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Ahmed et al.

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(45) **Date of Patent: Feb. 19, 2019**

(54) **ANTIBODIES DIRECTED AGAINST INFLUENZA**

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(73) Assignees: **Emory University**, Atlanta, GA (US); **The University of Chicago**, Chicago, IL (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/083,515**

(22) Filed: **Mar. 29, 2016**

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Related U.S. Application Data

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(51) **Int. Cl.**

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C07K 16/10	(2006.01)
G01N 33/569	(2006.01)
A61K 39/00	(2006.01)

(52) **U.S. Cl.**
CPC ... ***C07K 16/1018*** (2013.01); ***G01N 33/56983*** (2013.01); *A61K 2039/505* (2013.01); *C07K 2317/21* (2013.01); *C07K 2317/33* (2013.01); *C07K 2317/54* (2013.01); *C07K 2317/55* (2013.01); *C07K 2317/565* (2013.01); *C07K 2317/622* (2013.01); *C07K 2317/624* (2013.01); *C07K 2317/76* (2013.01); *G01N 2469/00* (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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Primary Examiner — Michelle S Horning

(74) *Attorney, Agent, or Firm* — Emory Patent Group

(57) **ABSTRACT**

Antibodies that specifically bind influenza virus hemagglutinin A (HA), and antigen binding fragments thereof are disclosed herein. In several embodiments, these antibodies are broadly neutralizing. Nucleic acids encoding these monoclonal antibodies, vectors including these nucleic acids, and host cells transformed with these vectors are also disclosed. Compositions are disclosed that include these antibodies, antigen binding fragments, nucleic acids, vectors and host cells. Method of using these antibodies, and antigen binding fragments, nucleic acids, vectors and host cells, such as for diagnosis and treatment of an influenza virus infection are also provided.

13 Claims, 90 Drawing Sheets

Specification includes a Sequence Listing.

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GeneBank AFFK77943, immunoglobulin heavy chain variable region, partial [*Homo sapiens*].

GeneBank AFFK77953, immunoglobulin heavy chain variable region, partial [*Homo sapiens*].

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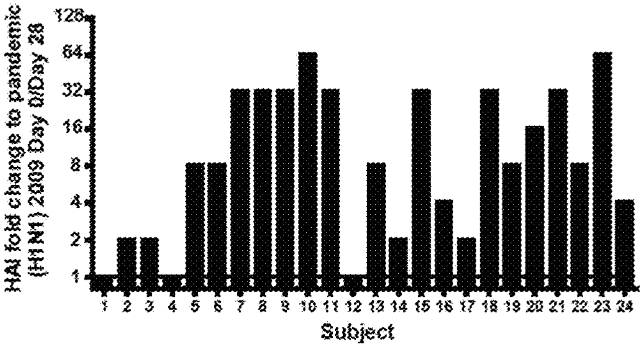

