro	Asp	Pro	Asp 135	Lys	Pro	Lys	Pro	Asn 140	Pro	Asp	Pro	Lys
Pro 145	Asp	Pro	Asp	Asn	Pro 150	Lys	Pro	Asn	Pro	Asp 155	Pro	Гла	Pro	Asp	Pro 160
Asp	Lys	Pro	Lys	Pro 165	Asn	Pro	Asp	Pro	Lys 170	Pro	Asp	Pro	Asp	Lys 175	Pro
ГЛа	Pro	Asn	Pro 180	Asn	Pro	Lys	Pro	Asp 185	Pro	Asn	Lys	Pro	Asn 190	Pro	Asn
Pro	Ser	Pro 195	Asp	Pro	Asp	Gln	Pro 200	Gly	Aab	Ser	Asn	His 205	Ser	Gly	Gly
Ser	Lys 210	Asn	Gly	Gly	Thr	Trp 215	Asn	Pro	Asn	Ala	Ser 220	Asp	Gly	Ser	Asn
Gln 225	Gly	Gln	Trp	Gln	Pro 230	Asn	Gly	Asn	Gln	Gly 235	Asn	Ser	Gln	Asn	Pro 240
Thr	Gly	Asn	Asp	Phe 245	Val	Ser	Gln	Arg	Phe 250	Leu	Ala	Leu	Ala	Asn 255	Gly
Ala	Tyr	Lys	Tyr 260	Asn	Pro	Tyr	Ile	Leu 265	Asn	Gln	Ile	Asn	Lys 270	Leu	Gly
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ГЛа	Gln 290	Asn	Phe	Ser	Gly	Asn 295	Ala	Tyr	Leu	Asn	Gly 300	Leu	Gln	Gln	Gln
Ser 305	Asn	Tyr	Phe	Arg	Phe 310	Gln	Tyr	Phe	Asn	Pro 315	Leu	Lys	Ser	Glu	Arg 320
Tyr	Tyr	Arg	Asn	Leu 325	Asp	Glu	Gln	Val	Leu 330	Ala	Leu	Ile	Thr	Gly 335	Glu
Ile	Gly	Ser	Met 340	Pro	Asp	Leu	ГЛа	Lys 345	Pro	Glu	Asp	Lys	Pro 350	Asp	Ser
Lys	Gln	Arg 355	Ser	Phe	Glu	Pro	His 360	Glu	Lys	Asp	Asp	Phe 365	Thr	Val	Val
ГЛа	Lys 370	Gln	Glu	Asp	Asn	Lys 375	Гла	Ser	Ala	Ser	Thr 380	Ala	Tyr	Ser	Lys
Ser 385	Trp	Leu	Ala	Ile	Val 390	Суз	Ser	Met	Met	Val 395	Val	Phe	Ser	Ile	Met 400
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Gln	Arg	Arg													

Gln Arg Arg

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Val	Ala	Gly	Asn 20	Ala	Gly	His	Glu	Ala 25	His	Ala	Ser	Glu	Ala 30	Asp	Leu
Asn	Lys	Ala 35	Ser	Leu	Ala	Gln	Met 40	Ala	Gln	Ser	Asn	Asp 45	Gln	Thr	Leu
Asn	Gln 50	Lys	Pro	Ile	Glu	Ala 55	Gly	Ala	Tyr	Asn	Tyr 60	Thr	Phe	Asp	Tyr
Glu 65	Gly	Phe	Thr	Tyr	His 70	Phe	Glu	Ser	Asp	Gly 75	Thr	His	Phe	Ala	Trp 80
Asn	Tyr	His	Ala	Thr 85	Gly	Thr	Asn	Gly	Ala 90	Asp	Met	Ser	Ala	Gln 95	Ala
Pro	Ala	Thr	Asn 100	Asn	Val	Ala	Pro	Ser 105	Ala	Val	Gln	Ala	Asn 110	Gln	Val
Gln	Ser	Gln 115	Glu	Val	Glu	Ala	Pro 120	Gln	Asn	Ala	Gln	Thr 125	Gln	Gln	Pro
Gln	Ala 130	Ser	Thr	Ser	Asn	Asn 135	Ser	Gln	Val	Thr	Ala 140	Thr	Pro	Thr	Glu
Ser 145	Lys	Ser	Ser	Glu	Gly 150	Ser	Ser	Val	Asn	Val 155	Asn	Ala	His	Leu	Lys 160
Gln	Ile	Ala	Gln	Arg 165	Glu	Ser	Gly	Gly	Asn 170	Ile	His	Ala	Val	Asn 175	Pro
Thr	Ser	Gly	Ala 180	Ala	Gly	ГЛа	Tyr	Gln 185	Phe	Leu	Gln	Ser	Thr 190	Trp	Asp
Ser	Val	Ala 195	Pro	Ala	Lys	Tyr	Lys 200	Gly	Val	Ser	Pro	Ala 205	Asn	Ala	Pro
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1	-		-	5		-	-		10					Thr 15	
			20				-	25					30	Phe	
		35					40					45		Val	
Lys	Pro 50	Ile	Pro	Thr	Leu	Phe 55	Leu	His	Gly	Phe	Gly 60	Gly	Ser	Ala	Asn
Ser 65	Glu	Lys	Phe	Met	Val 70	Lys	Gln	Ala	Glu	Lys 75	Arg	Gly	Val	Thr	LYa 80
Asp	Ile	Ile	Thr	Ala 85	Tyr	Val	Ser	Lys	Asp 90	Gly	Ala	Val	Thr	Phe 95	Lys
	T	Leu	Ara	Lvs	Asp	Ala	Val	Asn	Pro	Ile	Val	Lvs	Ile	Glu	Leu

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			100					105					110		
Glu	Asn	Asn 115	Arg	Gln	Gly	Tyr	Leu 120	Asp	Lys	Asn	Ala	Ala 125	Trp	Phe	Lys
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Phe 145	Val	Gly	His	Ser	Met 150	Gly	Asn	Leu	Thr	Phe 155	Ala	Gln	Tyr	Met	Met 160
Thr	Tyr	Gly	Asn	Asp 165	Lys	Ser	Leu	Pro	Gln 170	Leu	Asn	Lys	Gln	Val 175	Asn
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Glu	Ile	Thr 195	Val	Asp	Lys	Asp	Gly 200	Lys	Pro	Ser	Arg	Met 205	Asn	Gln	Pro
Tyr	Gln 210	Gln	Leu	Arg	Val	Leu 215	Lys	Asp	Ile	Tyr	Lys 220	Gly	Lys	Gly	Ile
Glu 225	Val	Leu	Asn	Ile	Tyr 230	Gly	Asp	Leu	Lys	Asp 235	Gly	Thr	His	Ser	Asp 240
Gly	Arg	Val	Ser	Asn 245	Ser	Ser	Ser	ГЛа	Ser 250	Leu	ГЛа	Tyr	Leu	Leu 255	Gly
Asn	Ser	Pro	Lys 260	Ser	Tyr	Arg	Glu	Ser 265	Lys	Tyr	Glu	Gly	Glu 270	Pro	Ala
Gln	His	Ser 275	Gln	Leu	His	Glu	Asn 280	Glu	Asn	Val	Ala	Asn 285	Glu	Leu	Ile
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Asp	Lys	His 35	Gln	Ile	Ala	Val	Ala 40	Asp	Thr	Asn	Val	Gln 45	Thr	Pro	Asp
Tyr	Glu 50	Lys	Leu	Arg	Asn	Thr 55	Trp	Leu	Asp	Val	Asn 60	Tyr	Gly	Tyr	Asp
Lys 65	Tyr	Asp	Glu	Asn	Asn 70	Pro	Asp	Met	Lys	Lys 75	ГЛа	Phe	Asp	Ala	Thr 80
Glu	Lys	Glu	Ala	Thr 85	Asn	Leu	Leu	Lys	Glu 90	Met	Lys	Thr	Glu	Ser 95	Gly
Arg	Lys	Tyr	Leu 100	Trp	Ser	Gly	Ala	Glu 105	Thr	Leu	Glu	Thr	Asn 110	Ser	Ser
His	Met	Thr 115	Arg	Thr	Tyr	Arg	Asn 120	Ile	Glu	Lys	Ile	Ala 125	Glu	Ala	Met
Arg	Asn 130	Pro	Lys	Thr	Thr	Leu 135	Asn	Thr	Asp	Glu	Asn 140	Lys	Lys	Lys	Val
Lys 145	Asp	Ala	Leu	Glu	Trp 150	Leu	His	Lys	Asn	Ala 155	Tyr	Gly	Lys	Glu	Pro 160
Asp	Lys	Lys	Val	Lys 165	Glu	Leu	Ser	Glu	Asn 170	Phe	Thr	Lys	Thr	Thr 175	Gly

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Ser	Leu	Thr 195	Asn	Thr	Leu	Ile	Leu 200	Leu	Asn	Asp	Gln	Phe 205	Ser	Asn	Glu
Glu	Lys 210	Lys	Гла	Phe	Thr	Ala 215	Pro	Ile	Гла	Thr	Phe 220	Ala	Pro	Asp	Ser
Asp 225	Lys	Ile	Leu	Ser	Ser 230	Val	Gly	Lys	Ala	Glu 235	Leu	Ala	Lys	Gly	Gly 240
Asn	Leu	Val	Asp	Ile 245	Ser	Lys	Val	Lys	Leu 250	Leu	Glu	Суз	Ile	Ile 255	Glu
Glu	Asp	Lys	Asp 260	Met	Met	Гла	Lys	Ser 265	Ile	Asp	Ser	Phe	Asn 270	Lys	Val
Phe	Thr	Tyr 275	Val	Gln	Asp	Ser	Ala 280	Thr	Gly	Lys	Glu	Arg 285	Asn	Gly	Phe
Tyr	Lys 290	Asp	Gly	Ser	Tyr	Ile 295	Asp	His	Gln	Asp	Val 300	Pro	Tyr	Thr	Gly
Ala 305	Tyr	Gly	Val	Val	Leu 310	Leu	Glu	Gly	Ile	Ser 315	Gln	Met	Met	Pro	Met 320
Ile	Lys	Glu	Thr	Pro 325	Phe	Asn	Asp	Гла	Thr 330	Gln	Asn	Asp	Thr	Thr 335	Leu
Lys	Ser	Trp	Ile 340	Aap	Asp	Gly	Phe	Met 345	Pro	Leu	Ile	Tyr	Lys 350	Gly	Glu
Met	Met	Asp 355	Leu	Ser	Arg	Gly	Arg 360	Ala	Ile	Ser	Arg	Glu 365	Asn	Glu	Thr
Ser	His 370	Ser	Ala	Ser	Ala	Thr 375	Val	Met	Lys	Ser	Leu 380	Leu	Arg	Leu	Ser
Asp 385	Ala	Met	Asp	-	Ser 390	Thr	Lys	Ala	Lys	Tyr 395	Lys	Lys	Ile	Val	Lys 400
Ser	Ser	Val	Glu	Ser 405	Asp	Ser	Ser	Tyr	Lys 410	Gln	Asn	Asp	Tyr	Leu 415	Asn
Ser	Tyr	Ser	Asp 420	Ile	Asp	Гла	Met	Lys 425	Ser	Leu	Met	Thr	Asp 430	Asn	Ser
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Asp	Arg 450	Val	Thr	Tyr	His	Asn 455	Lys	Asp	Leu	Asp	Phe 460	Ala	Phe	Gly	Leu
Ser 465	Met	Thr	Ser	Lys	Asn 470	Val	Ala	Arg	Tyr	Glu 475	Ser	Ile	Asn	Gly	Glu 480
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Lys	Arg	Leu 515	Ser	Gly	Thr	Thr	Thr 520	Leu	Asp	Asn	Glu	Ile 525	Leu	Гла	Asp
Thr	Asp 530	Asp	Lys	Lys	Ser	Ser 535	Lys	Thr	Phe	Val	Gly 540	Gly	Thr	Lys	Val
Asp 545	Asp	Gln	His	Ala	Ser 550	Ile	Gly	Met	Asp	Phe 555	Glu	Asn	Gln	Asp	Lys 560
Thr	Leu	Thr	Ala	Lys 565	Гла	Ser	Tyr	Phe	Ile 570	Leu	Asn	Asp	Гла	Ile 575	Val
Phe	Leu	Gly			Ile	Гла	Ser			Ser	Ser	Lys			Val
Thr	Thr	Ile	580 Glu	Asn	Arg	Lys	Ala	585 Asn	Gly	Tyr	Thr	Leu	590 Tyr	Thr	Asp

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		595					600					605			
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Lys	Pro	Lys	Ile	Thr 645	Val	Lys	Lys	Glu	Ser 650	His	Thr	Gly	Гла	Trp 655	Гла
Glu	Ile	Asn	Lys 660	Ser	Gln	Lys	Asp	Thr 665	Gln	Lys	Thr	Asp	Glu 670	Tyr	Tyr
Glu	Val	Thr 675	Gln	Lys	His	Ser	Asn 680	Ser	Asp	Asn	Lys	Tyr 685	Gly	Tyr	Val
Leu	Tyr 690	Pro	Gly	Leu	Ser	Lys 695	Asp	Val	Phe	Lys	Thr 700	ГЛа	ГЛЗ	Asp	Glu
Val 705	Thr	Val	Val	ГЛа	Gln 710	Glu	Asp	Asp	Phe	His 715	Val	Val	Lys	Asp	Asn 720
Glu	Ser	Val	Trp	Ala 725	Gly	Val	Asn	Tyr	Ser 730	Asn	Ser	Thr	Gln	Thr 735	Phe
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Leu	Lys	Lys 755	Lys	Aap	Asp	Asn	Thr 760	Tyr	Glu	Cys	Ser	Phe 765	Tyr	Asn	Pro
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Gly 785	Tyr	Ser	Ile	Thr	Asn 790	Lys	Asn	Thr	Ser	Thr 795	Ser	Asn	Glu	Ser	Gly 800
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Asn	Tyr	Asn 35	Asn	Tyr	Asn	Tyr	Asn 40	Thr	Thr	Gln	Thr	Thr 45	Thr	Thr	Thr
Thr	Thr 50	Thr	Thr	Thr	Thr	Ser 55	Ser	Ile	Ser	His	Ser 60	Gly	Asn	Leu	Tyr
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Ile	Gly	Ser	Thr	Trp 85	Gly	Asn	Ala	Asn	Asn 90	Trp	Ala	Ala	Ala	Ala 95	Gln
Gly	Ala	Gly	Phe 100	Thr	Val	Asn	His	Thr 105	Pro	Ser	Lys	Gly	Ala 110	Ile	Leu
Gln	Ser	Ser 115	Glu	Gly	Pro	Phe	Gly 120	His	Val	Ala	Tyr	Val 125	Glu	Ser	Val
Asn	Ser 130	Asp	Gly	Ser	Val	Thr 135	Ile	Ser	Glu	Met	Asn 140	Tyr	Ser	Gly	Gly
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Tyr Asn Tyr Ile His Ile 165

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Val Thr Ile Lys 35		Tyr Pro Leu 40	Gln Ser Phe 45	Ala Glu Gln
Ile Gly Gly Lys 50	His Val Lys 55	Val Ser Ser	Ile Tyr Pro 60	Ala Gly Thr
Asp Leu His Ser 65	Tyr Glu Pro 70	Thr Gln Lys	Asp Ile Leu 75	Ser Ala Ser 80
Lys Ser Asp Leu	Phe Met Tyr 85	Thr Gly Asp 90	Asn Leu Asp	Pro Val Ala 95
Lys Lys Val Ala 100		Lys Asp Lys 105	Asp Lys Lys	Leu Ser Leu 110
Glu Asp Lys Leu 115		Lys Leu Leu 120	Thr Asp Gln 125	His Glu His
Gly Glu Glu His 130	Glu His Glu 135	Gly His Asp	His Glu Lys 140	Glu Glu His
His His His His 145	Gly Gly Tyr . 150	Asp Pro His	Val Trp Leu 155	Asp Pro Lys 160
Ile Asn Gln Thr	Phe Ala Lys 165	Glu Ile Lys 170	Asp Glu Leu	Val Lys Lys 175
Asp Pro Lys His 180		Tyr Glu Lys 185	Asn Tyr Lys	Lys Leu Asn 190
Asp Asp Leu Lys 195		Asn Asp Met 200	Lys Gln Val 205	Thr Lys Asp
Lys Gln Gly Asn 210	Ala Val Phe 215	Ile Ser His	Glu Ser Ile 220	Gly Tyr Leu
Ala Asp Cys Tyr 225	Gly Phe Val 230	Gln Lys Gly	Ile Gln Asn 235	Met Asn Ala 240
Glu Asp Pro Ser	Gln Lys Glu 245	Leu Thr Lys 250	Ile Val Lys	Glu Ile Arg 255
Asp Ser Asn Ala 260		Leu Tyr Glu 265	Asp Asn Val	Ala Asn Lys 270
Val Thr Glu Thr 275		Glu Thr Asp 280	Ala Lys Pro 285	Leu Lys Phe
Tyr Asn Met Glu 290	Ser Leu Asn 295	Lys Glu Gln	Gln Lys Lys 300	Asp Asn Ile
Thr Tyr Gln Ser 305	Leu Met Lys 310	Ser Asn Ile	Glu Asn Ile 315	Gly Lys Ala 320
Leu Asp Ser Gly	Val Lys Val 325	Lya Asp Asp 330	Lys Ala Glu	Ser Lys His 335
Asp Lys Ala Ile 340		Tyr Phe Lys 345	Asp Glu Gln	Val Lys Asp 350
Arg Glu Leu Ser 355		Gly Glu Trp 360	Gln Ser Val 365	Tyr Pro Tyr

Leu	Lys 370	Asp	Gly	Thr	Leu	Asp 375	Glu	Val	Met	Glu	His 380	Гла	Ala	Glu	Asn
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Tyr	Lys	Thr	Asp	Ile 405	Thr	Asn	Ile	Asp	Ile 410	Lys	Gly	Asn	Glu	Ile 415	Thr
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ГЛа	Lys	Thr 435	Leu	ГЛа	Tyr	Pro	Lys 440	Gly	Asn	Arg	Gly	Val 445	Arg	Phe	Met
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Phe 465	Ser	Asp	His	Asn	Ile 470	Ala	Pro	Lys	Lys	Ala 475	Glu	His	Phe	His	Ile 480
Phe	Met	Gly	Asn	Asp 485	Asn	Asp	Ala	Leu	Leu 490	Lys	Glu	Met	Asp	Asn 495	Trp
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Ala	Pro	Leu	Ala 20	Asn	Pro	Phe	Ile	Glu 25	Ile	Ser	Гла	Ala	Glu 30	Asn	Гуз
Ile	Glu	Asp 35	Ile	Gly	Gln	Gly	Ala 40	Glu	Ile	Ile	Lys	Arg 45	Thr	Gln	Asp
Ile	Thr 50	Ser	ГЛа	Arg	Leu	Ala 55	Ile	Thr	Gln	Asn	Ile 60	Gln	Phe	Asp	Phe
Val 65	Lys	Asp	ГЛа	ГЛа	Tyr 70	Asn	Lys	Asp	Ala	Leu 75	Val	Val	ГЛа	Met	Gln 80
Gly	Phe	Ile	Ser	Ser 85	Arg	Thr	Thr	Tyr	Ser 90	Asp	Leu	Lys	Lys	Tyr 95	Pro
Tyr	Ile	Lys	Arg 100	Met	Ile	Trp	Pro	Phe 105	Gln	Tyr	Asn	Ile	Ser 110	Leu	Lys
Thr	Lys	Asp 115	Ser	Asn	Val	Asp	Leu 120	Ile	Asn	Tyr	Leu	Pro 125	Lys	Asn	Гла
Ile	Asp 130	Ser	Ala	Asp	Val	Ser 135	Gln	Lys	Leu	Gly	Tyr 140	Asn	Ile	Gly	Gly
Asn 145	Phe	Gln	Ser	Ala	Pro 150	Ser	Ile	Gly	Gly	Ser 155	Gly	Ser	Phe	Asn	Tyr 160
Ser		The	T 7 -	Cor	Tvr	Asn	Gln	Lys	Asn	Tyr	Val	Thr	Glu	Val	Glu
	Lys	1111	IIe	165	- 1 -				170					175	
Ser	Lys Gln			165	-		Гла	Trp 185		Val	Lys	Ala	Asn 190		Phe
	-	Asn	Ser 180	165 Lys	Gly	Val	-	185	Gly		-		190	Ser	

Gln Asp Pro Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn

210215220Gln 225Leu 230Ile 230Gln SerGly 235Phe 235Asn 235Pro SerPhe Ser PheIle 235Thr ThrLeu Ser 245Glu 245Arg SerGly Ser SerLeu Ser Ser SerPhe Ser Ser SerPhe Ser Ser Ser SerPhe Ser 	240
225 230 235 Thr Leu Ser His Glu Arg Gly Lys Gly Asp Lys Ser Glu Phe Glu 245 250 Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg	240
245 250 255 Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg	Ile
	His
Arg Leu Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn275280285	Val
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Pro His Val Tyr Gly Gly Ser Met Ser Ala Glu Ser Met Ile Tyr 50 55 60	Glu
Pro Leu Val Arg Asn Thr Lys Asp Gly Ile Lys Pro Leu Leu Ala 65 70 75	Lys 80
Lys Trp Asp Val Ser Glu Asp Gly Lys Thr Tyr Thr Phe His Leu 85 90 95	Arg
Asp Asp Val Lys Phe His Asp Gly Thr Pro Phe Asp Ala Asp Ala 100 105 110	Val
Lys Lys Asn Ile Asp Ala Val Gln Glu Asn Lys Lys Leu His Ser 115 120 125	Trp
Leu Lys Ile Ser Thr Leu Ile Asp Asn Val Lys Val Lys Asp Lys 130 135 140	Tyr
Thr Val Glu Leu Asn Leu Lys Glu Ala Tyr Gln Pro Ala Leu Ala 145 150 155	Glu 160
Leu Ala Met Pro Arg Pro Tyr Val Phe Val Ser Pro Lys Asp Phe 165 170 175	Lys
Asn Gly Thr Thr Lys Asp Gly Val Lys Lys Phe Asp Gly Thr Gly 180 185 190	Pro
Phe Lys Leu Gly Glu His Lys Lys Asp Glu Ser Ala Asp Phe Asn 195 200 205	LYa
Asn Asp Gln Tyr Trp Gly Glu Lys Ser Lys Leu Asn Lys Val Gln 210 215 220	Ala
Lys Val Met Pro Ala Gly Glu Thr Ala Phe Leu Ser Met Lys Lys 225 230 235	Gly 240
Glu Thr Asn Phe Ala Phe Thr Asp Asp Arg Gly Thr Asp Ser Leu 245 250 255	Aap
Lys Asp Ser Leu Lys Gln Leu Lys Asp Thr Gly Asp Tyr Gln Val 260 265 270	Lys

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Lys	Asp 290	Asn	Ala	Val	Ser	Asp 295	Гла	Thr	Val	Arg	Gln 300	Ala	Ile	Gly	His
Met 305	Val	Asn	Arg	Asp	Lys 310	Ile	Ala	Lys	Glu	Ile 315	Leu	Asp	Gly	Gln	Glu 320
Lys	Pro	Ala	Thr	Gln 325	Leu	Phe	Ala	Lys	Asn 330	Val	Thr	Asp	Ile	Asn 335	Phe
Asp	Met	Pro	Thr 340	Arg	Lys	Tyr	Asp	Leu 345	Lys	Lys	Ala	Glu	Ser 350	Leu	Leu
Asp	Glu	Ala 355	Gly	Trp	Lys	Lys	Gly 360	Lys	Asp	Ser	Asp	Val 365	Arg	Gln	Lys
Asp	Gly 370	Lys	Asn	Leu	Glu	Met 375	Ala	Met	Tyr	Tyr	Asp 380	Lys	Gly	Ser	Ser
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Arg	Arg	Thr	Ser 420	Gly	Asp	Tyr	Asp	Leu 425	Met	Phe	Asn	Gln	Thr 430	Trp	Gly
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Gly	Tyr 450	Glu	Ser	Ala	Thr	Ser 455	Gly	Ile	Glu	Asn	Lys 460	Asp	Lys	Ile	Tyr
Asn 465	Ser	Ile	Asp	Asp	Ala 470	Phe	Lys	Ile	Gln	Asn 475	Gly	Lys	Glu	Arg	Ser 480
Asp	Ala	Tyr	Lys	Asn 485	Ile	Leu	Lys	Gln	Ile 490	Asp	Asp	Glu	Gly	Ile 495	Phe
Ile	Pro	Ile	Ser 500	His	Gly	Ser	Met	Thr 505	Val	Val	Ala	Pro	Lys 510	Asp	Leu
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Asn	Ala	Gln 35	Ile	Lys	Asp	Thr	Phe 40	Asn	Gln	Thr	Leu	Lys 45	Leu	Tyr	Pro
Thr	Lys 50	Asn	Leu	Asp	Asp	Phe 55	Tyr	Asp	Lys	Glu	Gly 60	Phe	Arg	Asp	Gln
Glu 65	Phe	Lys	Lys	Gly	Asp 70	Lys	Gly	Thr	Trp	Ile 75	Val	Asn	Ser	Glu	Met 80
Val	Ile	Glu	Pro	Lys 85	Gly	Lys	Asp	Met	Glu 90	Thr	Arg	Gly	Met	Val 95	Leu
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Pro 145	Asn	Asp	Lys	Leu	Lys 150	Lys	Glu	Ile	Glu	Asn 155	Phe	Lys	Phe	Phe	Val 160
Gln	Tyr	Gly	Asn	Phe 165	Lys	Asp	Ile	Asn	Asp 170	Tyr	Lys	Asp	Gly	Asp 175	Ile
Ser	Tyr	Asn	Pro 180	Asn	Val	Pro	Ser	Tyr 185	Ser	Ala	Lys	Tyr	Gln 190	Leu	Asn
Asn	Aab	Asp 195	Tyr	Asn	Val	Gln	Gln 200	Leu	Arg	Lys	Arg	Tyr 205	Asp	Ile	Pro
Thr	Lys 210	Gln	Ala	Pro	Lys	Leu 215	Leu	Leu	Lys	Gly	Asp 220	Gly	Asp	Leu	Lys
Gly 225	Ser	Ser	Val	Gly	Ser 230	Arg	Ser	Leu	Glu	Phe 235	Thr	Phe	Val	Glu	Asn 240
ГÀа	Glu	Glu	Asn	Ile 245	Tyr	Phe	Thr	Asp	Ser 250	Val	Gln	Tyr	Thr	Pro 255	Ser
Glu	Asp	Thr	Arg 260	Tyr	Glu	Ser	Asn								
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	Ala Lys 50	35		-			40		-			45		-	
Thr	Lys	35 Asn	Leu	Asp	Asp	Phe 55	40 Tyr	Asp	Lys	Glu	Gly 60	45 Phe	Arg	Asp	Gln
Thr Glu 65	Lys 50	35 Asn Asp	Leu Lys	Asp Arg	Asp Asp 70	Phe 55 Lys	40 Tyr Gly	Asp Thr	Lys Trp	Glu Ile 75	Gly 60 Ile	45 Phe Tyr	Arg Ser	- Asp Glu	Gln Met 80
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Thr Glu 65 Val Tyr Glu	Lys 50 Phe Ile Ile	35 Asn Asp Glu Asn Thr 115	Leu Lys Pro Arg 100 Glu	Asp Arg Lys 85 Asn Asp	Asp 70 Gly Thr Ser	Phe 55 Lys Lys Arg Lys	40 Tyr Gly Asn Thr Gly 120	Asp Thr Met Thr 105 Tyr	Lys Trp Glu 90 Lys Ser	Glu 11e 75 Ser Gly Arg	Gly 60 Ile Arg Asn Ser	45 Phe Tyr Gly Phe Lys 125	Arg Ser Met Ile 110 Glu	Asp Glu Val 95 Val Lys	Gln Met 80 Leu Thr Lys
Thr Glu 65 Val Tyr Glu Tyr	Lys 50 Phe Ile Ile Ile Pro	35 Asn Asp Glu Asn Thr 115 Val	Leu Lys Pro Arg 100 Glu Lys	Asp Arg Lys 85 Asn Asp Met	Asp 70 Gly Thr Ser Glu	Phe 55 Lys Lys Arg Lys Lys Asn 135	40 Tyr Gly Asn Thr Gly 120 Asn	Asp Thr Met Thr 105 Tyr Arg	Lys Trp Glu 90 Lys Ser Ile	Glu Ile 75 Ser Gly Arg Ile	Gly 60 Ile Arg Asn Ser Pro 140	45 Phe Tyr Gly Phe Lys 125 Thr	Arg Ser Met Ile Il0 Glu Lys	Asp Glu Val 95 Val Lys Pro	Gln Met 80 Leu Thr Lys Ile
Thr Glu 65 Val Tyr Glu Tyr Pro 145	Lys 50 Phe Ile Ile Ile Pro 130	35 Asn Asp Glu Asn Thr 115 Val Asp	Leu Lys Pro Arg 100 Glu Lys Lys	Asp Arg Lys 85 Asn Asp Met Leu	Asp 70 Gly Thr Ser Glu Lys 150	Phe 55 Lys Lys Arg Lys Asn 135 Lys	40 Tyr Gly Asn Thr Gly 120 Asn Glu	Asp Thr Met Thr 105 Tyr Arg Ile	Lys Trp Glu 90 Lys Ser Ile Glu	Glu Ile 75 Ser Gly Arg Ile Asn 155	Gly 60 Ile Arg Asn Ser Pro 140 Phe	45 Phe Tyr Gly Phe Lys 125 Thr Lys	Arg Ser Met 110 Glu Lys Phe	Asp Glu Val 25 Val Lys Pro Phe	Gln Met 80 Leu Thr Lys Ile Val 160
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Thr Glu 65 Val Tyr Glu Tyr Pro 145 Gln Ser	Lys 50 Phe Ile Ile Pro 130 Asp Tyr	35 Asn Asp Glu Asn Thr 115 Val Asp Gly Asn	Leu Lys Pro Arg 100 Glu Lys Lys Asn Pro 180	Asp Arg Lys 85 Asn Asp Met Leu Phe 165 Asn	Asp 70 Gly Thr Ser Glu Lys Lys Lys Val	Phe 55 Lys Lys Arg Lys Asn 135 Lys Asp Pro	40 Tyr Gly Asn Thr Gly 120 Asn Glu Phe Ser	Asp Thr Met Thr 105 Tyr Arg Ile Lys Tyr 185	Lys Trp Glu 90 Lys Ser Ile Glu Asp 170 Ser	Glu Ile 75 Ser Gly Arg Ile Asn 155 Tyr Ala	Gly 60 Ile Arg Asn Ser Pro 140 Phe Lys Lys	45 Phe Gly Phe Lys Thr Lys Asn Tyr	Arg Ser Met Ile Ilo Glu Lys Phe Gly Gln 190	Asp Glu Val 95 Val Lys Pro Phe Asp 175 Leu	Gln Met 80 Leu Thr Lys Ile Val 160 Ile Asn

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Thr Gln Ly 3	-	Asp	Ala	Val	Lys 40	Ala	Leu	Lys	Glu	Leu 45	Pro	Lys	Ser
Glu Asn V 50	al Lys	Asn	Ile	Tyr 55	Gln	Asp	Tyr	Ala	Val 60	Thr	Asp	Val	Lys
Thr Asp L 65	үа Гуа	Gly	Phe 70	Thr	His	Tyr	Thr	Leu 75	Gln	Pro	Ser	Val	Asp 80
Gly Val H	is Ala	Pro 85	Asp	Lys	Glu	Val	Lys 90	Val	His	Ala	Asp	Lys 95	Ser
Gly Lys V	al Val 100	Leu	Ile	Asn	Gly	Asp 105	Thr	Asp	Ala	Lys	Lys 110	Val	Lys
Pro Thr A 1	sn Lys 15	Val	Thr	Leu	Ser 120	Lys	Asp	Asp	Ala	Ala 125	Asp	Lys	Ala
Phe Lys A 130	la Val	Lys	Ile	Asp 135	Lys	Asn	Lys	Ala	Lys 140	Asn	Leu	Lys	Asp
Lys Val I 145	le Lys	Glu	Asn 150	Lys	Val	Glu	Ile	Asp 155	Gly	Asp	Ser	Asn	Lys 160
Tyr Val T	yr Asn	Val 165	Glu	Leu	Ile	Thr	Val 170	Thr	Pro	Glu	Ile	Ser 175	His
Trp Lys V	al Lys 180	Ile	Asp	Ala	Gln	Thr 185	Gly	Glu	Ile	Leu	Glu 190	ГЛЗ	Met
Asn Leu V 1	al Lys 95	Glu	Ala	Ala	Glu 200	Thr	Gly	ГЛа	Gly	Lys 205	Gly	Val	Leu
Gly Asp T 210	nr Lys	Asp	Ile	Asn 215	Ile	Asn	Ser	Ile	Asp 220	Gly	Gly	Phe	Ser
Leu Glu A 225	sp Leu	Thr	His 230	Gln	Gly	Lys	Leu	Ser 235	Ala	Phe	Ser	Phe	Asn 240
Asp Gln T	nr Gly	Gln 245	Ala	Thr	Leu	Ile	Thr 250	Asn	Glu	Asp	Glu	Asn 255	Phe
Val Lys A	ap Glu 260	Gln	Arg	Ala	Gly	Val 265	Asp	Ala	Asn	Tyr	Tyr 270	Ala	Lys
Gln Thr T 2	yr Asp 75	Tyr	Tyr	Lys	Asp 280	Thr	Phe	Gly	Arg	Glu 285	Ser	Tyr	Asp
Asn Gln G 290	ly Ser	Pro	Ile	Val 295	Ser	Leu	Thr	His	Val 300	Asn	Asn	Tyr	Gly
Gly Gln A 305	sp Asn	Arg	Asn 310	Asn	Ala	Ala	Trp	Ile 315	Gly	Asp	Lys	Met	Ile 320

Tyr															
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Asp	Val	Val	Ala 340	His	Glu	Leu	Thr	His 345	Gly	Val	Thr	Gln	Glu 350	Thr	Ala
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Gln	Ile 450	Tyr	Tyr	Arg	Ala	Leu 455	Thr	Glu	Tyr	Leu	Thr 460	Ser	Asn	Ser	Asn
Phe 465	Lys	Asp	Суз	ГЛа	Asp 470	Ala	Leu	Tyr	Gln	Ala 475	Ala	Lys	Asp	Leu	Tyr 480
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												COII		ucu	
Glu	Ile	Val 195	Asn	Glu	Thr	Glu	Ile 200	Glu	Lys	Val	Gln	Pro 205	Gln	Gln	Asn
Asn	Gln 210	Ala	Asn	Asp	Гла	Ile 215	Thr	Asn	Tyr	Asn	Phe 220	Asn	Asn	Glu	Gln
Glu 225	Val	Lys	Pro	Gln	Lys 230	Asp	Glu	Lys	Thr	Leu 235	Ser	Val	Ser	Asp	Leu 240
Lys	Asn	Asn	Gln	Lys 245	Ser	Pro	Val	Glu	Pro 250	Thr	Гла	Asp	Asn	Asp 255	Lys
Lys	Asn	Gly	Leu 260	Asn	Leu	Leu	Lys	Ser 265	Ser	Ala	Val	Ala	Thr 270	Leu	Pro
Asn	Lys	Gly 275	Thr	Lys	Glu	Leu	Thr 280	Ala	Lys	Ala	Lys	Asp 285	Asp	Gln	Thr
Asn	Lys 290	Val	Ala	Lys	Gln	Gly 295	Gln	Tyr	Lys	Asn	Gln 300	Asp	Pro	Ile	Val
Leu 305	Val	His	Gly	Phe	Asn 310	Gly	Phe	Thr	Asp	Asp 315	Ile	Asn	Pro	Ser	Val 320
Leu	Ala	His	Tyr	Trp 325	Gly	Gly	Asn	ГЛа	Met 330	Asn	Ile	Arg	Gln	Asp 335	Leu
Glu	Glu	Asn	Gly 340	Tyr	Lys	Ala	Tyr	Glu 345	Ala	Ser	Ile	Ser	Ala 350	Phe	Gly
Ser	Asn	Tyr 355	Asp	Arg	Ala	Val	Glu 360	Leu	Tyr	Tyr	Tyr	Ile 365	Lys	Gly	Gly
Arg	Val 370	Asp	Tyr	Gly	Ala	Ala 375	His	Ala	Ala	Lys	Tyr 380	Gly	His	Glu	Arg
Tyr 385	Gly	Lys	Thr	Tyr	Glu 390	Gly	Ile	Tyr	Lys	Asp 395	Trp	Гла	Pro	Gly	Gln 400
ГЛа	Val	His	Leu	Val 405	Gly	His	Ser	Met	Gly 410	Gly	Gln	Thr	Ile	Arg 415	Gln
Leu	Glu	Glu	Leu 420	Leu	Arg	Asn	Gly	Asn 425	Arg	Glu	Glu	Ile	Glu 430	Tyr	Gln
Lys	Lys	His 435	Gly	Gly	Glu	Ile	Ser 440	Pro	Leu	Phe	ГЛЗ	Gly 445	Asn	His	Asp
Asn	Met 450	Ile	Ser	Ser	Ile	Thr 455	Thr	Leu	Gly	Thr	Pro 460	His	Asn	Gly	Thr
His 465	Ala	Ser	Asp	Leu	Ala 470	Gly	Asn	Glu	Ala	Leu 475	Val	Arg	Gln	Ile	Val 480
Phe	Asp	Ile	Gly	Lys 485	Met	Phe	Gly	Asn	Lys 490	Asn	Ser	Arg	Val	Asp 495	Phe
Gly	Leu	Ala	Gln 500	Trp	Gly	Leu	Lys	Gln 505	Lys	Pro	Asn	Glu	Ser 510	Tyr	Ile
Asp	Tyr	Val 515	Lys	Arg	Val	ГЛа	Gln 520	Ser	Asn	Leu	Trp	Lys 525	Ser	ГЛа	Asp
Asn	Gly 530	Phe	Tyr	Aap	Leu	Thr 535	Arg	Glu	Gly	Ala	Thr 540	Asp	Leu	Asn	Arg
Lys 545	Thr	Ser	Leu	Asn	Pro 550	Asn	Ile	Val	Tyr	Lys 555	Thr	Tyr	Thr	Gly	Glu 560
Ala	Thr	His	Lys	Ala 565	Leu	Asn	Ser	Asp	Arg 570	Gln	Lys	Ala	Asp	Leu 575	Asn
Met	Phe	Phe	Pro 580	Phe	Val	Ile	Thr	Gly 585	Asn	Leu	Ile	Gly	Lys 590	Ala	Thr
Glu	Lys	Glu 595	Trp	Arg	Glu	Asn	Asp 600	Gly	Leu	Val	Ser	Val 605	Ile	Ser	Ser
Gln	His	Pro	Phe	Asn	Gln	Ala	Tyr	Thr	Lys	Ala	Thr	Asp	Lys	Ile	Gln

-continued Lys Gly Ile Trp Gln Val Thr Pro Thr Lys His Asp Trp Asp His Val Asp Phe Val Gly Gln Asp Ser Ser Asp Thr Val Arg Thr Arg Glu Glu Leu Gln Asp Phe Trp His His Leu Ala Asp Asp Leu Val Lys Thr Glu

Lys Leu Thr Asp Thr Lys Gln Ala

<210> SEQ ID NO 99 <211> LENGTH: 328 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 99 Met Lys Lys Cys Ile Lys Thr Leu Phe Leu Ser Ile Ile Leu Val Val Met Ser Gly Trp Tyr His Ser Ala His Ala Ser Asp Ser Leu Ser Lys Ser Pro Glu Asn Trp Met Ser Lys Leu Asp Asp Gly Lys His Leu Thr Glu Ile Asn Ile Pro Gly Ser His Asp Ser Gly Ser Phe Thr Leu Lys Asp Pro Val Lys Ser Val Trp Ala Lys Thr Gln Asp Lys Asp Tyr Leu Thr Gln Met Lys Ser Gly Val Arg Phe Phe Asp Ile Arg Gly Arg Ala Ser Ala Asp Asn Met Ile Ser Val His His Gly Met Val Tyr Leu His His Glu Leu Gly Lys Phe Leu Asp Asp Ala Lys Tyr Tyr Leu Ser Ala Tyr Pro Asn Glu Thr Ile Val Met Ser Met Lys Lys Asp Tyr Asp Ser Asp Ser Lys Val Thr Lys Thr Phe Glu Glu Ile Phe Arg Glu Tyr Tyr Tyr Asn Asn Pro Gln Tyr Gln Asn Leu Phe Tyr Thr Gly Ser Asn Ala Asn Pro Thr Leu Lys Glu Thr Lys Gly Lys Ile Val Leu Phe Asn Arg Met Gly Gly Thr Tyr Ile Lys Ser Gly Tyr Gly Ala Asp Thr Ser Gly Ile Gln Trp Ala Asp Asn Ala Thr Phe Glu Thr Lys Ile Asn Asn Gly Ser Leu Asn Leu Lys Val Gln Asp Glu Tyr Lys Asp Tyr Tyr Asp Lys Lys Val Glu Ala Val Lys Asn Leu Leu Ala Lys Ala Lys Thr Asp Ser Asn Lys Asp Asn Val Tyr Val Asn Phe Leu Ser Val Ala Ser Gly Gly Ser Ala Phe Asn Ser Thr Tyr Asn Tyr Ala Ser His Ile Asn Pro Glu Ile Ala Lys Thr Leu Lys Ala As
n Gly Lys Ala Arg Thr Gly Tr
p Leu

Ile 305	Val	Asp	Tyr	Ala	Gly 310	Tyr	Thr	Trp	Pro	Gly 315	Tyr	Asp	Asp	Ile	Val 320
Ser	Glu	Ile	Ile	Asp 325	Ser	Asn	Lys								
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		YPE : RGAN		Staj	phyl	2000	cus a	aure	រទ						
< 400)> SI	EQUEI	NCE :	100											
Met 1	Lys	Ala	His	Lys 5	Ile	Phe	Trp	Leu	Asn 10	Leu	Ala	Ala	Ile	Ile 15	Ile
Ile	Ser	Ile	Val 20	Val	Ser	Gly	Asp	Met 25	Phe	Leu	Ala	Met	Lys 30	Trp	Glu
Gln	Ile	His 35	Leu	Lys	Asp	Gly	Leu 40	Lys	Lys	Val	Leu	Ser 45	Thr	Tyr	Pro
Ile	Lys 50	Asn	Leu	Glu	Thr	Leu 55	Tyr	Glu	Ile	Asp	Gly 60	His	Asp	Asn	Pro
His 65	Tyr	Glu	Asn	Asn	Asp 70	Gln	Asp	Thr	Trp	Tyr 75	Ile	Glu	Ser	Ser	Tyr 80
Ser	Val	Val	Gly	Ser 85	Asp	Glu	Leu	Leu	Lys 90	Glu	Aap	Arg	Met	Leu 95	Leu
Lys	Val	Asp	Lys 100	Asn	Thr	His	Lys	Ile 105	Thr	Gly	Glu	Tyr	Asp 110	Thr	Thr
Thr	Asn	Asp 115	Arg	Гла	Asn	Ala	Thr 120	Asp	Ser	Thr	Tyr	Lys 125	Ser	Tyr	Pro
Val	Lys 130	Val	Val	Asn	Asn	Lys 135	Ile	Val	Phe	Thr	Lys 140	Asp	Val	Lys	Asp
Pro 145	Ala	Leu	Lys	Gln	Lys 150	Ile	Glu	Asn	Asn	Gln 155	Phe	Leu	Ile	Gln	Ser 160
Gly	Asp	Leu	Thr	Ser 165	Ile	Leu	Asn	Ser	Asn 170	Asp	Leu	Lys	Val	Thr 175	His
Asp	Pro	Thr	Thr 180	Asp	Tyr	Tyr	Asn	Leu 185	Ser	Gly	Гла	Leu	Ser 190	Asn	Asp
Asn	Pro	Asn 195	Val	Lys	Gln	Leu	Lys 200	Arg	Arg	Tyr	Asn	Ile 205	Pro	Lys	Asn
Ala	Ser 210	Thr	Lys	Val	Glu	Leu 215	Lys	Gly	Met	Ser	Asp 220	Leu	Lys	Gly	Asn
Asn 225	His	Gln	Asp	Gln	Lys 230	Leu	Tyr	Phe	Tyr	Phe 235	Ser	Ser	Pro	Gly	Lys 240
	Gln	Ile	Ile	Tyr 245	Lys	Glu	Ser	Leu	Thr 250	Tyr	Asn	Lys	Ile	Ser 255	
His				·											
<210)> SI	EQ II	оис	101											
<212	2> T?	ENGTI YPE : RGAN	PRT		phv14	ococ	cus	aure	15						
		EQUEI			су.т.,			- 	~~						
					Terr	0	т1-	ጣኒ	T	ה ק -	T 7 - 7	17 - 7	M - +	T	T
1		-		5	-	СЛа			10					15	
Ile	Val	Thr	Ala 20	СЛа	Gly	Pro	Asn	Arg 25	Ser	LÀa	Glu	Asp	Ile 30	Asp	Lys
Ala	Leu	Asn	Lys	Asp	Asn	Ser	Гла	Asp	Lys	Pro	Asn	Gln	Leu	Thr	Met

												con	τın	uea	
		35					40					45			
Trp	Val 50	Asp	Gly	Asp	Гла	Gln 55	Met	Ala	Phe	Tyr	Lys 60	Lys	Ile	Thr	Asp
Gln 65	Tyr	Thr	Lys	Lys	Thr 70	Gly	Ile	Lys	Val	Lys 75	Leu	Val	Asn	Ile	Gly 80
Gln	Asn	Asp	Gln	Leu 85	Glu	Asn	Ile	Ser	Leu 90	Asp	Ala	Pro	Ala	Gly 95	Lys
Gly	Pro	Asp	Ile 100	Phe	Phe	Leu	Ala	His 105	Asp	Asn	Thr	Gly	Ser 110	Ala	Tyr
Leu	Gln	Gly 115	Leu	Ala	Ala	Glu	Ile 120	Lys	Leu	Ser	Lys	Asp 125	Glu	Leu	ГЛа
Gly	Phe 130	Asn	Lys	Gln	Ala	Leu 135	ГÀа	Ala	Met	Asn	Tyr 140	Asp	Asn	ГÀа	Gln
Leu 145	Ala	Leu	Pro	Ala	Ile 150	Val	Glu	Thr	Thr	Ala 155	Leu	Phe	Tyr	Asn	Lys 160
ГЛа	Leu	Val	Lys	Asn 165	Ala	Pro	Gln	Thr	Leu 170	Glu	Glu	Val	Glu	Ala 175	Asn
		-	180		-		Lys	185	-		-	-	190		
-		195			-		Asn 200	-				205	-		-
-	210			-	-	215	Gly			-	220				
225				-	230		Val	-		235		-			240
-	-	-	-	245	-		Pro	-	250					255	
	-		260	-		-	Lys	265	-				270	-	
-		275			-		Glu 280			-	-	285		-	
	290				-	295	Gly	-			300				-
305					310		Glu			315					320
-	-			325	-		Thr		330	-				335	-
	_		340				Thr	345	-		_		350		
		355		-			Glu 360	-			-	365			
Met	Pro 370	Asn	Ile	Pro	Glu	Met 375	Arg	Gln	Val	Trp	Glu 380	Pro	Met	Gly	Asn
Ala 385	Ser	Ile	Phe	Ile	Ser 390	Asn	Gly	ГÀа	Asn	Pro 395	Γλa	Gln	Ala	Leu	Asp 400
Glu	Ala	Thr	Asn	Asp 405	Ile	Thr	Gln	Asn	Ile 410	Lys	Ile	Leu	His	Pro 415	Ser
Gln	Asn	Asp	Lys 420	Lys	Gly	Asp									