FIG. 1A

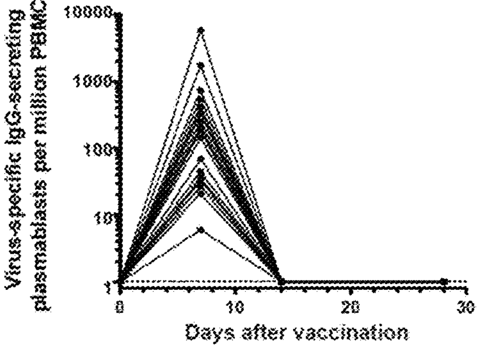

FIG. 1B

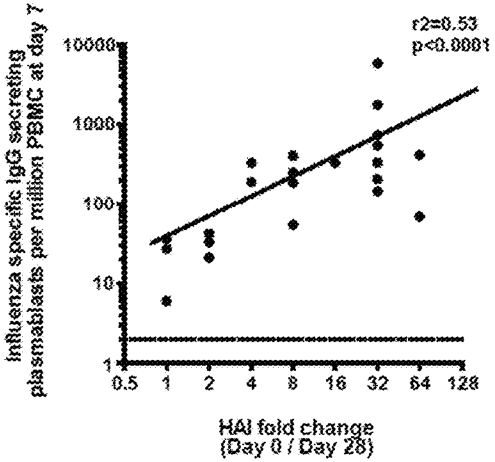

FIG. 1C

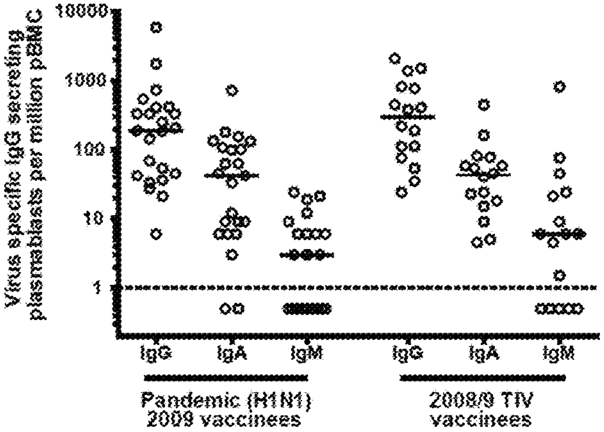

FIG. 1D

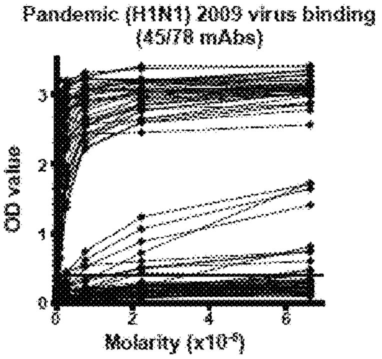

FIG. 2A

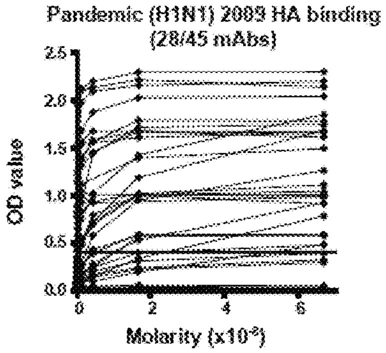