<210> SEQ ID NO 102 <211> LENGTH: 560 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus

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Gln A	Ala	Ala	Glu 20	Gln	Gln	Ser	Ile	Ser 25	Asp	Val	Tyr	Ser	Val 30	Ile	Thr
Asp A	Ala	Lys 35	Ser	Ala	Leu	Ser	Asn 40	Asn	Ser	Ile	Ser	Asn 45	Asp	Asn	Lys
Gln I 5	20 Dàr	Ala	Ile	Glu	Gln	Val 55	Val	Ser	Ala	Val	Lys 60	Lys	Leu	Ser	Leu
Glu A 65	/ab	Asn	Ser	Glu	Ser 70	Asn	Ala	Val	Lys	Ser 75	Asp	Val	Arg	Lys	Leu 80
Glu A	/ab	Ala	Lys	Ala 85	Asn	Asp	Asn	Gln	Lys 90	Asp	Thr	Leu	Ser	Gln 95	Leu
Thr L	yya	Ser	Leu 100	Ile	Ala	Tyr	Glu	Glu 105	Lys	Leu	Ala	Ser	Lys 110	Asp	Ala
Gly S	Ser	Lys 115	Ile	Lys	Leu	Leu	Gln 120	Gln	Gln	Val	Aap	Ala 125	Lys	Asp	Ala
Ala M 1	let L30	Thr	Lys	Ala	Ile	Lys 135	Asp	Lys	Asn	Lys	Ala 140	Glu	Leu	Glu	Ser
Leu A 145	\sn	Asn	Ser	Leu	Asn 150	Gln	Ile	Trp	Thr	Ser 155	Asn	Glu	Thr	Val	Ile 160
Arg A	\sn	Tyr	Asp	Ala 165	Asn	Gln	Tyr	Gly	Gln 170	Ile	Glu	Val	Ala	Leu 175	Leu
Gln I	Jeu	Arg	Ile 180	Ala	Ile	His	Lys	Ser 185	Pro	Leu	Asp	Thr	Ala 190	Lys	Val
Ser H	lis	Ala 195	Trp	Thr	Thr	Phe	Lys 200	Ser	Asn	Ile	Asp	His 205	Val	Asp	Lys
Lys S 2	Ser 210	Asn	Thr	Ser	Ala	Asn 215	Asp	Gln	Tyr	His	Val 220	Ser	Gln	Leu	Asn
Asp A 225	Ala	Leu	Glu	Lys	Ala 230	Ile	ГЛа	Ala	Ile	Asp 235	Asp	Asn	Gln	Leu	Ser 240
Asp A	Ala	Asp	Ala	Ala 245	Leu	Thr	His	Phe	Ile 250	Glu	Thr	Trp	Pro	Tyr 255	Val
Glu G	ly	Gln	Ile 260	Gln	Thr	Lys	Asp	Gly 265	Ala	Leu	Tyr	Thr	Lys 270	Ile	Glu
Asp I	Ъз	Ile 275	Pro	Tyr	Tyr	Gln	Ser 280	Val	Leu	Asp	Glu	His 285	Asn	ГЛЗ	Ala
His V 2	7al 290	Lys	Asp	Gly	Leu	Val 295	Asp	Leu	Asn	Asn	Gln 300	Ile	Lys	Glu	Val
Val G 305	€ly	His	Ser	Tyr	Ser 310	Phe	Val	Asp	Val	Met 315	Ile	Ile	Phe	Leu	Arg 320
Glu G	€ly	Leu	Glu	Val 325	Leu	Leu	Ile	Val	Met 330	Thr	Leu	Thr	Thr	Met 335	Thr
Arg A	Asn	Val	Lys 340	Asp	Lys	Lys	Gly	Thr 345	Ala	Ser	Val	Ile	Gly 350	Gly	Ala
Ile A	Ala	Gly 355	Leu	Val	Leu	Ser	Ile 360	Ile	Leu	Ala	Ile	Thr 365	Phe	Val	Glu
Thr L 3	Jeu 870	Gly	Asn	Ser	Gly	Ile 375	Leu	Arg	Glu	Ser	Met 380	Glu	Ala	Gly	Leu
Gly I 385	lle	Val	Ala	Val	Ile 390	Leu	Met	Phe	Ile	Val 395	Gly	Val	Trp	Met	His 400
Lys A	\rg	Ser	Asn	Ala	Lys	Arg	Trp	Asn	Asp	Met	Ile	Lys	Asn	Met	Tyr

cont	

						•••	0								
											-	con	tin	ued	
				405					410					415	
Ala	Asn	Ala	Ile 420	Ser	Asn	Gly	Asn	Leu 425	Val	Leu	Leu	Ala	Thr 430	Ile	Gly
Leu	Ile	Ser 435	Val	Leu	Arg	Glu	Gly 440		Glu	Val	Ile	Ile 445	Phe	Tyr	Met
Gly	Met 450	Ile	Gly	Glu	Leu	Ala 455		Lys	Asp	Phe	Ile 460	Ile	Gly	Ile	Ala
Leu 465	Ala	Ile	Val	Ile	Leu 470		Ile	Phe	Ala	Leu 475	Leu	Phe	Arg	Phe	Ile 480
Val	Lys	Leu	Ile	Pro 485	Ile	Phe	Tyr	Ile	Phe 490	Arg	Val	Leu	Ser	Ile 495	Phe
Ile	Phe	Ile	Met 500	Gly	Phe	Lys	Met	Leu 505	Gly	Val	Ser	Ile	Gln 510	ГЛа	Leu
Gln	Leu	Leu 515	Gly	Ala	Met	Pro	Arg 520	His	Val	Ile	Glu	Gly 525	Phe	Pro	Thr
Ile	Asn 530	Trp	Leu	Gly	Phe	Tyr 535		Ser	Tyr	Glu	Pro 540	Leu	Ile	Ala	Gln
Gly 545		Tyr	Ile	Met	Val 550	Val		Ile	Leu	Ile 555		Lys	Phe	Lys	Lys 560
					550										500
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		YPE : RGAN		Staj	phyl	ococ	cus a	aureu	ıs						
<400)> SI	EQUEI	NCE :	103											
Met 1	Gln	Lys	Гла	Val 5	Leu	Ala	Ala	Ile	Ile 10	Gly	Thr	Ser	Ala	Ile 15	Ser
Ala	Val	Ala	Ala 20	Thr	Gln	Ala	Asn	Ala 25	Ala	Thr	Thr	His	Thr 30	Val	Lys
Pro	Gly	Glu 35	Ser	Val	Trp	Ala	Ile 40	Ser	Asn	Lys	Tyr	Gly 45	Ile	Ser	Ile
Ala	Lys 50	Leu	Гла	Ser	Leu	Asn 55	Asn	Leu	Thr	Ser	Asn 60	Leu	Ile	Phe	Pro
Asn 65	Gln	Val	Leu	ГЛа	Val 70	Ser	Gly	Ser	Ser	Asn 75	Ser	Thr	Ser	Asn	Ser 80
Ser	Arg	Pro	Ser	Thr 85	Asn	Ser	Gly	Gly	Gly 90	Ser	Tyr	Tyr	Thr	Val 95	Gln
Ala	Gly	Asp	Ser 100		Ser	Leu	Ile	Ala 105	Ser	Lys	Tyr	Gly	Thr 110		Tyr
Gln	Asn	Ile 115		Arg	Leu	Asn	Gly 120		Asn	Asn	Phe	Phe 125	Ile	Tyr	Pro
Gly	Gln 130	Lys	Leu	Lys	Val	Ser 135	Gly	Thr	Ala	Ser	Ser 140		Asn	Ala	Ala
Ser 145			Ser	Arg	Pro 150			Asn	Ser	Gly 155		Gly	Ser	Tyr	Tyr 160
	Val	Gln	Ala	-		Ser	Leu	Ser			Ala	Ser	Lys	-	
Thr	Thr	Tyr	Gln	165 Lys	Ile	Met	Ser	Leu	170 Asn	Gly	Leu	Asn	Asn	175 Phe	Phe
			180					185					190 Ser		
	-	195	-		-		200			-		205			
Ser	Gly 210	Ser	Ala	Thr	Thr	Thr 215	Asn	Arg	Gly	Tyr	Asn 220	Thr	Pro	Val	Phe

Ser His Gln Asn Leu Tyr Thr Trp Gly Gln Cys Thr Tyr His Val Phe225230235240

-continued

Asn	Arg	Arg	Ala	Glu 245	Ile	Gly	Lys	Gly	Ile 250	Ser	Thr	Tyr	Trp	Trp 255	Asn
Ala	Asn	Asn	Trp 260	Asp	Asn	Ala	Ala	Ala 265	Ala	Asp	Gly	Tyr	Thr 270	Ile	Asp
Asn	Arg	Pro 275	Thr	Val	Gly	Ser	Ile 280	Ala	Gln	Thr	Asp	Val 285	Gly	Tyr	Tyr
Gly	His 290	Val	Met	Phe	Val	Glu 295	Arg	Val	Asn	Asn	Asp 300	Gly	Ser	Ile	Leu
Val 305	Ser	Glu	Met	Asn	Tyr 310	Ser	Ala	Ala	Pro	Gly 315	Ile	Leu	Thr	Tyr	Arg 320
Thr	Val	Pro	Ala	Tyr 325	Gln	Val	Asn	Asn	Tyr 330	Arg	Tyr	Ile	His		
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<400)> SB	EQUEI	ICE :	104											
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Ala	Leu	Asn	Asn 20	Ala	Ala	His	Ala	Gln 25	Gln	His	Gly	Thr	Gln 30	Val	Lys
Thr	Pro	Val 35	Gln	His	Asn	Tyr	Val 40	Ser	Asn	Val	Gln	Ala 45	Gln	Thr	Gln
Ser	Pro 50	Thr	Thr	Tyr	Thr	Val 55	Val	Ala	Gly	Asp	Ser 60	Leu	Tyr	Lys	Ile
Ala 65	Leu	Glu	His	His	Leu 70	Thr	Leu	Asn	Gln	Leu 75	Tyr	Ser	Tyr	Asn	Pro 80
Gly	Val	Thr	Pro	Leu 85	Ile	Phe	Pro	Gly	Asp 90	Val	Ile	Ser	Leu	Val 95	Pro
Gln	Asn	Lys	Val 100	Lys	Gln	Thr	Lys	Ala 105	Val	Lys	Ser	Pro	Val 110	Arg	Lys
Ala	Ser	Gln 115	Ala	Lys	Lys	Val	Val 120	Lys	Gln	Pro	Val	Gln 125	Gln	Ala	Ser
Lys	Lys 130	Val	Val	Val	Lys	Gln 135	Ala	Pro	Lys	Gln	Ala 140	Val	Thr	Гла	Thr
Val 145	Asn	Val	Ala	Tyr	Lys 150	Pro	Ala	Gln	Val	Gln 155	ГЛа	Ser	Val	Pro	Thr 160
Val	Pro	Val	Ala	His 165	Asn	Tyr	Asn	Гла	Ser 170	Val	Ala	Asn	Arg	Gly 175	Asn
Leu	Tyr	Ala	Tyr 180	Gly	Asn	Сүз	Thr	Tyr 185	Tyr	Ala	Phe	Asp	Arg 190	Arg	Ala
Gln	Leu	Gly 195	Arg	Ser	Ile	Gly	Ser 200	Leu	Trp	Gly	Asn	Ala 205	Asn	Asn	Trp
Asn	Tyr 210	Ala	Ala	Lys	Val	Ala 215	Gly	Phe	Lys	Val	Asp 220	Гла	Thr	Pro	Glu
Val 225	Gly	Ala	Ile	Phe	Gln 230	Thr	Ala	Ala	Gly	Pro 235	Tyr	Gly	His	Val	Gly 240
Val	Val	Glu	Ser	Val 245	Asn	Pro	Asn	Gly	Thr 250	Ile	Thr	Val	Ser	Glu 255	Met
Asn	Tyr	Ala	Gly 260		Asn	Val	Гла	Ser 265		Arg	Thr	Ile	Leu 270		Pro

Gly Lys Tyr Asn Tyr Ile His

<210> SEQ ID NO 105 <211> LENGTH: 346 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 105 Met Ile Ile Ala Ile Ile Ile Leu Ile Phe Ile Ser Phe Phe Phe Ser Gly Ser Glu Thr Ala Leu Thr Ala Ala Asn Lys Thr Lys Phe Lys Thr Glu Ala Asp Lys Gly Asp Lys Lys Ala Lys Gly Ile Val Lys Leu Leu Glu Lys Pro Ser Glu Phe Ile Thr Thr Ile Leu Ile Gly Asn Asn Val 50 55 60 Ala Asn Ile Leu Leu Pro Thr Leu Val Thr Leu Met Ala Leu Arg Trp 65 70 75 80 Gly Ile Ser Val Gly Ile Ala Ser Ala Val Leu Thr Val Val Ile Ile Leu Ile Ser Glu Val Ile Pro Lys Ser Val Ala Ala Thr Phe Pro Asp Lys Ile Thr Arg Leu Val Tyr Pro Ile Ile Asn Ile Cys Val Ile Val Phe Arg Pro Ile Thr Leu Leu Leu Asn Lys Leu Thr Asp Ser Ile Asn Arg Ser Leu Ser Lys Gly Gln Pro Gln Glu His Gln Phe Ser Lys Glu Glu Phe Lys Thr Met Leu Ala Ile Ala Gly His Glu Gly Ala Leu Asn Glu Ile Glu Thr Ser Arg Leu Glu Gly Val Ile Asn Phe Glu Asn Leu Lys Val Lys Asp Val Asp Thr Thr Pro Arg Ile Asn Val Thr Ala Phe Ala Ser Asn Ala Thr Tyr Glu Glu Val Tyr Glu Thr Val Met Asn Lys Pro Tyr Thr Arg Tyr Pro Val Tyr Glu Gly Asp Ile Asp Asn Ile Ile Gly Val Phe His Ser Lys Tyr Leu Leu Ala Trp Ser Asn Lys Lys Glu Asn Gln Ile Thr Asn Tyr Ser Ala Lys Pro Leu Phe Val Asn Glu His Asn Lys Ala Glu Trp Val Leu Arg Lys Met Thr Ile Ser Arg Lys His Leu Ala Ile Val Leu Asp Glu Phe Gly Gly Thr Glu Ala Ile Val Ser His Glu Asp Leu Ile Glu Glu Leu Leu Gly Met Glu Ile Glu Asp Glu Met Asp Lys Lys Glu Lys Glu Lys Leu Ser Gln Gln Gln Ile Gln Phe Gln Gln Arg Lys Asn Arg Asn Val Ser Ile

	<210> SEQ ID NO 106 <211> LENGTH: 391 <212> TYPE: PRT														
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Met 1	Lys	Leu	Lys	Pro 5	Phe	Leu	Pro	Ile	Leu 10	Ile	Ser	Gly	Ala	Val 15	Phe
Ile	Val	Phe	Leu 20	Leu	Leu	Pro	Ala	Ser 25	Trp	Phe	Thr	Gly	Leu 30	Val	Asn
Glu	Lys	Thr 35	Val	Glu	Asp	Asn	Arg 40	Thr	Ser	Leu	Thr	Asp 45	Gln	Val	Leu
Lys	Gly 50	Thr	Leu	Ile	Gln	Asp 55	ГЛа	Leu	Tyr	Glu	Ser 60	Asn	ГЛа	Tyr	Tyr
Pro 65	Ile	Tyr	Gly	Ser	Ser 70	Glu	Leu	Gly	Lys	Asp 75	Asp	Pro	Phe	Asn	Pro 80
Ala	Ile	Ala	Leu	Asn 85	Lys	His	Asn	Ala	Asn 90	Lys	ГЛа	Ala	Phe	Leu 95	Leu
Gly	Ala	Gly	Gly 100	Ser	Thr	Asp	Leu	Ile 105	Asn	Ala	Val	Glu	Leu 110	Ala	Ser
Gln	Tyr	Asp 115	Lys	Leu	Lys	Gly	Lys 120	Lys	Leu	Thr	Phe	Ile 125	Ile	Ser	Pro
Gln	Trp 130	Phe	Thr	Asn	His	Gly 135	Leu	Thr	Asn	Gln	Asn 140	Phe	Asp	Ala	Arg
Met 145	Ser	Gln	Thr	Gln	Ile 150	Asn	Gln	Met	Phe	Gln 155	Gln	Гла	Asn	Met	Ser 160
Thr	Glu	Leu	Lys	Arg 165	Arg	Tyr	Ala	Gln	Arg 170	Leu	Leu	Gln	Phe	Pro 175	His
Val	His	Asn	Lys 180	Glu	Tyr	Leu	Lys	Ser 185	Tyr	Ala	Lys	Asn	Pro 190	Lys	Glu
Thr	Lys	Asp 195	Ser	Tyr	Ile	Ser	Gly 200	Phe	Lys	Glu	Asn	Gln 205	Leu	Ile	Lys
Ile	Glu 210	Ala	Ile	Lys	Ser	Leu 215	Phe	Ala	Met	Asp	Lys 220	Ser	Pro	Leu	Glu
His 225	Val	Lys	Pro	Ala	Thr 230	ГЛЗ	Pro	Asp	Ala	Ser 235	Trp	Asp	Glu	Met	Lys 240
Gln	Lys	Ala	Val	Glu 245	Ile	Gly	Lys	Ala	Asp 250	Thr	Thr	Ser	Asn	Lys 255	Phe
Gly	Ile	Arg	Asp 260	Gln	Tyr	Trp	Lys	Leu 265	Ile	Gln	Glu	Ser	Lys 270	Arg	Lys
Val	Arg	Arg 275	Asp	Tyr	Glu	Phe	Asn 280	Val	Asn	Ser	Pro	Glu 285	Phe	Gln	Asp
Leu	Glu 290	Leu	Leu	Val	Lys	Thr 295	Met	Arg	Ala	Ala	Gly 300	Ala	Asp	Val	Gln
Tyr 305	Val	Ser	Ile	Pro	Ser 310	Asn	Gly	Val	Trp	Tyr 315	Asp	His	Ile	Gly	Ile 320
Asp	Lys	Glu	Arg	Arg 325	Gln	Ala	Val	Tyr	Lys 330	Lys	Ile	His	Ser	Thr 335	Val
Val	Asp	Asn	Gly 340	Gly	ГЛа	Ile	Tyr	Asp 345	Met	Thr	Asp	Lys	Asp 350	Tyr	Glu
Lys	Tyr	Val 355	Ile	Ser	Asp	Ala	Val 360	His	Ile	Gly	Trp	Lys 365	Gly	Trp	Val
Tyr	Met 370	Asp	Glu	Gln	Ile	Ala 375	Lys	His	Met	Lys	Gly 380	Glu	Pro	Gln	Pro

375		

Glu Val Asp Lys Pro Lys Asn

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 Asn Ile Ser Gly Thr Gln Val Tyr Gln Asp Pro Ala Ile Val Gln Pro

 65
 70
 75
 80
 Lys Thr Ala As
n Asn Lys Thr Gly Asn Ala Gl
n Val Ser Gl
n Lys Val Asp Thr Ala Gln Val Asn Gly Asp Thr Arg Ala Asn Gln Ser Ala Thr Thr Asn Asn Thr Gln Pro Val Ala Lys Ser Thr Ser Thr Thr Ala Pro Lys Thr As
n Thr As
n Val Thr As
n Ala Gly Tyr Ser Leu Val As
p As
p $\ensuremath{\mathsf{Asp}}$ Glu Asp Asp Asn Ser Glu Asn Gln Ile Asn Pro Glu Leu Ile Lys Ser Ala Ala Lys Pro Ala Ala Leu Glu Thr Gln Tyr Lys Thr Ala Ala Pro Lys Ala Ala Thr Thr Ser Ala Pro Lys Ala Lys Thr Glu Ala Thr Pro Lys Val Thr Thr Phe Ser Ala Ser Ala Gln Pro Arg Ser Val Ala Ala 2.05 Thr Pro Lys Thr Ser Leu Pro Lys Tyr Lys Pro Gln Val Asn Ser Ser Ile Asn Asp Tyr Ile Cys Lys Asn Asn Leu Lys Ala Pro Lys Ile Glu Glu Asp Tyr Thr Ser Tyr Phe Pro Lys Tyr Ala Tyr Arg Asn Gly Val Gly Arg Pro Glu Gly Ile Val Val His Asp Thr Ala Asn Asp Arg Ser Thr Ile Asn Gly Glu Ile Ser Tyr Met Lys Asn Asn Tyr Gln Asn Ala Phe Val His Ala Phe Val Asp Gly Asp Arg Ile Ile Glu Thr Ala Pro Thr Asp Tyr Leu Ser Trp Gly Val Gly Ala Val Gly Asn Pro Arg Phe Ile Asn Val Glu Ile Val His Thr His Asp Tyr Ala Ser Phe Ala Arg Ser Met Asn Asn Tyr Ala Asp Tyr Ala Ala Thr Gln Leu Gln Tyr Tyr Gly Leu Lys Pro Asp Ser Ala Glu Tyr Asp Gly Asn Gly Thr Val Trp

Thr	His	Tyr	Ala	Val	Ser		Tyr	Leu	Gly	Gly		Asp	His	Ala	Asp
Pro	370 His	Gly	Tyr	Leu	Arg	375 Ser	His	Asn	Tyr	Ser	380 Tyr	Asp	Gln	Leu	Tyr
385	Leu	710	7 an	<i>c</i> 1.,	390	Tr r r r	Lou	T1 o	Inc	395 Mot	C 1	I.u.a	Vol	710	400 Drco
Авр	цец	шe	ASII	405	цув	тут	цец	шe	ЦуБ 410	Met	GIY	цув	Val	415	PIO
Trp	Gly	Thr	Gln 420	Ser	Thr	Thr	Thr	Pro 425	Thr	Thr	Pro	Ser	Lys 430	Pro	Thr
Thr	Pro	Ser 435	Lys	Pro	Ser	Thr	Gly 440	ГЛа	Leu	Thr	Val	Ala 445	Ala	Asn	Asn
Gly	Val 450	Ala	Gln	Ile	Lys	Pro 455	Thr	Asn	Ser	Gly	Leu 460	Tyr	Thr	Thr	Val
Tyr 465	Asp	Lys	Thr	Gly	Lys 470	Ala	Thr	Asn	Glu	Val 475	Gln	Lys	Thr	Phe	Ala 480
Val	Ser	Lys	Thr	Ala 485	Thr	Leu	Gly	Asn	Gln 490	Lys	Phe	Tyr	Leu	Val 495	Gln
Aap	Tyr	Asn	Ser 500	Gly	Asn	Lys	Phe	Gly 505	Trp	Val	Lys	Glu	Gly 510	Asp	Val
Val	Tyr	Asn 515	Thr	Ala	Lys	Ser	Pro 520	Val	Asn	Val	Asn	Gln 525	Ser	Tyr	Ser
Ile	Lys 530	Pro	Gly	Thr	Lys	Leu 535	Tyr	Thr	Val	Pro	Trp 540	Gly	Thr	Ser	Lys
Gln 545	Val	Ala	Gly	Ser	Val 550	Ser	Gly	Ser	Gly	Asn 555	Gln	Thr	Phe	Lys	Ala 560
Ser	Lys	Gln	Gln	Gln 565	Ile	Asp	Lys	Ser	Ile 570	Tyr	Leu	Tyr	Gly	Ser 575	Val
Asn	Gly	Lys	Ser 580	Gly	Trp	Val	Ser	Lys 585	Ala	Tyr	Leu	Val	Asp 590	Thr	Ala
Lys	Pro	Thr 595	Pro	Thr	Pro	Thr	Pro 600	Lys	Pro	Ser	Thr	Pro 605	Thr	Thr	Asn
Asn	Lys 610	Leu	Thr	Val	Ser	Ser 615	Leu	Asn	Gly	Val	Ala 620	Gln	Ile	Asn	Ala
Lys 625	Asn	Asn	Gly	Leu	Phe 630	Thr	Thr	Val	Tyr	Asp 635	Lys	Thr	Gly	Lys	Pro 640
Thr	Lys	Glu	Val	Gln 645	Lys	Thr	Phe	Ala	Val 650	Thr	Lys	Glu	Ala	Ser 655	Leu
Gly	Gly	Asn	Lys 660	Phe	Tyr	Leu	Val	Lys 665	Asp	Tyr	Asn	Ser	Pro 670	Thr	Leu
Ile	Gly	Trp 675	Val	Lys	Gln	Gly	Asp 680	Val	Ile	Tyr	Asn	Asn 685	Ala	Lys	Ser
Pro	Val 690	Asn	Val	Met	Gln	Thr 695	Tyr	Thr	Val	Lys	Pro 700	Gly	Thr	Lys	Leu
Tyr 705	Ser	Val	Pro	Trp	Gly 710	Thr	Tyr	Lys	Gln	Glu 715	Ala	Gly	Ala	Val	Ser 720
Gly	Thr	Gly	Asn	Gln 725	Thr	Phe	Lys	Ala	Thr 730	Lys	Gln	Gln	Gln	Ile 735	Asp
Lys	Ser	Ile	Tyr 740	Leu	Phe	Gly	Thr	Val 745	Asn	Gly	Lys	Ser	Gly 750	Trp	Val
Ser	Lys	Ala 755	Tyr	Leu	Ala	Val	Pro 760	Ala	Ala	Pro	Гла	Lys 765	Ala	Val	Ala
Gln	Pro 770	Lys	Thr	Ala	Val	Lys 775	Ala	Tyr	Thr	Val	Thr 780	Lys	Pro	Gln	Thr

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Th: 78!		ln	Thr	Val	Ser	Lys 790	Ile	Ala	Gln	Val	և Աչ 79		Pro	Asn	. Asr	ı Thr	Gly 800
Lei	ı Ar	g	Ala	Ser	Val 805	Tyr	Glu	ГÀа	Thr	Ala 810		/s /	Asn	Gly	Ala	a Lys 815	Tyr
Ala	a As	p	Arg	Thr 820	Phe	Tyr	Val	Thr	Lys 825		ı Ar	g i	Ala	His	Gly 830		ı Glu
Th:	r Ty		Val 835	Leu	Leu	Asn	Asn	Thr 840	Ser	His	a As	an 1	Ile	Pro 845		ı Gly	7 Trp
Phe	e As 85		Val	Lys	Asp	Leu	Asn 855	Val	Gln	Ası	n L∈		31y 360	Lys	Glu	ı Val	. Lys
Th: 86!		ır	Gln	Lys	Tyr	Thr 870	Val	Asn	Lys	Sei	r As 87		Asn	Gly	Leu	ı Ser	Met 880
Va	l Pr	:0	Trp	Gly	Thr 885	Lys	Asn	Gln	Val	Ile 890		eu 1	「hr	Gly	Asr	n Asr 895	lle
Ala	a Gl	ln	Gly	Thr 900	Phe	Asn	Ala	Thr	Lys 905		n Va	al S	Ser	Val	Gl} 910		a Asp
Va	l Ty		Leu 915	Tyr	Gly	Thr	Ile	Asn 920	Asn	Arg	g Th	nr (Gly	Trp 925		. Asr	n Ala
Ly	s As 93		Leu	Thr	Ala	Pro	Thr 935	Ala	Val	Lys	s Pr		Fhr 940	Thr	Sei	: Ala	a Ala
Ly: 94!		ab	Tyr	Asn	Tyr	Thr 950	Tyr	Val	Ile	Lys	3 As 95		Gly	Asn	Glγ	7 Tyr	Tyr 960
Ту	r Va	al	Thr	Pro	Asn 965	Ser	Asp	Thr	Ala	Ly: 970	-	r ۲	Ser	Leu	. Цуа	975	h Phe
Ası	n Gl	Lu	Gln	Pro 980	Phe	Ala	Val	Val	Lys 985		ı Gl	ln V	/al	Ile	Asr 990		/ Gln
Th:	r Ti		Tyr 995	Tyr	Gly	Гла	Leu	Ser 100		n Gl	ly I	ъ	Leı		a 1 05	rp I	le Ly
Se:		nr 010		p Let	u Ala	a Ly:	5 Glu 101		eu I	le I	ys	ту		3n 020	Gln	Thr	Gly
Met		ır)25		ı Ası	n Glr	n Val	L Ala 103		ln I	le (Jln	Ala		ly 035	Leu	Gln	Tyr
Ly		:0)40		n Vai	l Glr	n Arç	g Val 104		ro G	ly I	ya	Trj		nr 050	Asp	Ala	ГЛа
Phe		9n 955		o Va	l Ly:	s His	5 Ala 106		et A	ap 1	「hr	LY		rg 065	Leu	Ala	Gln
Asj		:0)70		a Lei	u Ly:	з Туз	Glr 107		ne L	eu A	Arg	Leı		280 ab	Gln	Pro	Gln
Ası		Le 085		r Ile	e Asp	p Ly:	5 Ile 109		sn G	ln I	?he	Leı		ខ្លួន 295	Gly	LÀa	Gly
Va		eu LOO		ı Ası	n Glr	n Gly	7 Ala 110		la P	he A	Asn	Ly:		la 110	Ala	Gln	Met
Ту:		ly 15		e Ası	n Glı	ı Val	L Tyi 112		eu I	le S	Ser	Hi		la 125	Leu	Leu	Glu
Th:		Ly 130		ı Gly	y Thi	r Sei	Glr 113		eu A	la I	Jya	Gl		la 140	Asp	Val	Val
Ası	n As		LYS	s Vai	l Val	l Thi		n Se	ər A	sn 1	「hr	Ly:	s Tj		His	Asn	Val
Phe	e Gl	Lу	Leu	ı Ala	a Ala	а Туз		> A	sn A	ap I	Pro?	Lei	ı Ai	rg	Glu	Gly	Ile
Ly:	з Ту		Ala	a Ly:	s Glr	n Ala	a Gly	7 Т:	rp A	ap 1	「hr	Va:	l Se		rya	Ala	Ile
Va		175 Ly		/ Ala	a Ly:	s Phe	118 e Ile		ly A	sn S	Ser	туз		185 al	Lys	Ala	Gly

	1190)				119	95				12	200			
Gln	Asn 1205		r Lei	а Туз	r Lys	s Mei 12:	t A1 10	rg Ti	rp As	an Pi		la 1 215	His 1	Pro (Gly
Thr	His 1220		а Туз	r Ala	a Thi	r Asj 122	9 Va 25	al As	зр Ті	rp Ai		sn 1 230	Ile 2	Asn J	Ala
Lys	Ile 1235		e Ly:	a Gly	ү Туз	r Ty: 124	r A: 40	зр Цу	ys II	le G		lu ' 245	Val (Gly I	Lys
Tyr	Phe 1250		p Ile	e Pro	o Glr	n Ty: 129	r Ly 55	\a							
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L'Aa	His	Phe	Lуз 20	His	Tyr	Thr	Gln	Ser 25	Ile	Glu	Leu	Tyr	Asn 30	Tyr	Arg
Asn	Lys	Ile 35	Asn	His	Glu	Ala	His 40	Ile	Val	Gly	Val	Lys 45	Asn	Asp	Lys
Asn	Glu 50	Val	Leu	Ala	Ala	Сув 55	Leu	Leu	Thr	Glu	Ala 60	Arg	Ile	Phe	Lys
Phe 65	Tyr	Lys	Tyr	Phe	Tyr 70	Ser	His	Arg	Gly	Pro 75	Leu	Leu	Asp	Tyr	Phe 80
Aap	Ala	Lys	Leu	Val 85	Сүз	Tyr	Phe	Phe	Lys 90	Glu	Leu	Ser	Lys	Phe 95	Ile
Tyr	Lys	Asn	Arg 100	Gly	Val	Phe	Ile	Leu 105	Val	Asp	Pro	Tyr	Leu 110	Ile	Glu
Asn	Leu	Arg 115	Asp	Ala	Asn	Gly	Arg 120	Ile	Ile	Гла	Asn	Tyr 125	Asn	Asn	Ser
Val	Ile 130	Val	Lys	Met	Leu	Gly 135	Lys	Ile	Gly	Tyr	Leu 140	His	Gln	Gly	Tyr
Thr 145	Thr	Gly	Tyr	Ser	Asn 150	Lys	Ser	Gln	Ile	Arg 155	Trp	Ile	Ser	Val	Leu 160
Asp	Leu	Lys	Asp	Lys 165	Asp	Glu	Asn	Gln	Leu 170	Leu	ГЛа	Glu	Met	Glu 175	
Gln	Thr	Arg	Arg 180	Asn	Ile	Lys	Lys	Thr 185	Ile	Glu	Ile	Gly	Val 190	Lys	Val
Glu	Asp	Leu 195	Ser	Ile	Glu	Glu	Thr 200	Asn	Arg	Phe	Tyr	Lys 205	Leu	Phe	Gln
Met	Ala 210	Glu	Glu	Lys	His	Gly 215	Phe	His	Phe	Met	Asn 220	Glu	Asp	Tyr	Phe
Lys 225		Met	Gln	Glu	Ile 230		Lys	Asp	Lys	Ala 235		Leu	Lys	Ile	Ala 240
	Ile	Asn	Leu	Asn 245		Tyr	Gln	Asp	Lys 250		Гла	Ile	Gln	Leu 255	
ГЛа	Ile	Glu			Met	Met	Thr			Arg	Ala	Leu			Asn
Pro	Asn	Ser	260 Lys	Lys	Asn	Lys	Ser	265 Lys	Leu	Asn	Gln	Leu	270 Asn	Met	Gln
Leu	Ser	275 Ser	Ile	Asn	Asn	Arq	280 Ile	Ser	Lys	Thr	Glu	285 Glu	Leu	Ile	Phe
	290					295			- <u>1</u> ~		300				

Glu Asp Gly Pro Val Leu Asp Leu Ala Ala Ala Leu Phe Ile Cys Thr Asp Asp Glu Val Tyr Tyr Leu Ser Ser Gly Ser Asn Pro Lys Tyr Asn Gln Tyr Met Gly Ala Tyr His Leu Gln Trp His Met Ile Lys Tyr Ala Lys Ser His Asn Ile Asn Arg Tyr Asn Phe Tyr Gly Ile Thr Gly Val Phe Ser Asn Glu Asp Asp Phe Gly Val Gln Gln Phe Lys Lys Gly Phe Asn Ala His Val Glu Glu Leu Ile Gly Asp Phe Ile Lys Pro Val Arg Pro Ile Leu Tyr Lys Phe Ala Lys Leu Ile Tyr Lys Val <210> SEQ ID NO 109 <211> LENGTH: 428 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 109 Met Lys Glu Arg Tyr Tyr Glu Leu Ile Asp Glu Arg Val Phe Glu Gln Glu Leu Glu Asn Gly Leu Arg Leu Phe Ile Ile Pro Lys Pro Gly Phe Gln Lys Thr Phe Val Thr Tyr Thr Thr Gln Phe Gly Ser Leu Asp Asn Gln Phe Lys Pro Leu Gly Gln Asp Gln Phe Val Thr Val Pro Asp Gly Val Ala His Phe Leu Glu His Lys Leu Phe Glu Lys Glu Glu Glu Asp Leu Phe Thr Ala Phe Ala Glu Asp Asn Ala Gln Ala Asn Ala Phe Thr Ser Phe Asp Arg Thr Ser Tyr Leu Phe Ser Ala Thr Asp Asn Ile Glu Asn Asn Ile Lys Arg Leu Leu Thr Met Val Glu Thr Pro Tyr Phe Thr Lys Glu Thr Val Asp Lys Glu Lys Gly Ile Ile Ala Glu Glu Ile Lys Met Tyr Gln Glu Gln Pro Gly Tyr Lys Leu Met Phe Asn Thr Leu Arg Ala Met Tyr Gln Gln His Pro Ile Arg Val Asp Ile Ala Gly Ser Val Glu Ser Ile Tyr Asp Ile Thr Lys Asp Asp Leu Tyr Leu Cys Tyr Glu Thr Phe Tyr His Pro Ser Asn Met Val Leu Phe Val Val Gly Asp Val Asp Pro Glu Ala Ile Cys Arg Ile Val Lys Gln His Glu Asp Ala Arg Asn Lys Val Asn Gln Pro Lys Ile Glu Arg Gly Leu Val Asp Glu Pro Glu Asp Val Lys Glu Ala Phe Val Thr Glu Ser Met Lys Ile Gln Ser Pro Arg Leu Met Leu Gly Phe Lys Asn Lys Pro Leu Gln Glu Ala Pro

Gln	Lys	Tyr 275	Val	Gln	Arg	Asp	Leu 280	Glu	Met	Ser	Leu	Phe 285	Phe	Glu	Leu
Ile	Phe 290	Gly	Glu	Glu	Thr	Asp 295	Phe	Tyr	Gln	Asn	Leu 300	Leu	Asn	Glu	Gly
Leu 305	Ile	Asp	Asp	Thr	Phe 310	Gly	Tyr	Gln	Phe	Val 315	Leu	Glu	Pro	Thr	Tyr 320
Ser	Phe	Ser	Ile	Val 325	Thr	Ser	Ala	Thr	Glu 330	Glu	Pro	Asp	Lys	Leu 335	Lys
Lys	Leu	Leu	Leu 340	Asp	Glu	Leu	Arg	Asp 345	Lys	Lys	Gly	Asn	Phe 350	Gln	Asp
Ala	Glu	Ala 355	Phe	Glu	Leu	Leu	Lys 360	ГЛЗ	Gln	Phe	Ile	Gly 365	Glu	Phe	Ile
Ser	Ser 370	Leu	Asn	Ser	Pro	Glu 375	Tyr	Ile	Ala	Asn	Gln 380	Tyr	Thr	ГЛа	Leu
Tyr 385	Phe	Glu	Gly	Val	Ser 390	Val	Phe	Asb	Met	Leu 395	Asp	Ile	Val	Glu	Asn 400
Ile	Thr	Leu	Asp	Ser 405	Ile	Asn	Glu	Thr	Ser 410	Ser	Leu	Tyr	Leu	Asn 415	Leu
Aap	Gln	Gln	Val 420	Asp	Ser	Arg	Leu	Glu 425	Ile	rÀa	ГÀа				
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	Val	Gly	Gly 20		Val	Val	Ala	Arg 25		Leu	Leu	Leu	Gln 30		Gln
Ser	Gln	Ala 35		Gln	Thr	Ala	Glu 40		Ile	Val	Asn	Gln 45		His	Lys
Glu	Ala 50	Asp	Asn	Ile	Lys	Lys 55	Glu	Гуз	Leu	Leu	Glu 60	Ala	Гла	Glu	Glu
Asn 65	Gln	Ile	Leu	Arg	Glu 70	Gln	Thr	Glu	Ala	Glu 75	Leu	Arg	Glu	Arg	Arg 80
Ser	Glu	Leu	Gln	Arg 85	Gln	Glu	Thr	Arg	Leu 90	Leu	Gln	Lys	Glu	Glu 95	Asn
Leu	Glu	Arg	Lys 100	Ser	Asp	Leu	Leu	Asp 105	Lys	Lys	Asp	Glu	Ile 110	Leu	Glu
Gln	Lys	Glu 115	Ser	Lys	Ile	Glu	Glu 120	Lys	Gln	Gln	Gln	Val 125	Asp	Ala	Lys
Glu	Ser 130	Ser	Val	Gln	Thr	Leu 135	Ile	Met	Lys	His	Glu 140	Gln	Glu	Leu	Glu
Arg 145	Ile	Ser	Gly	Leu	Thr 150	Gln	Glu	Glu	Ala	Ile 155	Asn	Glu	Gln	Leu	Gln 160
Arg	Val	Glu	Glu	Glu 165	Leu	Ser	Gln	Asp	Ile 170	Ala	Val	Leu	Val	Lys 175	Glu
Lys	Glu	Lys	Glu 180	Ala	Lys	Glu	Lys	Val 185	Asp	Гла	Thr	Ala	Lys 190	Glu	Leu
Leu	Ala	Thr 195	Ala	Val	Gln	Arg	Leu 200	Ala	Ala	Asp	His	Thr 205	Ser	Glu	Ser
Thr	Val	Ser	Val	Val	Asn	Leu	Pro	Asn	Asp	Glu	Met	Lys	Gly	Arg	Ile

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Ile Gl 225	y Arg	Glu	Gly	Arg 230	Asn	Ile	Arg	Thr	Leu 235	Glu	Thr	Leu	Thr	Gly 240
Ile As	p Leu	Ile	Ile 245	Asp	Asp	Thr	Pro	Glu 250	Ala	Val	Ile	Leu	Ser 255	Gly
Phe As	p Pro	Ile 260	Arg	Arg	Glu	Ile	Ala 265	Arg	Thr	Ala	Leu	Val 270	Asn	Leu
Val Se	r Asp 275	Gly	Arg	Ile	His	Pro 280	Gly	Arg	Ile	Glu	Asp 285	Met	Val	Glu
Lys Al 29	-	Lys	Glu	Val	Asp 295	Asp	Ile	Ile	Arg	Glu 300	Ala	Gly	Glu	Gln
Ala Th 305	r Phe	Glu	Val	Asn 310	Ala	His	Asn	Met	His 315	Pro	Asp	Leu	Val	Lys 320
Ile Va	l Gly	Arg	Leu 325	Asn	Tyr	Arg	Thr	Ser 330	Tyr	Gly	Gln	Asn	Val 335	Leu
Lys Hi	s Ser	Ile 340	Glu	Val	Ala	His	Leu 345	Ala	Ser	Met	Leu	Ala 350	Ala	Glu
Leu Gl	y Glu 355	Asp	Glu	Thr	Leu	Ala 360	Lys	Arg	Ala	Gly	Leu 365	Leu	His	Asp
Val Gl 37		Ala	Ile	Asp	His 375	Glu	Val	Glu	Gly	Ser 380	His	Val	Glu	Ile
Gly Va 385	l Glu	Leu	Ala	Lys 390	Lys	Tyr	Gly	Glu	Asn 395	Glu	Thr	Val	Ile	Asn 400
Ala Il	e His	Ser	His 405	His	Gly	Asp	Val	Glu 410	Pro	Thr	Ser	Ile	Ile 415	Ser
Ile Le	u Val	Ala 420	Ala	Ala	Asp	Ala	Leu 425	Ser	Ala	Ala	Arg	Pro 430	Gly	Ala
Arg Ly	s Glu 435	Thr	Leu	Glu	Asn	Tyr 440	Ile	Arg	Arg	Leu	Glu 445	Arg	Leu	Glu
Thr Le 45		Glu	Ser	Tyr	Asp 455	Gly	Val	Glu	Lys	Ala 460	Phe	Ala	Ile	Gln
Ala Gl 465	y Arg	Glu	Ile	Arg 470	Val	Ile	Val	Ser	Pro 475	Glu	Glu	Ile	Asp	Asp 480
Leu Ly	s Ser	Tyr	Arg 485	Leu	Ala	Arg	Asp	Ile 490	Lys	Asn	Gln	Ile	Glu 495	Asp
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Val Ty	r Ala 35	Arg	Lys	Gln	Leu	Ile 40	Lys	Lys	Asn	Lys	Ala 45	Leu	Ser	Ala
a1 -		~ 1			a				a	a				
Glu As 50		GIU	ьeu	Arg	Ser 55	GIN	met	ьeu	ser	Ser 60	Asn	Asn	Asb	va⊥