FIG. 2B

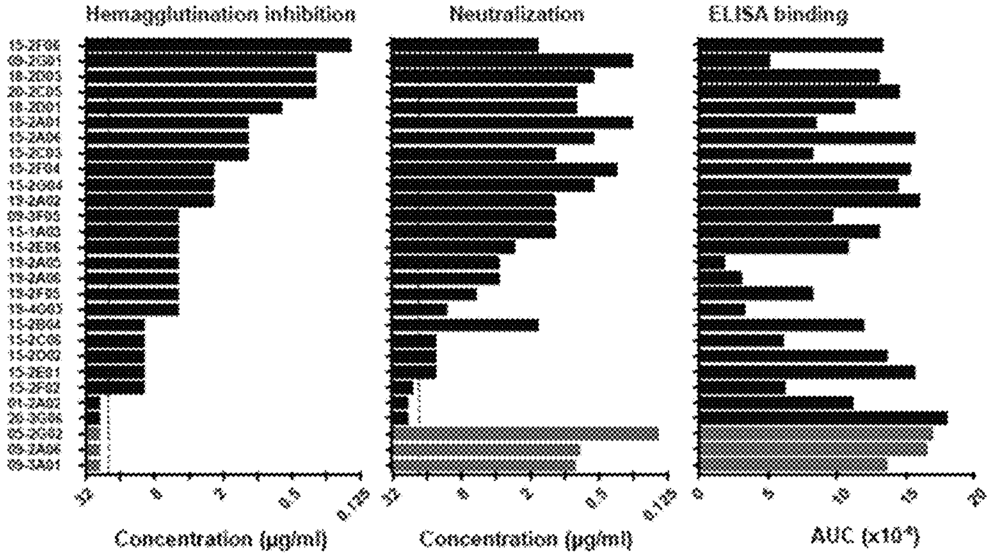

FIG. 2C

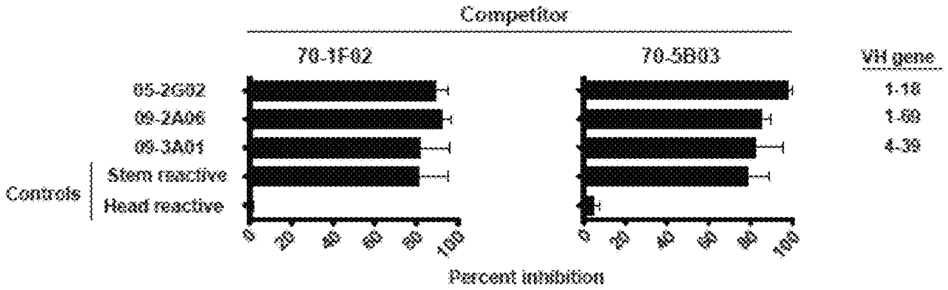

FIG. 2D

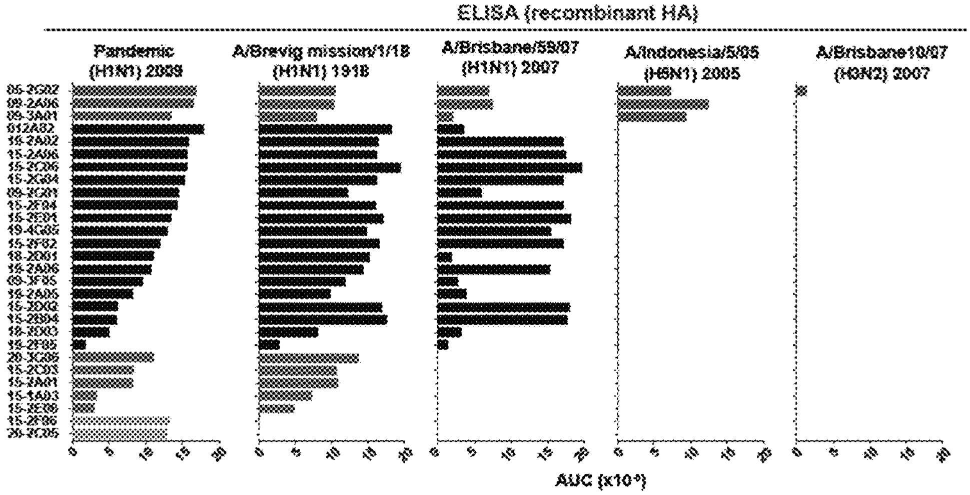

FIG. 3A

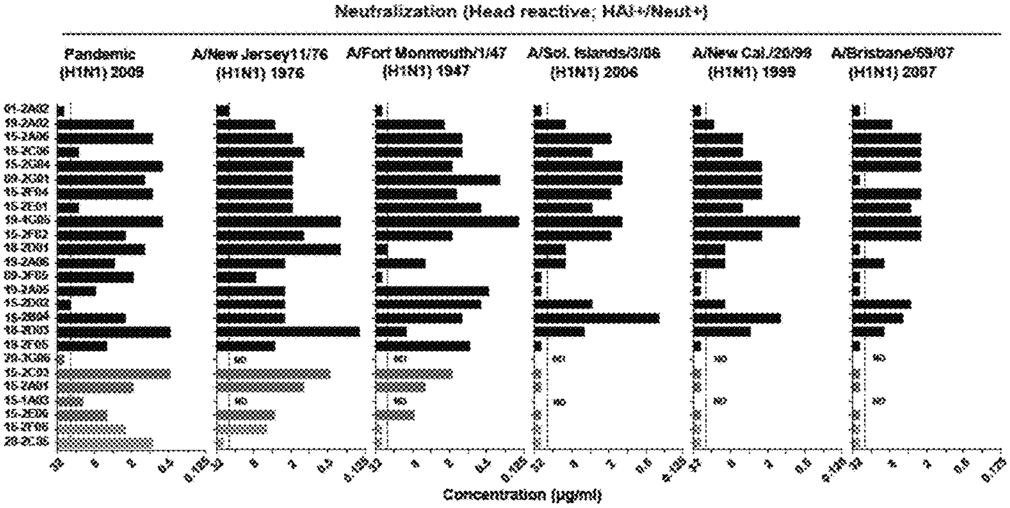

FIG. 3B