Gly His His Ala Tyr Lys Asn Ala Lys Arg Glu Leu Arg Lys IIe Leu 50 Asp Ser Tyr Leu Glu Asn Gly Lys Leu Yo Tyr Tyr Asp IIe IIe Val 95 Thr Ser Ann Leu Ala Thr Lys His Pro Phe Phe Glu Tyr Ala Arg Ser 100 Phe Asp Phe IIe IIe Val Ser Asp IIe Cly Leu IIe Asm Val Asp Val 115 Lys Ser Trp Gly Glu Lys Thr Phe Tyr His Phe Asp Val Pro Asp Glu 1150 Tyr IIe Ser Gln Gln Tyr His Asp Gln Lys Val Val Gly His 160 Tyr IIe Ser Gln Gln Tyr His Asp Gln Phe Asn Ser Ser Arg Lys Ser 175 IIe Tyr Thr Phe Thr Glu Thr Val Gln Pro Asn Arg Val IIe Tyr Asp 190 Phe Tyr Asp Tyr Asp Pro Tyr Gln Leu Ala Ala Asm Asm Ala Lys Ala 205 Leu Lys Asp His IIe Glu Gln Asm Phe Asm Phe Lys Val Gln Ser Thr 210 Gly 41 IIe Tyr Phe Ser Asp Gly Thr Val Asm IIe IIe Gln Gly Ser 220 Glu Glu Arg Asp Lys Tyr Val Asp Thr Val Ser Thr Lys Ser Ser Leu 260 Clu Glu Val Asp Gln IIe Thr Ala IIe Phe Lys 275 Lys Ger TTP De Asp Lys Clu Asp Thr Val Ser Thr Lys Ser Ser Leu 260 Clu Glu Val Asp Gln IIe Thr Ala IIe Phe Lys 275 Lys Glu Gln Val Asp Clu Jie Vas Asp Glu Glu Ser Gln Asm 116 Club SEQ TD INO 112 Club Clu Ser TTP De Asp Lys Lys Lys Asg Arg Gln Glu Ser Gln Asm 118 Asp Leu IIe His Axg Lys Lys Lys Arg Arg Gln Glu Ser Gln Asm 118 Asp Luc IIe His Axg Lys Lys Lys Arg Arg Gln Glu Ser Gln Asm 118 Asp Luc IIe His Axg Lys Lys Lys Arg Arg Gln Glu Ser Gln Asm 118	_												con		uea		
as so so ss Thr Ser Aon Leu Ala Thr Lyø His pro Phe Phe Glu Tyr Alla Arg Ser 1100 Tyr Alla Arg Ser 1100 Phe Aop Phe Ile Ile Val Ser Aop Ile Gly Leu Ile Aon Val Aop Val 1150 For Aop Clu 120 Lyø Ser Typ Gly Glu Lyø Thr Phe Tyr Hiø Phe Aop Val Pro Aop Glu 1100 For Aop Clu 120 His Aop Thr Glu Ile Ser Aon Ser Aon Ile Glu Lyø Val Val Gly Hig 180 For Aop Clu 190 Tyr Ile Ser Gln Gln Tyr Hiø Aop Gln Phe Aon Ser Ser Arg Lyø Ser 196 For Aop Clu 190 Phe Tyr Aop Tyr Aop Pro Tyr Gln Leu Ala Ala Aon Aon Ala Lyø Ala 195 For Aop Clu Clug Aop Hiø Ile Glu Gln Aon Phe Aon Phe Lyø Val Gln Gly Ser 225 For Aop Clu Ala Ser Glu Ala The Glu Fry Val Ser Thr 240 Glu Glu Arg Ap Lyø Tyr Val Ap Thr Val Ser Thr Lyø Fro Ese Leu 240 For Aop Clu Ala The Clu Fry Val Ser Thr 240 Glu Glu Arg Ap Lyø Tyr Val Ap Thr Val Ser Thr Lyø Fro Ese Leu 240 For Aop Clu Her Ang Ap Club Sto ID Do 112 For Aop Clu Her Ang Ap For Aop Ap Club Sto UD NO 112 For Adp Lyø Ap For Adp Ap Club Sto UD NO 112 For Adp Lyø Lyø Arg Ap For Adp Ang Ap Club Sto ID NO 112 For Adp Ap For Adp Ap Club Sto ID NO 112 For Adp Ap For Adp Ap Club Sto ID NO 112 For Adp Ap For Ad	-	His	His	Ala	Tyr		Asn	Ala	Lys	Arg		Leu	Arg	Lys	Ile		
100 105 110 Pho App Pho P	Asp	Ser	Tyr	Leu		Asn	Gly	Lys	Leu		Tyr	Tyr	Asp	Ile		Val	
115 120 125 Lyg Ser Trp Gly Glu Lyg Thr phe Tyr His Phe Amp Val Pro Amp Glu 140 Amp Thr Glu 1le Ser Am Ser Am 1le Glu Lyg Val Val Gly Hig 145 Am Thr Glu 1le Ser Am Ser Am 1le Glu Lyg Val Val Gly Hig 166 Tyr Ile Ser Gln Gln Tyr His Amp Gln Phe Am Ser Ser Arg Lyg Ser 116 Tyr Thr Phe Thr Glu Thr Val Gln Pro Am Arg Val Ile Tyr Amp Phe Tyr Amp Tyr Amp Pro Tyr Gln Leu Ala Ala Am Am Am Ala Lyg Ala 210 Leu Lyg Amp His Ile Glu Gln Am Phe Am Phe Lyg Val Gln Ser Thr 211 Tyr Phe Ser Amp Gly Thr Val Ser Thr Lyg Ser Ser Leu 225 Val Ile Tyr Phe Ser Amp Gly Thr Val Ser Thr Lyg Ser Ser Leu 2260 Glu Gln Arg Amp Gln Ile Thr Ala Ile Glu Lue Ser Lyg His Pro Leu Am 2260 Thr Val Amp Gln Ile Thr Ala Ile Phe Lyg 210 SEQ TD NO 112 211 Ser Tr Phe Amp Lyg Lyg Lyg Lyg Arg Gln Glu Ser Gln Am Amp 212 TPH PH T 213 SGRAMISM: Staphylococccus aureus <400 SEQUENCE: 112	Thr	Ser	Asn		Ala	Thr	Lys	His		Phe	Phe	Glu	Tyr		Arg	Ser	
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145150155160TyrIle SerGin Gin TyrHis Asp Gin Phe Asn Ser Ser Arg Lyg Ser 175175Ile TyrThr Phe Thr Glu Thr Val Gin Pro Asn Arg Val Ile Tyr Asp 195Tyr Gin Leu Ala Ala Asn Asn Ala Lyg Ala 205110Phe TyrAsp Tyr Asp Pro Tyr Gin Leu Ala Ala Asn Asn Ala Lyg Ala 215110Gin Ser Thr 220Gly Val Ile TyrPhe Ser Asp Gly Thr Val Asp The Lyg Val Gin Ser Thr 210220Gly Val Ile TyrPhe Ser Asp Gly Thr Val Ser Thr Lyg Ser Ser Leu 244246Clu Ala 11e 265Glu Leu Ser Lyg Hig Pro Leu Asn 275Arg Arg Ile Ile Ser Glu Ala Ile Glu Leu Ser Lyg Hig Pro Leu Asn 2662711EMNORTH:27212802722Clu Gin Val Asp Gin Ile 275273Clu Asp Ser Asp Ser Asp Asp 112274212275280275280276112277213278Clu Asp Asp Asp Ser Asp Asp 115279120270121271EMNORTH:274212TYPE: PRT 213213ORGANISM: Staphylococccus aureus<400	Lys		Trp	Gly	Glu	ГЛа		Phe	Tyr	His	Phe		Val	Pro	Asp	Glu	
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210 215 220 Gly Val Ile Tyr Phe Ser Asp Gly Thr Val Asp Th' Zas Ile Ile Gln Gly Ser 240 Glu Glu Arg Asp Lys Tyr Val Asp Th' Val Ser Thr Lys Ser Ser Leu 245 Arg Arg Ile Ile Ser Glu Ala Ile Glu Leu Ser Lys His Pro Leu Asp 260 Lys Glu Gln Val Asp Gln Ile Thr Ala Ile Phe Lys 275 2211> LENGTH: 1274 2212> TYPE: PRT 2213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 112 Met Ser Trp Phe Asp Lys Leu Phe Gly Glu Asp Asp Asp Ser Asp Asp 11 Asp Asp Asp His Asp Ser Leu Leu Pro Gln Asp Asp Asp Ser Asp 15 Asp Asp Asp His Asp Ser Leu Leu Pro Gln Asp Asp Asp 11 Asp Asp Asp Asp Asp Asp Asp Asp Ser Asp Asp 11 Asp	Phe	Tyr		Tyr	Asp	Pro	Tyr		Leu	Ala	Ala	Asn		Ala	ГЛа	Ala	
225230235240Glu Glu Arg Asp Lys Tyr Val Asp Thr Val Ser Thr Lys Ser Ser Leu 245235240Arg Arg Ile Ile Ser Glu Ala Ile Glu Leu Ser Lys His Pro Leu Asn 260265Ser Lys His Pro Leu Asn 270Lys Glu Gln Val Asp Gln Ile Thr Ala Ile Phe Lys 275280Ser Lys His Pro Leu Asn 270<210> SEQ ID NO 112 <211> LENGTH: 1274 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus<400> SEQUENCE: 112Met Ser Trp Phe Asp Lys Leu Phe Gly Glu Asp Asn Asp Ser Asn Asp 1Asp Leu Ile His Arg Lys Lys Lys Lys Arg Arg Gln Glu Ser Gln Asn Ile 20Asp Asn Asp His Asp Ser Leu Leu Pro Gln Asn Asn Asp Ile Tyr Ser 40Arg Pro Arg Gly Lys Phe Arg Phe Pro Met Ser Val Ala Tyr Glu Asn 55Glu Asn Val Glu Gln Ser Ala Asp Thr Ile Ser Asp Glu Lys Glu Gln 65Glu Asn Val Glu Gln Ser Lis Asp Ser Arg Ser Gln Lys 90Arg His Arg Arg Arg Arg Asn Gln Thr Thr Glu Glu Gln Asn Tyr Ser 100Glu Gln Arg Gly Asn Ser Lys Ile Ser Gln Gln Ser Ile Lys Tyr Lys 122Arg His Arg Gly Asn Ser Lys Ile Ser Gln Gln Ser Ile Lys Tyr Lys 120Asp His Ser His Tyr His Thr Asn Lys Pro Cly Thr Tyr Val Ser Ala 130His Asn Gly Ile Glu Lys Glu Thr His Lys Pro Lys Thr His Asn Met	Leu		Asp	His	Ile	Glu		Asn	Phe	Asn	Phe		Val	Gln	Ser	Thr	
Arg Arg Ile Ile Ser Glu Ala Ile Glu Leu Ser Lys His Pro Leu Asn 260255Arg Arg Ile Ile Ser Glu Ala Ile Glu Leu Ser Lys His Pro Leu Asn 260265Lys Glu Gln Val Asp Gln Ile Thr Ala Ile Phe Lys 275275<210> SEQ ID NO 112 <211> LENGTH: 1274 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus<400> SEQUENCE: 112Met Ser Trp Phe Asp Lys Leu Phe Gly Glu Asp Asn Asp Ser Asn Asp 10Asp Leu Ile His Arg Lys Lys Lys Arg Arg Gln Glu Ser Gln Asn Ile 20Asp Asn Asp His Asp Ser Leu Leu Pro Gln Asn Asn Asp Ile Tyr Ser 40Arg Pro Arg Gly Lys Phe Arg Phe Pro Met Ser Val Ala Tyr Glu Asn 50Glu Asn Val Glu Gln Ser Ala Asp Thr Ile Ser Asp Glu Lys Glu Gln 80Tyr His Arg Arg Arg Arg Cln Ser His Asp Ser Arg Ser Gln Lys 90Arg His Arg Arg Arg Arg Arg Gln Ser His Asp Ser Arg Ser Gln Lys 90Arg His Arg Arg Arg Arg Asn Gln Thr Thr Glu Glu Gln Asn Tyr Ser 100Glu Gln Arg Gly Asn Ser Lys Ile Ser Gln Gln Ser Ile Lys Tyr Lys 120Asp His Ser His Tyr His Thr Asn Lys Pro Gly Thr Tyr Val Ser Ala 140Ile Asn Gly Ile Glu Lys Glu Thr His Lys Pro Lys Thr His Asn Met		Val	Ile	Tyr	Phe		Asp	Gly	Thr	Val		Ile	Ile	Gln	Gly		
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65 70 75 80 Tyr His Arg Asg Tyr Arg Lys Gln Ser His Asg Ser Arg Ser Gln Lys 95 90 Ser Arg Ser Gln Lys 95 Arg His Arg Arg Arg Arg Arg Arg Arg Gln Lys 100 Ser Gln Thr Thr Glu Glu Gln Asn Tyr Ser 110 Ser 110 Glu Gln Arg Gly Asn Ser Lys 11e Ser Gln Lys 120 Ser Gln Lys 125 Tyr Lys 125 Asg His Ser His Tyr His Thr Asn Lys Pro Gly Thr Tyr Val Ser Ala Ser Ala Ile Asn Gly Ile Glu Lys Glu Thr His Lys Pro Lys Thr His Asn Met	-	50	-	-	-		55					60		-			
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Ala	Ile	Gln	Arg	Ala 325	Ile	Asp	Glu	Met	Tyr 330	Ala	ГÀа	Gln	Ala	Glu 335	Arg
Tyr	Val	Gly	Asp 340	Ser	Ser	Leu	Asn	Asp 345	Asp	Ser	Asp	Leu	Thr 350	Asp	Asn
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Ala	Pro 530	Arg	His	ГЛа	ГЛа	Asp 535	Asp	Gln	Thr	Asn	Leu 540	Ser	Val	Asn	Ser
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Gln	Ser	Lys	Gln	Ala 645	Val	Ser	Glu	Arg	Met 650	Pro	Ala	Ser	Gln	Ala 655	Thr
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Ser	Ser	Val	Ser 740	Glu	Val	Ser	Asp	Ile 745	Thr	Glu	Glu	Ser	Glu 750	Glu	Thr
Thr	His	Pro 755	Asn	Asn	Thr	Ser	Gly 760	Gln	Gln	Asp	Asn	Asp 765	Asp	Gln	Gln
ГЛЗ	Asp 770	Leu	Gln	Ser	Ser	Phe 775	Ser	Asn	Lys	Asn	Glu 780	Asp	Thr	Ala	Asn
Glu 785	Asn	Arg	Pro	Arg	Thr 790	Asn	Gln	Gln	Asp	Val 795	Ala	Thr	Asn	Gln	Ala 800
Val	Gln	Thr	Ser	Lys 805	Pro	Met	Ile	Arg	Lys 810	Gly	Pro	Asn	Ile	Lys 815	Leu
Pro	Ser	Val	Ser 820	Leu	Leu	Glu	Glu	Pro 825	Gln	Val	Ile	Glu	Ser 830	Asp	Glu
Asp	Trp	Ile 835	Thr	Asp	Lys	Lys	Lys 840	Glu	Leu	Asn	Asp	Ala 845	Leu	Phe	Tyr
Phe	Asn 850	Val	Pro	Ala	Glu	Val 855	Gln	Aab	Val	Thr	Glu 860	Gly	Pro	Ser	Val
Thr 865	Arg	Phe	Glu	Leu	Ser 870	Val	Glu	Lys	Gly	Val 875	Lys	Val	Ser	Arg	Ile 880
Thr	Ala	Leu	Gln	Asp 885	Asp	Ile	Lys	Met	Ala 890	Leu	Ala	Ala	Lys	Asp 895	Ile
Arg	Ile	Glu	Ala 900	Pro	Ile	Pro	Gly	Thr 905	Ser	Arg	Val	Gly	Ile 910	Glu	Val
Pro	Asn	Gln 915	Asn	Pro	Thr	Thr	Val 920	Asn	Leu	Arg	Ser	Ile 925	Ile	Glu	Ser
Pro	Ser 930	Phe	ГЛЗ	Asn	Ala	Glu 935	Ser	Lys	Leu	Thr	Val 940	Ala	Met	Gly	Tyr
Arg 945	Ile	Asn	Asn	Glu	Pro 950	Leu	Leu	Met	Asp	Ile 955	Ala	Lys	Thr	Pro	His 960
Ala	Leu	Ile	Ala	Gly 965	Ala	Thr	Gly	Ser	Gly 970	Lys	Ser	Val	Сув	Ile 975	Asn
Ser	Ile	Leu	Met 980	Ser	Leu	Leu	Tyr	Lys 985	Asn	His	Pro	Glu	Glu 990	Leu	Arg
Leu	Leu	Leu	Ile	Asp	Pro	Гла	Met	Va:	l Glu	ı Leı	ı Ala	a Pro	o Ty	yr As	an Gly

_													- CC	ont	cin	lued	1
		995					1	1000					:	100	5		
Leu	Pro 1010		s Le	eu	Val	Ala	Pro 1015		1 11	.e T	hr	Asp	Val 1020		ya	Ala	Ala
Thr	Gln 1025		: Le	eu	Lys	Trp	Ala 1030		1 G]	.u G	lu	Met	Glu 103!		rg	Arg	Tyr
Lys	Leu 1040		e A.	La	His	Tyr	His 1045		l Aı	g A	sn	Ile	Thr 1050		la	Phe	Asn
Lys	Lys 1055		ı Pı	ro	Tyr	Asp	Glu 1060		g Me	et P	ro	Lys	Ile 106!		al	Ile	Val
Ile	Asp 1070		ı L€	∋u	Ala	Asp	Leu 1075		t Me	et M	et	Ala	Pro 1080		ln	Glu	Val
Glu	Gln 1085		: 1]	Le	Ala	Arg	Ile 1090		a G]	n L	уs	Ala	Arg 109!		la	Сүз	Gly
Ile	His 1100		: Le	∋u	Val	Ala	Thr 1109		n Ai	g P	ro	Ser	Val 1110		sn	Val	Ile
Thr	Gly 1115		ı L€	∋u	ГЛа	Ala	Asn 112(e Pi	:0 T	hr	Arg	Ile 112!		la	Phe	Met
Val	Ser 1130		: S€	∍r	Val	Asp	Ser 1135		g Tł	nr I	le	Leu	Asp 1140		er	Gly	Gly
Ala	Glu 1145		j L€	∋u	Leu	Gly	Tyr 1150		γ Αε	sp M	et	Leu	Tyr 115!		eu	Gly	Ser
Gly	Met 1160		ı Lj	វទ	Pro	Ile	Arg 1165		1 G]	.n G	ly	Thr	Phe 1170		al	Ser	Asp
Asp	Glu 1175		e As	₹Þ	Asp	Val	Val 1180		p Pł	ne I	le	Lys	Gln 118!		ln	Arg	Glu
Pro	Asp 1190	-	: Le	∋u	Phe	Glu	Glu 1195	-	s G]	u L.	eu	Leu	Lys 1200		ıув	Thr	Gln
Thr	Gln 1205		G	ln	Asp	Glu	Leu 1210		e As	sp A	ap	Val	Cys 121!		la	Phe	Met
Val	Asn 1220		ιG	Ly	His	Ile	Ser 1225		r Se	er L	eu	Ile	Gln 1230		rg	His	Phe
Gln	Ile 1235	-	ν Т	ŗr	Asn	Arg	Ala 1240		a Ai	g I	le	Ile	Asp 124!		ln	Leu	Glu
Gln	Leu 1250	-	ν Т <u>3</u>	ŗ	Val	Ser	Ser 1255		a As	sn G	ly	Ser	Lys 1260		ro	Arg	Asp
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Thr	Ser	Ile	Th: 20	r G	iy v	Val	Gly 1		Thr 25	Met	Va	al G	lu G	-	I1∈ 30	e Glr	ı Gln
Thr	Ala	Lys 35	Ala	a G	3lu 2	Asn		/al 10	Lys	Gln	Il	le T	hr As 49		Thr	Ası	n Val
Ala	Pro 50	Tyr	Sei	r G	sly v		Thr 1 55	Irp	Met	Gly	Al	la G 6		nr	Gly	Phe	e Val
Val 65	Gly	Asn	Hi	з Т		Ile 70	Ile 1	[hr	Asn	Lys	Hi 75		al Tì	nr	Tyr	Hi	8 Met 80

Lys	Val	Gly	Asp	Glu 85	Leu	Lys	Ala	His	Pro 90	Asn	Gly	Phe	Tyr	Asn 95	Asn
Gly	Gly	Gly	Leu 100	Tyr	Гла	Val	Thr	Lys 105	Ile	Val	Asp	Tyr	Pro 110	Gly	Lys
Glu	Asp	Ile 115	Ala	Val	Val	Gln	Val 120	Glu	Glu	Lys	Ser	Thr 125	Gln	Pro	Lys
Gly	Arg 130	Lys	Phe	Lys	Asp	Phe 135	Thr	Ser	Lys	Phe	Asn 140	Ile	Ala	Ser	Glu
Ala 145	Lys	Glu	Asn	Glu	Pro 150	Ile	Ser	Val	Ile	Gly 155	Tyr	Pro	Asn	Pro	Asn 160
Gly	Asn	Lys	Leu	Gln 165	Met	Tyr	Glu	Ser	Thr 170	Gly	Lys	Val	Leu	Ser 175	Val
Asn	Gly	Asn	Ile 180	Val	Ser	Ser	Asp	Ala 185	Ile	Ile	Gln	Pro	Gly 190	Ser	Ser
Gly	Ser	Pro 195	Ile	Leu	Asn	Ser	Lys 200	His	Glu	Ala	Ile	Gly 205	Val	Ile	Tyr
Ala	Gly 210	Asn	Lys	Pro	Ser	Gly 215	Glu	Ser	Thr	Arg	Gly 220	Phe	Ala	Val	Tyr
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Thr	Ala	Lys 35	Ala	Glu	His	Asn	Val 40	Lys	Leu	Ile	Lys	Asn 45	Thr	Asn	Val
Ala	Pro 50	Tyr	Asn	Gly	Val	Val 55	Ser	Ile	Gly	Ser	Gly 60	Thr	Gly	Phe	Ile
Val 65	Gly	Lys	Asn	Thr	Ile 70	Val	Thr	Asn	Lys	His 75	Val	Val	Ala	Gly	Met 80
Glu	Ile	Gly	Ala	His 85	Ile	Ile	Ala	His	Pro 90	Asn	Gly	Glu	Tyr	Asn 95	Asn
Gly	Gly	Phe	Tyr 100	Гла	Val	ГЛЗ	Гла	Ile 105	Val	Arg	Tyr	Ser	Gly 110	Gln	Glu
Asp	Ile	Ala 115	Ile	Leu	His	Val	Glu 120	Asp	Lys	Ala	Val	His 125	Pro	Lys	Asn
Arg	Asn 130	Phe	Lys	Asp	Tyr	Thr 135	Gly	Ile	Leu	Гла	Ile 140	Ala	Ser	Glu	Ala
Lys 145	Glu	Asn	Glu	Arg	Ile 150	Ser	Ile	Val	Gly	Tyr 155	Pro	Glu	Pro	Tyr	Ile 160
Asn	Lys	Phe	Gln	Met 165	Tyr	Glu	Ser	Thr	Gly 170	ГÀа	Val	Leu	Ser	Val 175	Гла
Gly	Asn	Met	Ile 180	Ile	Thr	Asp	Ala	Phe 185	Val	Glu	Pro	Gly	Asn 190	Ser	Gly
Ser	Ala	Val 195	Phe	Asn	Ser	ГЛа	Tyr 200	Glu	Val	Val	Gly	Val 205	His	Phe	Gly
Gly	Asn	Gly	Pro	Gly	Asn	-	Ser	Thr	Lys	Gly	-	Gly	Val	Tyr	Phe
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Lys Val Gly Asp Arg Ile Thr Ala His Pro Asn Gly Asp Lys Gly Asn Gly Gly Ile Tyr Lys Ile Lys Ser Ile Ser Asp Tyr Pro Gly Asp Glu Asp Ile Ser Val Met Asn Ile Glu Glu Gln Ala Val Glu Arg Gly Pro Lys Gly Phe Asn Phe Asn Glu Asn Val Gln Ala Phe Asn Phe Ala Lys Asp Ala Lys Val Asp Asp Lys Ile Lys Val Ile Gly Tyr Pro Leu Pro Ala Gln Asn Ser Phe Lys Gln Phe Glu Ser Thr Gly Thr Ile Lys Arg Ile Lys Asp As
n Ile Leu Asn Phe Asp Ala Tyr Ile Glu Pro Gly As
n Ser Gly Ser Pro Val Leu Asn Ser Asn Asn Glu Val Ile Gly Val Val Tyr Gly Gly Ile Gly Lys Ile Gly Ser Glu Tyr Asn Gly Ala Val Tyr Phe Thr Pro Gln Ile Lys Asp Phe Ile Gln Lys His Ile Glu Gln <210> SEQ ID NO 117 <211> LENGTH: 240 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 117 Met Asn Lys Asn Val Val Ile Lys Ser Leu Ala Ala Leu Thr Ile Leu Thr Ser Val Thr Gly Ile Gly Thr Thr Leu Val Glu Glu Val Gln Gln Thr Ala Lys Ala Glu Asn Asn Val Thr Lys Val Lys Asp Thr Asn Ile Phe Pro Tyr Thr Gly Val Val Ala Phe Lys Ser Ala Thr Gly Phe Val Val Gly Lys Asn Thr Ile Leu Thr Asn Lys His Val Ser Lys Asn Tyr Lys Val Gly Asp Arg Ile Thr Ala His Pro Asn Ser Asp Lys Gly Asn Gly Gly Ile Tyr Ser Ile Lys Lys Ile Ile Asn Tyr Pro Gly Lys Glu Asp Val Ser Val Ile Gln Val Glu Glu Arg Ala Ile Glu Arg Gly Pro Lys Gly Phe Asn Phe Asn Asp Asn Val Thr Pro Phe Lys Tyr Ala Ala Gly Ala Lys Ala Gly Glu Arg Ile Lys Val Ile Gly Tyr Pro His Pro Tyr Lys Asn Lys Tyr Val Leu Tyr Glu Ser Thr Gly Pro Val Met Ser Val Glu Gly Ser Ser Ile Val Tyr Ser Ala His Thr Glu Ser Gly Asn Ser Gly Ser Pro Val Leu Asn Ser Asn Asn Glu Leu Val Gly Ile His Phe Ala Ser Asp Val Lys Asn Asp Asp Asn Arg Asn Ala Tyr Gly Val