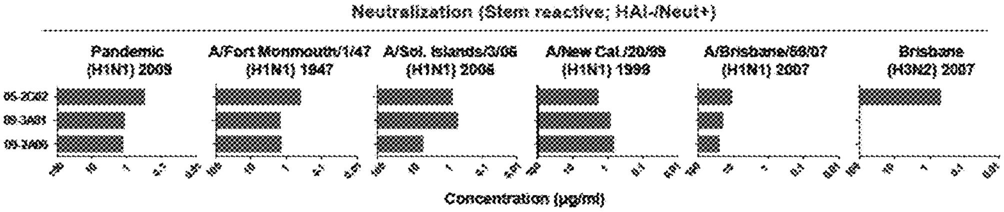

FIG. 3C

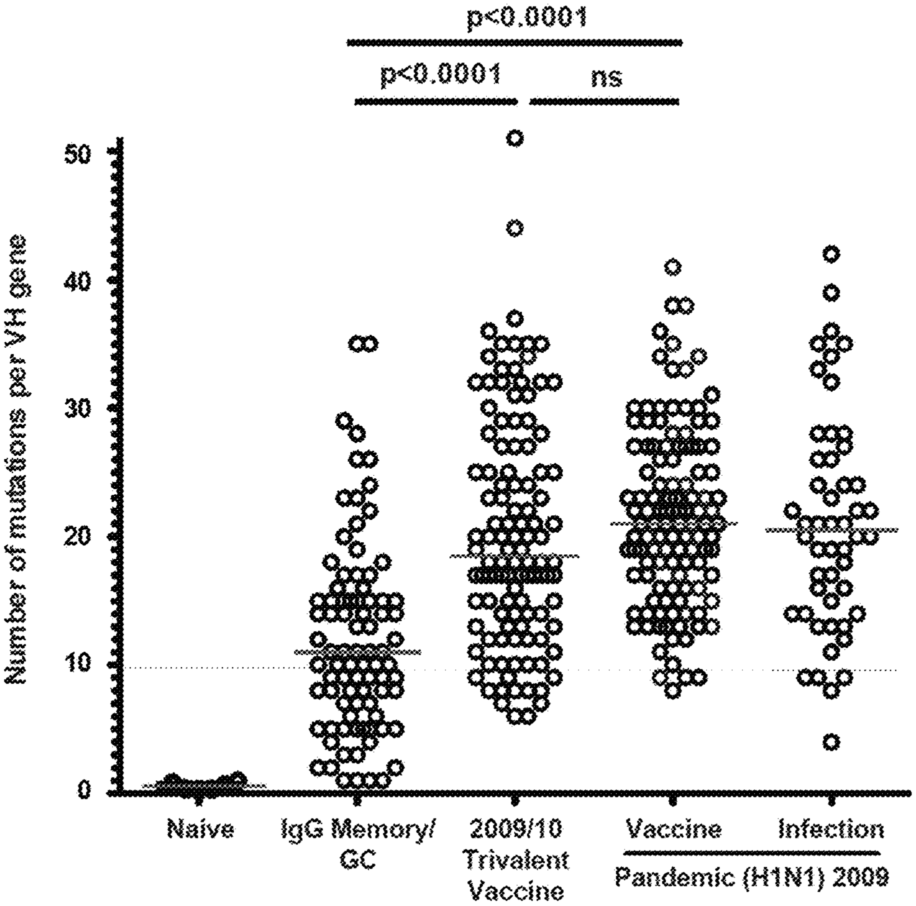
p<0.0001
p<0.0001
ns
Number of mutations per VH gene
50
40
30
20
10
0
Naive
IgG Memory/
GC
2009/10
Trivalent
Vaccine
Vaccine
Infection
Pandemic (H1N1) 2009