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Thr	Ser	Leu	Gly 20	Phe	Ala	Glu	Asn	Ile 25	Ser	Asn	Gln	Pro	His 30	Ser	Ile
Ala	Lys	Ala 35	Glu	Lys	Asn	Val	Lys 40	Glu	Ile	Thr	Asp	Ala 45	Thr	ГЛа	Glu
Pro	Tyr 50	Asn	Ser	Val	Val	Ala 55	Phe	Val	Gly	Gly	Thr 60	Gly	Val	Val	Val
Gly 65	LÀa	Asn	Thr	Ile	Val 70	Thr	Asn	Lys	His	Ile 75	Ala	Lys	Ser	Asn	Asp 80
Ile	Phe	Lys	Asn	Arg 85	Val	Ser	Ala	His	His 90	Ser	Ser	Lys	Gly	Lys 95	Gly
Gly	Gly	Asn	Tyr 100	Asp	Val	Lys	Asp	Ile 105	Val	Glu	Tyr	Pro	Gly 110	Lys	Glu
Asp	Leu	Ala 115	Ile	Val	His	Val	His 120	Glu	Thr	Ser	Thr	Glu 125	Gly	Leu	Asn
Phe	Asn 130	Гла	Asn	Val	Ser	Tyr 135	Thr	Lys	Phe	Ala	Asp 140	Gly	Ala	ГЛа	Val
Lys 145	Asp	Arg	Ile	Ser	Val 150	Ile	Gly	Tyr	Pro	Lys 155	-	Ala	Gln	Thr	Lys 160
Tyr	Lys	Met	Phe	Glu 165	Ser	Thr	Gly	Thr	Ile 170	Asn	His	Ile	Ser	Gly 175	Thr
Phe	Met	Glu	Phe 180	Asp	Ala	Tyr	Ala	Gln 185	Pro	Gly	Asn	Ser	Gly 190	Ser	Pro
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Gly	Lys 210	Asp	Glu	Ser	Glu	Lys 215	Asn	Phe	Gly	Val	Tyr 220	Phe	Thr	Pro	Gln
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Ser	Phe	Ser	Ser 20	Ile	Thr	Asn	Glu	Val 25	Ser	Ala	Ser	Ser	Ser 30	Phe	Asp
Lys	Gly	Lуя 35	Tyr	Lys	Lys	Gly	Asp 40	Asp	Ala	Ser	Tyr	Phe 45	Glu	Pro	Thr
Gly	Pro 50	Tyr	Leu	Met	Val	Asn 55	Val	Thr	Gly	Val	Asp 60	Gly	Гла	Gly	Asn
Glu	Leu	Leu	Ser	Pro	His	Tyr	Val	Glu	Phe	Pro	Ile	Lya	Pro	Gly	Thr

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Thr Leu	u Ti	hr	Lys	Glu 85	Lys	Ile	Glu	Tyr	Tyr 90	Val	Glu	Trp	Ala	Leu 95	Asp
Ala Thi	rΑ		Tyr 100	Lys	Glu	Phe	Arg	Val 105	Val	Glu	Leu	Asp	Pro 110	Ser	Ala
Lys Ile		lu 15	Val	Thr	Tyr	Tyr	Asp 120	Lys	Asn	Lys	Lys	Lys 125	Glu	Glu	Thr
Lys Sei 13(he	Pro	Ile	Thr	Glu 135		Gly	Phe	Val	Val 140	Pro	Asp	Leu	Ser
Glu His 145	s I	le	Lys	Asn	Pro 150	Gly	Phe	Asn	Leu	Ile 155	Thr	ГЛа	Val	Ile	Ile 160
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Leu Ala	a G	-	Cys 20	Asp	Tyr	Ser	Lys	Pro 25	Glu	Lys	Arg	Ser	Gly 30	Phe	Phe
Tyr Asr	n Ti 31		Phe	Val	Asp	Pro	Met 40	Lys	Asn	Val	Leu	Asp 45	Trp	Leu	Gly
Asn Asr 50	n L	eu	Leu	Asn	Asp	Asn 55	Tyr	Gly	Leu	Ala	Ile 60	Ile	Ile	Leu	Val
Leu Val 65	1 I	le	Arg	Ile	Ile 70	Leu	Leu	Pro	Phe	Met 75	Leu	Ser	Asn	Tyr	Lys 80
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Glu Ly:	s I		Gln 100	Glu	Гла	Val	Lys	Arg 105	Ala	Arg	Thr	Gln	Glu 110	Glu	Lys
Met Ala		la 15	Asn	Gln	Glu	Leu	Met 120	Gln	Val	Tyr	Lys	Lys 125	Tyr	Asp	Met
Asn Pro 130		le	Lys	Ser	Met	Leu 135	Gly	Суз	Leu	Pro	Met 140	Leu	Ile	Gln	Leu
Pro Ile 145	eΙ	le	Met	Gly	Leu 150	Tyr	Phe	Val	Leu	Lys 155	Asp	Gln	Leu	Val	Asp 160
Gly Leu	u Pi	he	Lys	Tyr 165	Pro	His	Phe	Leu	Trp 170	Phe	Asp	Leu	Gly	Arg 175	Pro
Asp Ile	e T	-	Ile 180	Thr	Ile	Ile	Ala	Gly 185	Val	Leu	Tyr	Phe	Ile 190	Gln	Ala
Tyr Val		er 95	Ser	Lys	Thr	Met	Pro 200	Asp	Glu	Gln	Arg	Gln 205	Met	Gly	Tyr
Met Met 210		et	Val	Ile	Ser	Pro 215	Ile	Met	Ile	Ile	Trp 220	Ile	Ser	Leu	Ser
Ser Ala 225	a S	er	Ala	Leu	Gly 230	Leu	Tyr	Trp	Ser	Val 235	Ser	Ala	Ala	Phe	Leu 240
Val Val	1 G	ln	Thr	His 245	Phe	Ala	Asn	Ile	Tyr 250	Tyr	Glu	Гла	Val	Ala 255	Lys
Lys Glu	u V		Gln 260		Phe	Ile	Glu	Ala 265		Glu	Arg	Glu	His 270		Gly
Gly Sei	r A			Lys	Gly	Lys	Asn		Gln	Val	Val	Ser		Lys	Lys

115
445

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Arg	Lys	Ser 35	Thr	Asp	Glu	Asp	Ile 40	Gln	Thr	Asn	Asn	Ile 45	Lys	Met	Arg
Lys	Met 50	Val	Pro	Trp	Ala	Ile 55	Gly	Phe	Phe	Ile	Leu 60	Ile	Leu	Ile	Ile
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Thr	Leu	Leu	Ser 100		Lys	Asp	Asn	Lys 105		Asp	Ser	Glu	Glu 110	Ala	Lys
Val	Tyr	Ile 115		Tyr	Ile	ГЛа	Asp 120		Val	Gly	Leu	Lys 125		Phe	Val
Ser	Asp 130		Гла	Asn	Thr	Val 135		Lys	Leu	Asn	Lys 140		Гла	Thr	Ser
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	Lys	Asn	Gly			Tyr	Ile	Phe			Asn	Met	Ser	Phe	
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Glu	Phe		180 Ser	Gly	Gly	Гла	Lys	185 Lys	Met	Val	Ile	Ala	190 Glu	Ala	Asn
Lys	Val	195 Thr	Pro	Ile	Gly	Asn	200 Phe	Ile	Pro	Gly	Thr	205 Tyr	Arg	Ile	Pro
Ala	210 Met	Lvs	Ser	Thr	Glu	215 Asn	Glv	Asp	Phe	Ala	220 Glv	His	Leu	Lys	Phe
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				245					250					255	
			260					265					270	Leu	
Asb	Ser	Ser 275	Lys	Lys	Val	Thr	Ile 280	Asn	Asp	His	Glu	Met 285	Ala	Phe	Ser
Ser	Ser 290	LÀa	Thr	Tyr	Gly	Pro 295	Tyr	Pro	Gln	Asn	Lуз 300	Asp	Ile	Thr	Ile
Ser 305	Ala	Ser	Gly	Lys	Ala 310	Lys	Asp	Lys	Thr	Phe 315	Thr	Thr	Gln	Thr	Lys 320
Thr	Leu	Lys	Ala	Ser 325	Asp	Leu	Lys	Tyr	Asn 330	Thr	Glu	Ile	Thr	Leu 335	Asn
Phe	Asp	Ser	Glu 340	Asp	Ile	Glu	Asp	Tyr 345	Val	Glu	Lys	Гла	Glu 350	Lys	Glu

Glu	Asn	Ser 355	Leu	Lys	Asn	Lys	Leu 360	Ile	Glu	Phe	Phe	Ala 365	Gly	Tyr	Ser
Leu	Ala 370	Asn	Asn	Ala	Ala	Phe 375	Asn	Gln	Ser	Asp	Phe 380	Asp	Phe	Val	Ser
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Ala	Glu	Lys	His 420	Gly	Asp	ГЛЗ	Ile	Thr 425	Ala	Thr	Val	Arg	Leu 430	Ile	Asn
Glu	Asn	Gly 435	Lys	Gln	Val	Asp	Lys 440	Glu	Tyr	Glu	Leu	Glu 445	Gln	Gly	Ser
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1 Tvr	Ala	His	Ile	5 Ara	Ile	Lvs	Glu	Lvs	10 Arg	Ser	Val	Lvs	Ser	15 Tvr	Met
•			20	Ū		-		25	Ū			-	30	-	
		35	-		Arg		40	-		-	-	45			-
Lys	Glu 50	Glu	Ala	Met	Гла	Ala 55	Leu	Glu	Lys	Met	Ala 60	Pro	Gln	Thr	Ala
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Lys	His	Gln	Arg 100	Val	Val	Leu	Tyr	Ala 105	His	Gly	Gly	Ala	Trp 110	Phe	Gln
Asp	Pro	Leu 115	Lys	Ile	His	Phe	Glu 120	Phe	Ile	Asp	Glu	Leu 125	Ala	Glu	Thr
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Leu	Asn	Gln	Val	Ala 165	Asp	Ser	Lys	Gln	Ile 170	Val	Val	Met	Gly	Asp 175	Ser
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	Thr	Pro	Leu		Asn	Tyr	Lys	Val			Ile	Asn	Gly		
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His	Val 130	Thr	Thr	Thr	Ala	Ala 135	Pro	Ser	Ser	Asn	Gly 140	Arg	Ser	Ile	Ser
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Tyr	Tyr	Val	Phe	Asp 165	Arg	Val	Gly	Gly	Lys 170	Ile	Gly	Ser	Thr	Trp 175	Gly
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Arg 225	Val	Ser	Glu	Met	Asn 230	Tyr	Gly	His	Gly	Ala 235	Gly	Val	Val	Thr	Ser 240
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Asn	Gln	-		Asp	Lys	Leu			Asn	His	Гла	-		Gly	His
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Ser 65	Gln	Lys	Phe	Glu	Glu 70	Arg	Lys	Thr	Gln	Leu 75	Glu	Glu	Thr	Val	Ala 80
	Thr	Lys	Glu	Arg 85	Val	Glu	Gly	Phe	Leu 90	Asn	Lys	Ser	Гла	Asn 95	Glu
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Ala	Asn	Asn 115		Ser	Asp	Thr	Ser 120	_	Glu	Ala	Gln	Glu 125	Ile	Gln	Glu
Ala	-		Glu	Ala	Gln			Ala	Asp	Lys			Ala	Val	Ser
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			180					185					190		
Ser	Ala	Ala 195	Val	Ser	Asn	Glu	Glu 200	Pro	ГЛЗ	Ala	Val	Ala 205	Leu	гла	Ala
Gln	Gln 210	Ala	Ala	Ile	ГЛа	Glu 215	Glu	Ala	Ser	Ala	Asn 220	Asn	Leu	Ser	Asp
Thr 225	Ser	Gln	Glu	Ala	Gln 230	Glu	Val	Gln	Glu	Ala 235	Lys	Lys	Glu	Ala	Gln 240
Ala	Glu	Thr	Asp	Lys 245	Ser	Ala	Ala	Val	Ser 250	Asn	Glu	Glu	Pro	Lys 255	Ala

Val	Ala	Leu	Lys 260	Ala	Gln	Gln	Ala	Ala 265	Ile	Lys	Glu	Glu	Ala 270	Ser	Ala
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Lys	Lys 290	Glu	Ala	Gln	Ala	Glu 295	Lys	Asp	Ser	Asp	Thr 300	Leu	Thr	Lys	Asp
Ala 305	Ser	Ala	Ala	Lys	Val 310	Glu	Val	Ser	Lys	Pro 315	Glu	Ser	Gln	Ala	Glu 320
Arg	Leu	Ala	Asn	Ala 325	Ala	Lys	Gln	Lys	Gln 330	Ala	Lys	Leu	Thr	Pro 335	Gly
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Gln	Ser	Lys	Lys 420	Thr	Thr	Pro	Ser	Asn 425	Lys	Arg	Asn	Ala	Ser 430	Lys	Ala
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Ser	Gln 450	Gly	Ala	Lys	Lys	Gln 455	Ser	Ser	Ser	Ser	Lys 460	Ser	Thr	Gln	Lys
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Gly Asp Asp Met Ser Thr Leu Val Gly Thr Val Leu Ser Gly Phe Glu Tyr Arg Thr Gln Lys Glu Lys Tyr Asp Asn Leu Tyr Lys Phe Phe Lys Asp Asn Glu Glu Lys Tyr Gln Tyr Thr Gly Phe Thr Lys Glu Ala Ile Asn Lys Thr Gln Asn Val Gly Tyr Lys Asn Glu Tyr Phe Tyr Ile Thr Tyr Ser Ser Arg Ser Leu Lys Glu Tyr Arg Lys Tyr Tyr Glu Pro Leu Ile His Lys Asn Asp Lys Glu Phe Lys Glu Gly Met Glu Gln Ala Arg Lys Glu Val Asn Tyr Ala Ala Asn Thr Asp Thr Val Thr Thr Leu Phe Ser Thr Lys Glu As
n Phe Thr Lys Asp As
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Tyr Ser Ann (1) Leu Lyo Gin Gly Coin Ile Thr He Thr Met Ban Ang 195 Giv Thr Thr He Thr He Ap Leu Ser Gin Lyo Leu Clu Lyo Giu Arg 205 Met Cly Glu Ser He Ang (1) Thr Lyo He Ann Lyo He Leu Val Glu 210 Met Lyo 215 Set Clo SEC ID NO 130 Cills LEWOTH: 231 Cills SEC HENR Cills Cills Sec Henr Cills Cills For Ser He Glu Ann Ser Lyo Lyo Leu Lyo Ala Tyr Tyr 40 Ann Cill Pro Ser He Glu Ann Ser Lyo Lyo Leu Lyo Ala Tyr Tyr 40 Ann Cill Pro Ser He Glu Jyo Ann Ser Lyo Lyo Leu Lyo Ala Tyr Tyr 40 Ann Cill Pro Ser He Glu Jyo Ann Ser Lyo Lyo Leu Lyo Ala Tyr Tyr 40 Ann Cill Pro Ser He Glu Jyo Ann Ser Lyo Lyo Leu Lyo Ala Tyr Tyr 40 Ann Ann He Ala Leu He Me Tyr Lyo Ann Thr Gly Tyr He Ser Phe 50 Cills Cill Pro Ser He Glu Jyo Ann Ser Lyo Cill His Tyr His Thr Cilly 70 Ann Ann He Ala Leu He Me Thr Thr Er Ala Men Anp Lyo 110 Glu Qi Ma Lyo Tyr Ser He Gly Lyo App Lyo Cill His Tyr His Thr 110 Glu Qi Ma Lyo Tyr Ser He Gly Lyo App Lyo Cill He Thr 110 Glu Qi Yi Ang Tyr Ang Phe Phe Pro Phe Lyo Cill Ang His Thr 110 Glu Qi Yi Ang Tyr Ang Phe Phe Pro Phe Lyo Lie Ang Lyo Cill Ang 145 Cills Cill Cills Cills Cill Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Cills Ci																			
195 200 205 Net GLy GLU Ser Ile Asp GLY Thr Lys Tle Asn Lys Tle Leu Val GLU 210 225 ************************************	Tyr	Ser	Asn	-	Leu	Гла	Gln	Gly		Ile	Thr	Ile	Thr		Asn	Азр			
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50 55 60 11e Gln Pro Ser Ile Lys Phe Met Asn Ile Ile Asp Gly Asn Ser Val 70 80 Asn Asn Ile Ala Leu Ile Gly Lys Asp Lys Gln His Tyr His Thr Gly 95 95 Val His Arg Asn Leu Asn Ile Phe Tyr Val Asn Glu Asp Lys Arg Phe 100 110 Glu Gly Ala Lys Tyr Ser Ile Gly Gly Ile Thr Ser Ala Asn Asp Lys 115 120 Ala Val Asp Leu Ile Ala Glu Ala Arg Val Ile Lys Glu Asp His Thr 130 135 Ala Val Asp Leu Ile Ala Glu Ala Arg Val Ile Lys Glu Asp Lys Glu Ala 150 160 Gly Glu Tyr Asp Tyr Asp Phe Phe Pro Phe Lys Ile Asp Lys Glu Ala 160 160 Met Ser Leu Lys Glu Ile Asp Phe Lys Leu Arg Lys Tyr Leu Ile Asp 180 170 Net Ser Leu Lys Glu Jur Styr Thr Phe Glu Leu Asp Lys Lys Lys Leu Gln 210 190 Lys Tyr Tyr Gly Lys Tyr Thr Phe Glu Leu Asp Lys Lys Leu Gln 220 200 Glu Asp Arg Met Ser Asp Val Ile Asn Val Thr Asp Ile Asp Arg Ile 210 230 <210 > SEQ ID NO 131 <211 > LENGTH: 356 230 <212 > TYE: PRT 230 <213 > ORGANISM: Staphylococcus aureus 400 > EQUENCE: 131 Met Lys Met Arg Thr Ile Ala Lys Thr Ser Leu Ala Leu Gly Leu Leu 10 15 Thr Thr Gly Ala Ile Thr Val Thr Thr Gln Ser Val Lys Ala Glu Lys	Lys	Pro		Val	Ile	Ser	Glu		Ser	Lys	Lys	Leu		Ala	Tyr	Tyr			
65 70 75 80 Asm Asn Ile Ala Leu Ile Gly Lys Asp Lys Gln His Tyr His Thr Gly 95 90 Nam Asp Tyr Bar Leu Asp Ile Phe Tyr Val Asp Glu Asp Lys Arg Phe 100 Glu Gly Ala Lys Tyr Ser Ile Gly Gly Ile Thr Ser Ala Asp Asp Lys 115 110 100 Glu Gly Ala Lys Tyr Ser Ile Gly Gly Ile Thr Ser Ala Asp Asp Lys 115 110 Ala Val Asp Leu Ile Ala Glu Ala Arg Val Ile Lys Glu Asp His Thr 130 115 Gly Glu Tyr Asp Tyr Asp Phe Phe Pro Phe Lys Ile Asp Lys Glu Ala 160 160 Met Ser Leu Lys Glu Ile Asp Phe Lys Leu Arg Lys Tyr Leu Ile Asp 176 116 Asn Tyr Gly Leu Tyr Gly Glu Met Ser Thr Gly Lys Ile Thr Val Lys 190 190 Lys Lys Tyr Tyr Gly Lys Tyr Thr Phe Glu Leu Asp Lys Lys Lys Leu Gln 205 190 Glu Asp Arg Met Ser Asp Val Ile Asp Val Thr Asp Ile Asp Arg Ile 210 210 Sec ID No 131 230 212> SEQ ID No 131 230 212> TPF: PRT 213 213> ORGANISM: Staphylococccus aureus <400> SEQUENCE: 131 Met Lys Met Arg Thr Ile Ala Lys Thr Ser Leu Ala Leu Gly Leu Leu 15 Thr Thr Gly Ala Ile Thr Val Thr Thr Gln Ser Val Lys Ala Glu Lys	Asn		Pro	Ser	Ile	Glu	-	Lys	Asn	Val	Thr	-	Tyr	Ile	Ser	Phe			
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115120125Ala Val Asp Leu Ile Ala Glu Ala Arg Val Ile Lys Glu Asp His Thr 130135Gly Glu Tyr Asp Tyr Asp Phe Phe Pro Phe Lys Ile Asp Lys Glu Ala 145145Met Ser Leu Lys Glu Ile Asp Phe Lys Leu Arg Lys Tyr Leu Ile Asp 165Asn Tyr Gly Leu Tyr Gly Glu Met Ser Thr Gly Lys Ile Thr Val Lys 180Lys Lys Tyr Tyr Gly Lys Tyr Thr Phe Glu Leu Asp Lys Lys Lys Leu Gln 200Glu Asp Arg Met Ser Asp Val Ile Asn Val Thr Asp Ile Asp Arg Ile 210Clu Ile Lys Val Leu Lys Ala 220SEQ ID NO 131 <211> LENGTH: 356 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus<400> SEQUENCE: 131Met Lys Met Arg Thr Ile Ala Lys Thr Ser Leu Ala Leu Gly Leu Leu 10115Thr Gly Ala Ile Thr Val Thr Thr Gln Ser Val Lys Ala Glu Lys	Val	His	Arg		Leu	Asn	Ile	Phe	-	Val	Asn	Glu	Asp	-	Arg	Phe			
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Ile	Gln	Ser 35	Thr	Lys	Val	Asp	Lys 40	Val	Pro	Thr	Leu	Lys 45	Ala	Glu	Arg
Leu	Ala 50	Met	Ile	Asn	Ile	Thr 55	Ala	Gly	Ala	Asn	Ser 60	Ala	Thr	Thr	Gln
Ala 65	Ala	Asn	Thr	Arg	Gln 70	Glu	Arg	Thr	Pro	Lys 75	Leu	Glu	Lys	Ala	Pro 80
Asn	Thr	Asn	Glu	Glu 85	ГЛЗ	Thr	Ser	Ala	Ser 90	Lys	Ile	Glu	Lys	Ile 95	Ser
Gln	Pro	Lys	Gln 100	Glu	Glu	Gln	Lys	Thr 105	Leu	Asn	Ile	Ser	Ala 110	Thr	Pro
Ala	Pro	Lys 115	Gln	Glu	Gln	Ser	Gln 120	Thr	Thr	Thr	Glu	Ser 125	Thr	Thr	Pro
Lys	Thr 130		Val	Thr	Thr	Pro 135	Pro	Ser	Thr	Asn	Thr 140		Gln	Pro	Met
Gln 145		Thr	Lys	Ser	Asp 150		Pro	Gln	Ser	Pro 155		Ile	Lys	Gln	Ala 160
	Thr	Asp	Met	Thr 165		Lys	Tyr	Glu	Asp 170		Arg	Ala	Tyr	Tyr 175	
Lys	Pro	Ser			Phe	Glu	Lys			Gly	Phe	Met			Pro
Trp	Thr		180 Val	Arg	Phe	Met	Asn	185 Val	Ile	Pro	Asn	-	190 Phe	Ile	Tyr
Lys	Ile	195 Ala	Leu	Val	Gly	Lys	200 Asp	Glu	Lys	Lys	Tyr	205 Lys	Asp	Gly	Pro
Tyr	210 Asp	Asn	Ile	Asp	Val	215 Phe	Ile	Val	Leu	Glu	220 Asp	Asn	Lys	Tyr	Gln
225	-			-	230		Gly			235	-		-	-	240
				245			Ser		250					255	
			260					265		-	-	_	270		-
		275					Glu 280					285			
Ser	Leu 290	Lys	Glu	Leu	Asp	Phe 295	Гла	Leu	Arg	Lys	Gln 300	Leu	Ile	Glu	Lys
His 305	Asn	Leu	Tyr	Gly	Asn 310	Met	Gly	Ser	Gly	Thr 315	Ile	Val	Ile	ГЛЗ	Met 320
Lys	Asn	Gly	Gly	Lуя 325	Tyr	Thr	Phe	Glu	Leu 330	His	ГЛа	ГЛа	Leu	Gln 335	Glu
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Leu Ser Ser Thr Lys Val Glu Ala Pro Gln Ser Thr Pro Pro Ser Thr 35 40 45

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Гла	Ile 50	Glu	Ala	Pro	Gln	Ser 55	Lys	Pro	Asn	Ala	Thr 60	Thr	Pro	Pro	Ser
Thr 65	Lys	Val	Glu	Ala	Pro 70	Gln	Gln	Thr	Ala	Asn 75	Ala	Thr	Thr	Pro	Pro 80
Ser	Thr	Lys	Val	Thr 85	Thr	Pro	Pro	Ser	Thr 90	Asn	Thr	Pro	Gln	Pro 95	Met
Gln	Ser	Thr	Lys 100	Ser	Asp	Thr	Pro	Gln 105	Ser	Pro	Thr	Thr	Lys 110	Gln	Val
Pro	Thr	Glu 115	Ile	Asn	Pro	Lys	Phe 120	Lys	Asp	Leu	Arg	Ala 125	Tyr	Tyr	Thr
ГЛЗ	Pro 130	Ser	Leu	Glu	Phe	Lys 135	Asn	Glu	Ile	Gly	Ile 140	Ile	Leu	Гλа	Lys
Trp 145	Thr	Thr	Ile	Arg	Phe 150	Met	Asn	Val	Val	Pro 155	Asp	Tyr	Phe	Ile	Tyr 160
Lys	Ile	Ala	Leu	Val 165	Gly	Lys	Asp	Asp	Lys 170	Lys	Tyr	Gly	Glu	Gly 175	Val
His	Arg	Asn	Val 180	Asp	Val	Phe	Val	Val 185	Leu	Glu	Glu	Asn	Asn 190	Tyr	Asn
Leu	Glu	Lys 195	Tyr	Ser	Val	Gly	Gly 200	Ile	Thr	Lys	Ser	Asn 205	Ser	Lys	Lys
Val	Asp 210	His	Lys	Ala	Gly	Val 215	Arg	Ile	Thr	Lys	Glu 220	Asp	Asn	Lys	Gly
Thr 225	Ile	Ser	His	Asp	Val 230	Ser	Glu	Phe	Lys	Ile 235	Thr	Lys	Glu	Gln	Ile 240
Ser	Leu	Lys	Glu	Leu 245	Asp	Phe	Lys	Leu	Arg 250	Lys	Gln	Leu	Ile	Glu 255	Lys
Asn	Asn	Leu	Tyr 260	Gly	Asn	Val	Gly	Ser 265	Gly	Lys	Ile	Val	Ile 270	Гла	Met
Lys	Asn	Gly 275	Gly	Lys	Tyr	Thr	Phe 280	Glu	Leu	His	Lys	Lys 285	Leu	Gln	Glu
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His	Lys	Ala 35	Lys	Tyr	Glu	Asn	Val 40	Thr	Lys	Asp	Ile	Phe 45	Asp	Leu	Arg
Asp	Tyr 50	Tyr	Ser	Gly	Ala	Ser 55	Гла	Glu	Leu	Lys	Asn 60	Val	Thr	Gly	Tyr
Arg 65	Tyr	Ser	Гла	Gly	Gly 70	Lys	His	Tyr	Leu	Ile 75	Phe	Asp	Гла	Asn	Arg 80
Lys	Phe	Thr	Arg	Val 85	Gln	Ile	Phe	Gly	Lys 90	Asp	Ile	Glu	Arg	Phe 95	Lys
Ala	Arg	Lys	Asn	Pro	Gly	Leu	Aab	Ile	Phe	Val	Val	Lys	Glu	Ala	Glu

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Asn	Arg	Asn 115	Gly	Thr	Val	Phe	Ser 120	Tyr	Gly	Gly	Val	Thr 125	Lys	Lys	Asn
Gln	Asp 130	Ala	Tyr	Tyr	Asp	Tyr 135	Ile	Asn	Ala	Pro	Arg 140	Phe	Gln	Ile	Lys
Arg 145	Asp	Glu	Gly	Asp	Gly 150	Ile	Ala	Thr	Tyr	Gly 155	Arg	Val	His	Tyr	Ile 160
Tyr	Lys	Glu	Glu	Ile 165	Ser	Leu	Lys	Glu	Leu 170	Asp	Phe	Lys	Leu	Arg 175	Gln
Tyr	Leu	Ile	Gln 180	Asn	Phe	Asp	Leu	Tyr 185	Lys	ГÀа	Phe	Pro	Lys 190	Asp	Ser
ГЛа	Ile	Lys 195	Val	Ile	Met	Lya	Asp 200	Gly	Gly	Tyr	Tyr	Thr 205	Phe	Glu	Leu
Asn	Lys 210	Lys	Leu	Gln	Thr	Asn 215	Arg	Met	Ser	Asp	Val 220	Ile	Asp	Gly	Arg
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Ala	Thr	Gly	Val 20	Ile	Thr	Thr	Glu	Ser 25	Gln	Thr	Val	Lys	Ala 30	Ala	Glu
Ser	Thr	Gln 35	Gly	Gln	His	Asn	Tyr 40	Lys	Ser	Leu	Lys	Tyr 45	Tyr	Tyr	Ser
Lys	Pro 50	Ser	Ile	Glu	Leu	Lys 55	Asn	Leu	Asp	Gly	Leu 60	Tyr	Arg	Gln	Lys
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Val	Gly	Leu	Leu	Gly 85	Lys	Asp	Ile	Glu	Lys 90	Tyr	Pro	Gln	Gly	Glu 95	His
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Arg	Gln	Tyr 115	Ser	Ile	Gly	Gly	Leu 120	Ser	Гла	Thr	Asn	Ser 125	ГÀа	Glu	Phe
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Glu 145	Lys	Ser	Lys	Asp	Ser 150	Lys	Phe	Lys	Ile	Thr 155	Lys	Glu	Glu	Ile	Ser 160
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Pro	His 210	Arg	Met	Gly	Asp	Thr 215	Ile	Asp	Gly	Thr	Lys 220	Ile	Lys	Glu	Ile
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 Glu Asn Tyr Asn Gly Ser Asn Val Val Arg
 Phe Asn Gln Glu Asn Gln

 65
 70
 75
 80
 Asn His Gln Leu Phe Leu Leu Gly Lys Asp Lys Glu Lys Tyr Lys Glu Gly Ile Glu Gly Lys Asp Val Phe Val Val Lys Glu Leu Ile Asp Pro Asn Gly Arg Leu Ser Thr Val Gly Gly Val Thr Lys Lys Asn Asn Lys Ser Ser Glu Thr As
n Thr His Leu Phe Val As
n Lys Val Tyr Gly Gly $% \left({\left({{{\left({{{\left({{{}} \right)}} \right)}} \right)}} \right)$ Asn Leu Asp Ala Ser Ile Asp Ser Phe Ser Ile Asn Lys Glu Glu Val Ser Leu Lys Glu Leu Asp Phe Lys Ile Arg Gln His Leu Val Lys Asn Tyr Gly Leu Tyr Lys Gly Thr Thr Lys Tyr Gly Lys Ile Thr Ile Asn Leu Lys Asp Gly Glu Lys Gln Glu Ile Asp Leu Gly Asp Lys Leu Gln Phe Glu Arg Met Gly Asp Val Leu Asn Ser Lys Asp Ile Asn Lys Ile Glu Val Thr Leu Lys Gln Ile <210> SEQ ID NO 136 <211> LENGTH: 232 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 136 Met Lys Phe Thr Val Ile Ala Lys Ala Ile Phe Ile Leu Gly Ile Leu Thr Thr Ser Val Met Ile Thr Glu Asn Gln Ser Val Asn Ala Lys Gly Lys Tyr Glu Lys Met Asn Arg Leu Tyr Asp Thr Asn Lys Leu His Gln Tyr Tyr Ser Gly Pro Ser Tyr Glu Leu Thr Asn Val Ser Gly Gln Ser Gln Gly Tyr Tyr Asp Ser Asn Val Leu Leu Phe Asn Gln Gln Asn Gln Lys Phe Gl
n Val Phe Leu Leu Gly Lys Asp
 Glu Asn Lys Tyr Lys Glu

												0011	CIII	ucu	
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Asp	Gly	Arg 115	Ile	Phe	Ser	Val	Ser 120	Gly	Val	Thr	Lys	Lys 125	Asn	Val	Lys
Ser	Ile 130	Phe	Glu	Ser	Leu	Arg 135	Thr	Pro	Asn	Leu	Leu 140	Val	Lys	Lys	Ile
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Glu	Glu	Val	Ser	Leu 165	Гла	Glu	Leu	Asp	Phe 170	Lys	Ile	Arg	Lys	Leu 175	Leu
Ile	Lys	Lys	Tyr 180	Lys	Leu	Tyr	Glu	Gly 185	Ser	Ala	Asp	Lys	Gly 190	Arg	Ile
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ГЛа	Leu 210	Asp	Phe	Glu	Arg	Met 215	Ala	Asp	Val	Ile	Asn 220	Ser	Glu	Gln	Ile
Lys 225	Asn	Ile	Glu	Val	Asn 230	Leu	Lys								
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Glu	Leu	Asp 35		Thr	Gln	Arg	Lys 40		Tyr	Ile	Asn	Met 45	Leu	His	Gln
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Glu 65	Asp	Tyr	Tyr	Gly	Ser 70	Asn	Val	Leu	Asn	Phe 75	Lys	Gln	Arg	Asn	Lys 80
Ala	Phe	Lys	Val	Phe 85	Leu	Leu	Gly	Asp	Asp 90	Lys	Asn	Lys	Tyr	Lys 95	Glu
Lys	Thr	His	Gly 100		Asp			105	Val	Pro	Glu	Leu	Ile 110	Asp	Ile
Lys	Gly	Gly 115			Ser				Ile	Thr	Lys	Lys 125		Val	Arg
Ser	Val 130		Gly	Phe	Val	Ser 135		Pro	Ser	Leu	Gln 140		Lys	Lys	Val
Asp 145	Ala	Lys	Asn	Gly	Phe 150	Ser	Ile	Asn	Glu	Leu 155	Phe	Phe	Ile	Gln	Lys 160
Glu	Glu	Val	Ser	Leu 165	Lys	Glu	Leu	Asp	Phe 170	Lys	Ile	Arg	Lys	Leu 175	Leu
Ile	Glu	Lys	Tyr 180	Arg	Leu	Tyr	Lys	Gly 185	Thr	Ser	Aap	Lys	Gly 190	Arg	Ile
Val	Ile	Asn 195	Met	Lys	Asp	Glu	Lys 200	Lys	His	Glu	Ile	Asp 205	Leu	Ser	Glu
Lya	Leu 210		Phe	Glu	Arg	Met 215		Asp	Val	Met	Asp 220		Гла	Gln	Ile
Lys 225		Ile	Glu	Val	Asn 230		Asn				_20				
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Asn Gln Lys Ser Val 35	Asn Lys His 40	Asp Lys Glu	Ala Leu Tyr 45	Arg Tyr
Tyr Thr Gly Lys Thr 50	Met Glu Met 55	Lys Asn Ile	Ser Ala Leu 60	Lys His
Gly Lys Asn Asn Leu 65	Arg Phe Lys 70	Phe Arg Gly 75	Ile Lys Ile	Gln Val 80
Leu Leu Pro Gly Asn 85	Asp Lys Ser	Lys Phe Gln 90	Gln Arg Ser	Tyr Glu 95
Gly Leu Asp Val Phe 100	Phe Val Glr	Glu Lys Arg 105	Asp Lys His 110	
Phe Tyr Thr Val Gly 115	Gly Val Ile 120		Lys Thr Ser 125	Gly Val
Val Ser Ala Pro Ile 130	Leu Asn Ile 135	e Ser Lys Glu	Lys Gly Glu 140	Asp Ala
Phe Val Lys Gly Tyr 145	Pro Tyr Tyr 150	Ile Lys Lys 155	Glu Lys Ile	Thr Leu 160
Lys Glu Leu Asp Tyr 165	Lys Leu Arg	Lys His Leu 170	Ile Glu Lys	Tyr Gly 175
Leu Tyr Lys Thr Ile 180	Ser Lys Asp	Gly Arg Val 185	Lys Ile Ser 190	Leu Lys
Asp Gly Ser Phe Tyr 195	Asn Leu Asp 200		Lys Leu Lys 205	Phe Lys
Tyr Met Gly Glu Val 210	Ile Glu Ser 215	Lys Gln Ile	Lys Asp Ile 220	Glu Val
Asn Leu Lys 225				
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Leu Glu Val Arg Ser 35	Gln Ala Thr 40	Gln Asp Leu	Ser Glu Tyr 45	Tyr Asn
Arg Pro Phe Phe Glu 50	Tyr Thr Asr 55	Gln Ser Gly	Tyr Lys Glu 60	Glu Gly
Lys Val Thr Phe Thr 65	Pro Asn Tyr 70	Gln Leu Ile 75	Asp Val Thr	Leu Thr 80
Gly Asn Glu Lys Gln 85	Asn Phe Gly	Glu Asp Ile 90	Ser Asn Val	Asp Ile 95

Phe Val Val Arg Glu Asn Ser Asp Arg Ser Gly Asn Thr Ala Ser Ile Gly Gly Ile Thr Lys Thr Asn Gly Ser Asn Tyr Ile Asp Lys Val Lys Asp Val Asn Leu Ile Ile Thr Lys Asn Ile Asp Ser Val Thr Ser Thr Ser Thr Ser Ser Thr Tyr Thr Ile Asn Lys Glu Glu Ile Ser Leu Lys Glu Leu Asp Phe Lys Leu Arg Lys His Leu Ile Asp Lys His Asn Leu Tyr Lys Thr Glu Pro Lys Asp Ser Lys Ile Arg Ile Thr Met Lys Asp Gly Gly Phe Tyr Thr Phe Glu Leu Asn Lys Lys Leu Gln Thr His Arg Met Gly Asp Val Ile Asp Gly Arg Asn Ile Glu Lys Ile Glu Val Asn Leu <210> SEO ID NO 140 <211> LENGTH: 116 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEOUENCE: 140 Met Lys Phe Lys Lys Tyr Ile Leu Thr Gly Thr Leu Ala Leu Leu Leu Ser Ser Thr Gly Ile Ala Thr Ile Glu Gly Asn Lys Ala Asp Ala Ser Ser Leu Asp Lys Tyr Leu Thr Glu Ser Gln Phe His Asp Lys Arg Ile Ala Glu Glu Leu Arg Thr Leu Leu Asn Lys Ser Asn Val Tyr Ala Leu Ala Ala Gly Ser Leu Asn Pro Tyr Tyr Lys Arg Thr Ile Met Met Asn Glu Tyr Arg Ala Lys Ala Ala Leu Lys Lys Asn Asp Phe Val Ser Met Ala Asp Ala Lys Val Ala Leu Glu Lys Ile Tyr Lys Glu Ile Asp Glu Ile Ile Asn Arg <210> SEQ ID NO 141 <211> LENGTH: 203 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 141 Met Phe Lys Lys Tyr Asp Ser Lys Asn Ser Ile Val Leu Lys Ser Ile Leu Ser Leu Gly Ile Ile Tyr Gly Gly Thr Phe Gly Ile Tyr Pro Lys Ala Asp Ala Ser Thr Gln Asn Ser Ser Ser Val Gln Asp Lys Gln Leu

Gln Lys Val Glu Glu Val Pro Asn Asn Ser Glu Lys Ala Leu Val Lys 50 55 60

Lys Leu Tyr Asp Arg Tyr Ser Lys Asp Thr Ile Asn Gly Lys Ser Asn 65 70 75 80 Lys Ser Arg Asn Trp Val Tyr Ser Glu Arg Pro Leu Asn Glu Asn Gln Val Arg Ile His Leu Glu Gly Thr Tyr Thr Val Ala Gly Arg Val Tyr Thr Pro Lys Arg Asn Ile Thr Leu Asn Lys Glu Val Val Thr Leu Lys Glu Leu Asp His Ile Ile Arg Phe Ala His Ile Ser Tyr Gly Leu Tyr Met Gly Glu His Leu Pro Lys Gly Asn Ile Val Ile Asn Thr Lys Asp Gly Gly Lys Tyr Thr Leu Glu Ser His Lys Glu Leu Gln Lys Asp Arg Glu Asn Val Lys Ile Asn Thr Ala Asp Ile Lys Asn Val Thr Phe Lys Leu Val Lys Ser Val Asn Asp Ile Glu Gln Val 195 200 <210> SEQ ID NO 142 <211> LENGTH: 146 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEOUENCE: 142 Met Asn Thr Lys Tyr Phe Leu Ala Ala Gly Ala Val Ile Thr Thr Leu Ala Leu Gly Ala Cys Gly Asn Ser Asn Ser Gln Asp Gln Gly Asn Lys Thr Glu Gln Lys Thr Lys Ser Glu Asp Ser Asn Val Lys Thr Asp Lys Thr Lys His Leu Thr Gly Thr Phe Ser Ser Lys Asn Gly Glu Thr Val Glu Gly Lys Ala Glu Ile Lys Asn Gly Lys Leu Met Leu Thr Asn Tyr Lys Ser Ser Lys Gly Pro Asp Leu Tyr Val Tyr Leu Thr Lys As
n Gly Asp Ile Lys Asn Gly Lys Glu Ile Ala Met Val Asp Tyr Asp Lys Glu Lys Gln Thr Phe Asp Leu Lys Asn Val Asp Leu Ser Lys Tyr Asp Glu Val Thr Ile Tyr Cys Lys Lys Ala His Val Ile Phe Gly Gly Ala Lys Leu Lys <210> SEQ ID NO 143 <211> LENGTH: 619 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 143 Met Pro Lys Asn Lys Ile Leu Ile Tyr Leu Leu Ser Thr Thr Leu Val Leu Pro Thr Leu Val Ser Pro Thr Ala Tyr Ala Asp Thr Pro Gln Lys

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Asp	Glu 50	Thr	Ser	Lys	Asp	Thr 55	Thr	Ser	Lys	Asp	Ile 60	Asp	Lys	Ala	Asp
Lys 65	Asn	Asn	Thr	Ser	Asn 70	Gln	Asp	Asn	Asn	Asp 75	Lys	Lys	Phe	Гла	Thr 80
Ile	Asp	Aap	Ser	Thr 85	Ser	Asp	Ser	Asn	Asn 90	Ile	Ile	Asp	Phe	Ile 95	Tyr
LYa	Asn	Leu	Pro 100	Gln	Thr	Asn	Ile	Asn 105	Gln	Leu	Leu	Thr	Lys 110	Asn	Lys
Tyr	Aab	Asp 115	Asn	Tyr	Ser	Leu	Thr 120	Thr	Leu	Ile	Gln	Asn 125	Leu	Phe	Asn
Leu	Asn 130	Ser	Asp	Ile	Ser	Asp 135	Tyr	Glu	Gln	Pro	Arg 140	Asn	Gly	Glu	Lys
Ser 145	Thr	Asn	Asp	Ser	Asn 150	Lys	Asn	Ser	Asp	Asn 155	Ser	Ile	Lys	Asn	Asp 160
Thr	Asb	Thr	Gln	Ser 165	Ser	Lys	Gln	Aab	Lys 170	Ala	Asp	Asn	Gln	Lys 175	Ala
Pro	Lys	Ser	Asn 180	Asn	Thr	Lys	Pro	Ser 185	Thr	Ser	Asn	Lys	Gln 190	Pro	Asn
Ser	Pro	Lys 195	Pro	Thr	Gln	Pro	Asn 200	Gln	Ser	Asn	Ser	Gln 205	Pro	Ala	Ser
Asp	Asp 210	ràa	Ala	Asn	Gln	Lys 215	Ser	Ser	Ser	rÀa	Asp 220	Asn	Gln	Ser	Met
Ser 225	Asp	Ser	Ala	Leu	Asp 230	Ser	Ile	Leu	Asb	Gln 235	Tyr	Ser	Glu	Asp	Ala 240
LYs	Lys	Thr	Gln	Lys 245	Asp	Tyr	Ala	Ser	Gln 250	Ser	Lys	Lys	Asp	Lys 255	Asn
Glu	Lys	Ser	Asn 260	Thr	Lys	Asn	Pro	Gln 265	Leu	Pro	Thr	Gln	Asp 270	Glu	Leu
Lys	His	Lys 275	Ser	Lys	Pro	Ala	Gln 280	Ser	Phe	Asn	Asn	Asp 285	Val	Asn	Gln
Lys	Asp 290	Thr	Arg	Ala	Thr	Ser 295	Leu	Phe	Glu	Thr	Asp 300	Pro	Ser	Ile	Ser
Asn 305	Asn	Asp	Asp	Ser	Gly 310	Gln	Phe	Asn	Val	Val 315	Asp	Ser	Гла	Asp	Thr 320
Arg	Gln	Phe	Val	Lys 325	Ser	Ile	Ala	Lys	Asp 330	Ala	His	Arg	Ile	Gly 335	Gln
Asp	Asn	Asp	Ile 340	Tyr	Ala	Ser	Val	Met 345	Ile	Ala	Gln	Ala	Ile 350	Leu	Glu
Ser	Asp	Ser 355	Gly	Arg	Ser	Ala	Leu 360	Ala	Lys	Ser	Pro	Asn 365	His	Asn	Leu
Phe	Gly 370	Ile	Lys	Gly	Ala	Phe 375	Glu	Gly	Asn	Ser	Val 380	Pro	Phe	Asn	Thr
Leu 385	Glu	Ala	Aab	Gly	Asn 390	Gln	Leu	Tyr	Ser	Ile 395	Asn	Ala	Gly	Phe	Arg 400
ГЛа	Tyr	Pro	Ser	Thr 405	Lys	Glu	Ser	Leu	Lys 410	Asp	Tyr	Ser	Asp	Leu 415	Ile
Lys	Asn	Gly	Ile 420	Asp	Gly	Asn	Arg	Thr 425	Ile	Tyr	Lys	Pro	Thr 430	Trp	Lys
Ser	Glu	Ala 435	Asp	Ser	Tyr	Lys	Asp 440	Ala	Thr	Ser	His	Leu 445	Ser	Lys	Thr

Tyr	Ala 450	Thr	Asp	Pro	Asn	Tyr 455	Ala	Lys	Lys	Leu	Asn 460	Ser	Ile	Ile	Lys
His 465	Tyr	Gln	Leu	Thr	Gln 470	Phe	Aab	Aab	Glu	Arg 475	Met	Pro	Asp	Leu	Asp 480
Lys	Tyr	Glu	Arg	Ser 485	Ile	Lys	Asp	Tyr	Asp 490	Asp	Ser	Ser	Asp	Glu 495	Phe
Lys	Pro	Phe	Arg 500	Glu	Val	Ser	Asp	Ser 505	Met	Pro	Tyr	Pro	His 510	Gly	Gln
Сув	Thr	Trp 515	Tyr	Val	Tyr	Asn	Arg 520	Met	Lys	Gln	Phe	Gly 525	Thr	Ser	Ile
Ser	Gly 530	Asp	Leu	Gly	Asp	Ala 535	His	Asn	Trp	Asn	Asn 540	Arg	Ala	Gln	Tyr
Arg 545	Asp	Tyr	Gln	Val	Ser 550	His	Thr	Pro	Lys	Arg 555	His	Ala	Ala	Val	Val 560
Phe	Glu	Ala	Gly	Gln 565	Phe	Gly	Ala	Asp	Gln 570	His	Tyr	Gly	His	Val 575	Ala
Phe	Val	Glu	Lys 580	Val	Asn	Ser	Asp	Gly 585	Ser	Ile	Val	Ile	Ser 590	Glu	Ser
Asn	Val	Lys 595	Gly	Leu	Gly	Ile	Ile 600	Ser	His	Arg	Thr	Ile 605	Asn	Ala	Ala
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Leu	Ala	Gly	Cys 20	Thr	Thr	Asp	Lys	Lys 25	Glu	Ile	Lys	Ala	Tyr 30	Leu	Lys
Gln	Val	Asp 35	Lys	Ile	Lys	Asp	Asp 40	Glu	Glu	Pro	Ile	Lys 45	Thr	Val	Gly
Lys	Lys 50	Ile	Ala	Glu	Leu	Asp 55	Glu	Lys	Lys	Lys	Lys 60	Leu	Thr	Glu	Asp
Val 65	Asn	Ser	Lys	Asp	Thr 70	Ala	Val	Arg	Gly	Lys 75	Ala	Val	Lys	Asp	Leu 80
Ile	Lys	Asn	Ala	_	Asp	Arg	Leu	Ivs							
				85		_		275	Glu 90	Phe	Glu	Lys	Glu	Glu 95	Asp
Ala	Ile	Lys	Lys 100		Glu	Gln		-	90			-		95	-
	Ile Asn	-	100	Ser			Asp	Phe 105	90 Lys	Lys	Ala	Lys	Ser 110	95 His	Val
Aap		Ile 115	100 Asp	Ser Asn	Asp	Val	Asp Lys 120	Phe 105 Arg	90 Lys Lys	Lys Glu	Ala Val	Lys Lys 125	Ser 110 Gln	95 His Leu	Val Asp
Asp Asp	Asn Val	Ile 115 Leu	100 Asp Lys	Ser Asn Glu	Азр Lys	Val Tyr 135	Asp Lys 120 Lys	Phe 105 Arg Leu	90 Lys Lys His	Lys Glu Ser	Ala Val Asp 140	Lys Lys 125 Tyr	Ser 110 Gln Ala	95 His Leu Lys	Val Asp Ala
Asp Asp Tyr 145	Asn Val 130	Ile 115 Leu Lys	100 Asp Lys Ala	Ser Asn Glu Val	Asp Lys Asn 150	Val Tyr 135 Ser	Asp Lys 120 Lys Glu	Phe 105 Arg Leu Lys	90 Lys Lys His Thr	Lys Glu Ser Leu 155	Ala Val Asp 140 Phe	Lys Lys 125 Tyr Lys	Ser 110 Gln Ala Tyr	95 His Leu Lys Leu	Val Asp Ala Asn 160
Asp Asp Tyr 145 Gln	Asn Val 130 Lys	Ile 115 Leu Lys Asp	100 Asp Lys Ala Ala	Ser Asn Glu Val Thr 165	Asp Lys Asn 150 Gln	Val Tyr 135 Ser Gln	Asp Lys 120 Lys Glu Gly	Phe 105 Arg Leu Lys Val	90 Lys Lys His Thr Asn 170	Lys Glu Ser Leu 155 Glu	Ala Val Asp 140 Phe Lys	Lys Lys 125 Tyr Lys Ser	Ser 110 Gln Ala Tyr Lys	95 His Leu Lys Leu Ala 175	Val Asp Ala Asn 160 Ile
Asp Asp Tyr 145 Gln Glu	Asn Val 130 Lys Asn	Ile 115 Leu Lys Asp Asn	100 Asp Lys Ala Ala Tyr 180	Ser Asn Glu Val Thr 165 Lys	Asp Lys Asn 150 Gln Lys	Val Tyr 135 Ser Gln Leu	Asp Lys 120 Lys Glu Gly Lys	Phe 105 Arg Leu Lys Val Glu 185	90 Lys Lys His Thr Asn 170 Val	Lys Glu Ser Leu 155 Glu Ser	Ala Val Asp 140 Phe Lys Asp	Lys Lys 125 Tyr Lys Ser Lys	Ser 110 Gln Ala Tyr Lys Tyr 190	95 His Leu Lys Leu Ala 175 Thr	Val Asp Ala Asn 160 Ile Lys

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 Thr Asp Lys Ile Lys Val Asp Gly Gln Ile Asp Thr Ser Lys Ser Gly
 Gly
 65
 70
 75
 80
 Lys Tyr Gln Ile Lys Tyr His Val Thr Asp Ser Asp Gly Ala Ile Lys 85 90 95 Ile Ser Thr Arg Tyr Ile Glu Val Lys <210> SEQ ID NO 146 <211> LENGTH: 312 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEOUENCE: 146 Met Lys Lys Leu Val Pro Leu Leu Leu Ala Leu Leu Leu Val Ala Ala Cys Gly Thr Gly Gly Lys Gln Ser Ser Asp Lys Ser Asn Gly Lys Leu Lys Val Val Thr Thr Asn Ser Ile Leu Tyr Asp Met Ala Lys Asn Val Gly Gly Asp Asn Val Asp Ile His Ser Ile Val Pro Val Gly Gln Asp Pro His Glu Tyr Glu Val Lys Pro Lys Asp Ile Lys Lys Leu Thr Asp Ala Asp Val Ile Leu Tyr Asn Gly Leu Asn Leu Glu Thr Gly Asn Gly Trp Phe Glu Lys Ala Leu Glu Gln Ala Gly Lys Ser Leu Lys Asp Lys Lys Val Ile Ala Val Ser Lys Asp Val Lys Pro Ile Tyr Leu Asn Gly Glu Glu Gly Asn Lys Asp Lys Gln Asp Pro His Ala Trp Leu Ser Leu Asp Asn Gly Ile Lys Tyr Val Lys Thr Ile Gln Gln Thr Phe Ile Asp Asn Asp Lys Lys His Lys Ala Asp Tyr Glu Lys Gln Gly Asn Lys Tyr Ile Ala Gln Leu Glu Lys Leu Asn Asn Asp Ser Lys Asp Ser Lys Asp Lys Phe Asn Asp Ile Pro Lys Glu Gln Arg Ala Met Ile Thr Ser Glu Gly Ala Phe Lys Tyr Phe Ser Lys Gln Tyr Gly Ile Thr Pro Gly

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Tyr Ile Trp Glu Ile Asn Thr Glu Lys Gln Gly Thr Pro Glu Gln Met Arg Gln Ala Ile Glu Phe Val Lys Lys His Lys Leu Lys His Leu Leu Val Glu Thr Ser Val Asp Lys Lys Ala Met Glu Ser Leu Ser Glu Glu Thr Lys Lys Asp Ile Phe Gly Glu Val Tyr Thr Asp Ser Ile Gly Lys Glu Gly Thr Lys Gly Asp Ser Tyr Tyr Lys Met Met Lys Ser Asn Ile Glu Thr Val His Gly Ser Met Lys <210> SEQ ID NO 147 <211> LENGTH: 646 <212> TYPE: PRT <213> ORGANISM: Staphylococcus aureus <400> SEQUENCE: 147 Met Ser Ser Gln Lys Lys Lys Ile Ser Leu Phe Ala Phe Phe Leu Leu Thr Val Ile Thr Ile Thr Leu Lys Thr Tyr Phe Ser Tyr Tyr Val Asp Phe Ser Leu Gly Val Lys Gly Leu Val Gln Asn Leu Ile Leu Leu Met Asn Pro Tyr Ser Leu Val Ala Leu Val Leu Ser Val Phe Leu Phe Phe Lys Gly Lys Lys Ala Phe Trp Phe Met Phe Ile Gly Gly Phe Leu Leu Thr Phe Leu Leu Tyr Ala Asn Val Val Tyr Phe Arg Phe Phe Ser Asp Phe Leu Thr Phe Ser Thr Leu Asn Gln Val Gly Asn Val Glu Ser Met Gly Gly Ala Val Ser Ala Ser Phe Lys Trp Tyr Asp Phe Val Tyr Phe Ile Asp Thr Leu Val Tyr Leu Phe Ile Leu Ile Phe Lys Thr Lys Trp Leu Asp Thr Lys Ala Phe Ser Lys Lys Phe Val Pro Val Val Met Ala Ala Ser Val Ala Leu Phe Phe Leu Asn Leu Ala Phe Ala Glu Thr Asp Arg Pro Glu Leu Leu Thr Arg Thr Phe Asp His Lys Tyr Leu Val Lys Tyr Leu Gly Pro Tyr Asn Phe Thr Val Tyr Asp Gly Val Lys Thr Ile Glu Asn Asn Gln Gln Lys Ala Leu Ala Ser Glu Asp Asp Leu Thr Lys Val Leu Asn Tyr Thr Lys Gln Arg Gln Thr Glu Pro Asn Pro Glu Tyr Tyr Gly Val Ala Lys Lys Asn Ile Ile Lys Ile His Leu Glu Ser Phe Gln Thr Phe Leu Ile Asn Lys Lys Val Asn Gly Lys Glu Val Thr Pro Phe Leu Asn Lys Leu Ser Ser Gly Lys Glu Gln Phe Thr Tyr Phe

-conti	nued
	iiucu

											-	con	tin	ued	
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Pro	Asn 290	Phe	Phe	His	Gln	Thr 295	Gly	Gln	Gly	Lys	Thr 300	Ser	Asp	Ser	Glu
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Ser	Leu	Lys	Gly	Asp 325	Asn	Thr	Tyr	Gln	Ser 330	Leu	Pro	Ala	Ile	Leu 335	Asp
Gln	Lys	Gln	Gly 340	Tyr	Lys	Ser	Asp	Val 345	Met	His	Gly	Asp	Tyr 350	Lys	Thr
Phe	Trp	Asn 355	Arg	Asp	Gln	Val	Tyr 360	Lys	His	Phe	Gly	Ile 365	Asp	Lys	Phe
Tyr	Asp 370	Ala	Thr	Tyr	Tyr	Asp 375	Met	Ser	Asp	ГÀа	Asn 380	Val	Val	Asn	Leu
Gly 385	Leu	Lys	Asp	ГЛа	Ile 390	Phe	Phe	ГЛа	Asp	Ser 395	Ala	Asn	Tyr	Gln	Ala 400
Lys	Met	Lys	Ser	Pro 405	Phe	Tyr	Ser	His	Leu 410	Ile	Thr	Leu	Thr	Asn 415	His
Tyr	Pro	Phe	Thr 420	Leu	Asp	Glu	ГЛа	Asp 425	Ala	Thr	Ile	Glu	Lys 430	Ser	Asn
Thr	Gly	Asp 435	Ala	Thr	Val	Asp	Gly 440	Tyr	Ile	Gln	Thr	Ala 445	Arg	Tyr	Leu
Asp	Glu 450	Ala	Leu	Glu	Glu	Tyr 455	Ile	Asn	Asp	Leu	Lys 460	Lys	Lys	Gly	Leu
Tyr 465	Asp	Asn	Ser	Val	Ile 470	Met	Ile	Tyr	Gly	Asp 475	His	Tyr	Gly	Ile	Ser 480
Glu	Asn	His	Asn	Asn 485	Ala	Met	Glu	Lys	Leu 490	Leu	Gly	Glu	Гла	Ile 495	Thr
Pro	Ala	Lys	Phe 500	Thr	Asp	Leu	Asn	Arg 505	Thr	Gly	Phe	Trp	Ile 510	Гла	Ile
Pro	Gly	Lys 515	Ser	Gly	Gly	Ile	Asn 520	Asn	Glu	Tyr	Ala	Gly 525	Gln	Val	Asp
Val	Met 530	Pro	Thr	Ile	Leu	His 535	Leu	Ala	Gly	Ile	Asp 540	Thr	Lys	Asn	Tyr
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Pro	Phe	Arg	Asn	Gly 565	Asp	Phe	Ile	Thr	Lys 570	Asp	Tyr	Гла	Tyr	Val 575	Asn
Gly	Lys	Ile	Tyr 580	Ser	Asn	ГÀа	Asn	Asn 585	Glu	Leu	Ile	Thr	Thr 590	Gln	Pro
Ala	Asp	Phe 595	Glu	Lys	Asn	Lys	Lys 600	Gln	Val	Glu	Lys	Asp 605	Leu	Glu	Met
Ser	Asp 610	Asn	Val	Leu	Asn	Gly 615	Asp	Leu	Phe	Arg	Phe 620	Tyr	Lys	Asn	Pro
Asp 625	Phe	Гла	Lys	Val	Asn 630	Pro	Ser	Гла	Tyr	Lys 635	Tyr	Glu	Thr	Gly	Pro 640
Lys	Ala	Asn	Ser	Lys 645	Lys										
625 Lys <210 <212 <212	Ala D> SI L> LI 2> TY	Asn EQ II ENGTI (PE :	Ser D NO H: 1 PRT	Lys 645 148 73	630 Lya		Ser		-	-	Tyr	Glu	Thr	Gly	

<400> SEQUENCE: 148

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Ala	Leu	Phe	Tyr 20	Phe	Val	Ser	Val	Ser 25	Val	Gln	Leu	Tyr	Gln 30	Met	Lys
Ile	Ser	Phe 35	Leu	Pro	Ala	Leu	Gly 40	Phe	Asn	Gln	Ile	Leu 45	Leu	Glu	Arg
Glu	Glu 50	Asp	Gln	Leu	Asn	Ile 55	Met	Asn	Ser	Ala	Thr 60	Glu	Glu	His	His
His 65	Lys	Asp	Tyr	Ile	Lys 70	Leu	Tyr	Asn	Leu	Gly 75	Gly	Gly	Ala	Ala	Lys 80
Lys	Ile	Ala	Ile	Glu 85	Val	Leu	Leu	Gly	Lys 90	Asp	Lys	Val	Ile	Gln 95	Lys
Lys	Tyr	Val	His 100	Ile	Leu	Pro	Ser	Lys 105	Glu	Gly	Tyr	Met	Leu 110	Pro	Ile
Asn	Lys	Asn 115	Val	Tyr	Glu	Glu	Leu 120	Glu	Arg	Thr	Ile	Glu 125	Asn	Asn	Gly
His	Glu 130	Ala	Asp	Leu	Asn	Val 135	Arg	Met	Thr	Tyr	Tyr 140	His	Asn	Val	Ser
Arg 145	Lys	Gln	Gln	Glu	Val 150	Ile	Leu	Lys	Gly	Gln 155	Ile	Asp	Arg	Phe	Asn 160
	Tyr	Asn	Asn	Lys 165	Glu	Ile	Tyr	Asp	Leu 170	Gln	Phe	Ile			
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Gln	Leu	Trp	His 20	Ser	Asn	His	Ala	Asn 25	Ala	Leu	Val	Thr	Glu 30	Ser	Gly
Ala	Asn	Asp 35	Thr	Lys	Gln	Phe	Thr 40	Glu	Ile	Val	Ser	Glu 45	Glu	ГЛЗ	Val
Ile	Thr 50	Val	Glu	His	Ala	Gln 55	Ile	Asn	Ile	Phe	Gln 60	Ser	Asn	Ser	Asn
Ser 65	Asn	Leu	Met	Glu	Phe 70	Asn	Ile	Leu	Thr	Met 75	Gly	Gly	Lys	Ser	Gly 80
Ala	Met	Val	Gly	Tyr 85	Ser	Glu	Ile	Asp	Ser 90	Ser	His	Phe	Thr	Asp 95	Arg
Aab	Lys	Arg	Val 100	Ile	Arg	Arg	Asp	His 105	Val	ГÀа	Glu	Ala	Gln 110	Ser	Leu
Val	Glu	Asn 115	Tyr	Lys	Asp	Thr	Gln 120	Ser	Ala	Asp	Ala	Arg 125	Met	Lys	Ala
Lys	Gln 130	Lys	Val	Asn	Thr	Leu 135	Ser	Lys	Pro	His	Gln 140	Asn	Tyr	Phe	Asn
Lys 145	Gln	Ile	Asp	ГЛа	Val 150	Tyr	Asn	Gly	Leu	Gln 155	Arg				
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Ala	Gly	Leu	Leu 20	Thr	Gln	Thr	Asn	Asp 25	Ala	ГÀа	Ala	Phe	Phe 30	Ser	Tyr
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Lys	Lys	Leu	Ser	Gln 85	Gly	Asp	Val	Lys	Lys 90	Ala	Val	Val	Arg	Ile 95	Lys
Aap	Gly	Gly	Pro 100	Arg	Asp	Tyr	Tyr	Thr 105	Phe	Asp	Leu	Thr	Arg 110	Pro	Leu
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Ile	Val	Ser	Lys	Tyr 85	Pro	Ile	Lys	Glu	Lys 90	Ile	Gln	His	Val	Phe 95	Lys
Ser	Gly	-	Gly 100		Asp		-			-	-		Val 110	-	Thr
ГЛа	Ile	Glu 115	Гла	Asn	Gly	ГЛа	Asn 120	Val	His	Val	Ile	Gly 125	Thr	His	Thr
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Val	Leu	Tyr 195	Ala	Gly	His	Asn	Ser 200	Thr	Trp	Aap	Pro	Gln 205	Ser	Asn	Ser
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What is claimed is:

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1. A method for eliciting an immune response against a *staphylococcus* bacterium in a subject comprising administering to the subject an effective amount of a staphylococcal ECM-binding protein homologue (Ebh) antigen and a staphylococcal Protein A (SpA) variant, wherein the Ebh antigen comprises amino acids 40-471 of SEQ ID NO: 24 or amino acids 2087-2544 of SEQ ID NO: 24 and the SpA variant comprises at least an amino acid substitution at one or more of positions 9, 10, 36, and 37 in Domain D.

2. The method of claim 1, where the subject is also administered an adjuvant.

3. The method of claim **1**, wherein the composition comprises an adjuvant.

4. The method of claim **1**, wherein the Ebh antigen is 60 coupled to an adjuvant.

5. The method of claim 1, wherein the Ebh antigen formulated in a pharmaceutically acceptable composition.

6. The method of claim 1, wherein the *staphylococcus* bacterium is a *S. aureus* bacterium. 65

7. The method of claim 1, wherein the *staphylococcus* bacterium is resistant to one or more treatments.

8. The method of claim **7**, wherein the bacterium is methicillin resistant.

9. The method of claim **1**, further comprising administering the Ebh antigen or SpA variant is in a composition that is administered more than one time to the subject.

10. The method of claim 1, wherein the composition is administered orally, parenterally, subcutaneously, intramus-cularly, or intravenously.

 The method of claim 1, further comprising administering to the subject a composition comprising a second staphy-55 lococcal antigen.

12. The method of claim 11, wherein the second staphylococcal antigen is one or more of SpA, Emp, EsxA, EsxB, EsaC, Eap, EsaB, Coa, vWbp, vWh, Hla, SdrC, SdrD, SdrE, IsdA, IsdB, IsdC, CIfA, CIfB, and SasF.

13. The method of claim **11**, wherein the second staphylococcal antigen is one or more of Sta006, Sta011, Hla and EsxA-EsxB.

14. The method of claim 1, wherein the subject is a mammal.

15. The method of claim 1, wherein the subject is human.16. A method of treating staphylococcal infection compris-

ing the step of administering a vaccine comprising an isolated

staphylococcal ECM-binding protein homolog (Ebh) antigen and a staphylococcal Protein A (SpA) variant, to a patient in need thereof, wherein the Ebh antigen comprises amino acids 40-471 of SEQ ID NO: 24 or amino acids 2087-2544 of SEQ ID NO: 24 and the SpA variant comprises at least an amino acid substitution at one or more of positions 9, 10, 36, and 37 in Domain D.

17. The method of claim **1**, wherein the Ebh antigen is at least 80% identical to SEQ ID NO:24.

18. The method of claim **1**, wherein the Ebh antigen is at 10 least 90% identical to SEQ ID NO:24.

19. The method of claim **1**, wherein the vaccine is administered multiple times.

20. A method of reducing staphylococcal load in kidney tissue in a subject having or suspected of having a staphylo-15 coccal infection comprising administering an effective amount of a composition comprising a staphylococcal ECMbinding protein homologue (Ebh) antigen and a staphylococcal Protein A (SpA) variant, wherein the Ebh antigen comprises amino acids 40-471 of SEQ ID NO: 24 or amino acids 20 2087-2544 of SEQ ID NO: 24 and the SpA variant comprises at least an amino acid substitution at one or more of positions 9, 10, 36, and 37 in Domain D.

21. The method of claim **1**, wherein the Ebh antigen comprises amino acids 40-2544 of SEQ ID NO: 24. 25

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