FIG. 4A

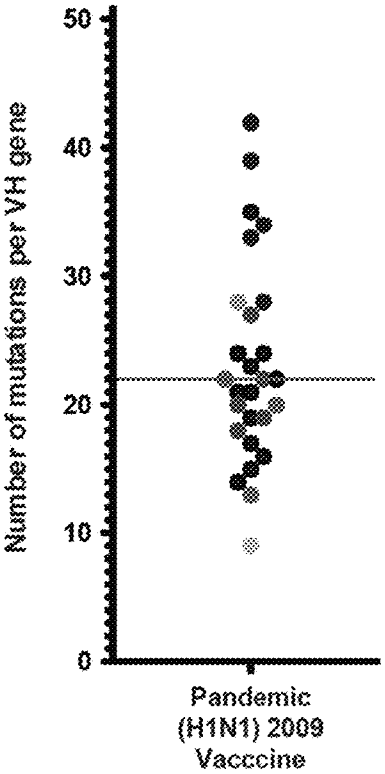
Number of mutations per VH gene
50
40
30
20
10
0
Pandemic
(H1N1) 2009
Vacccine

FIG. 4B

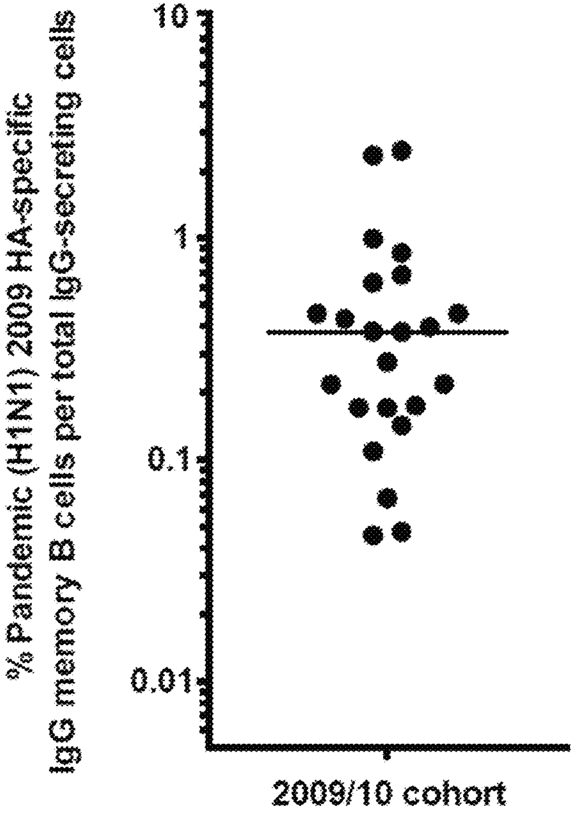
% Pandemic (H1N1) 2009 HA-specific
IgG memory B cells per total IgG-secreting cells
10
1
0.1
0.01
2009/10 cohort

FIG. 5A

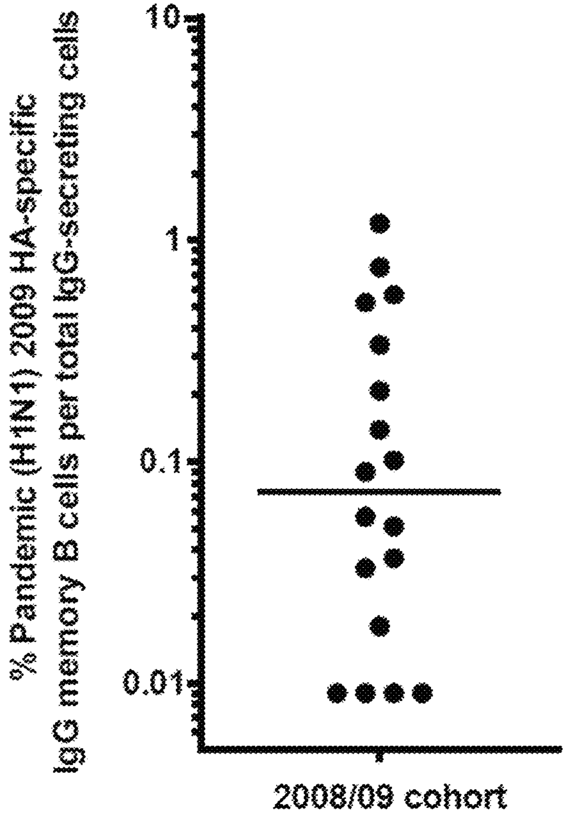
% Pandemic (H1N1) 2009 HA-specific
IgG memory B cells per total IgG-secreting cells
10
1
0.1
0.01
2008/09 cohort

FIG. 5B

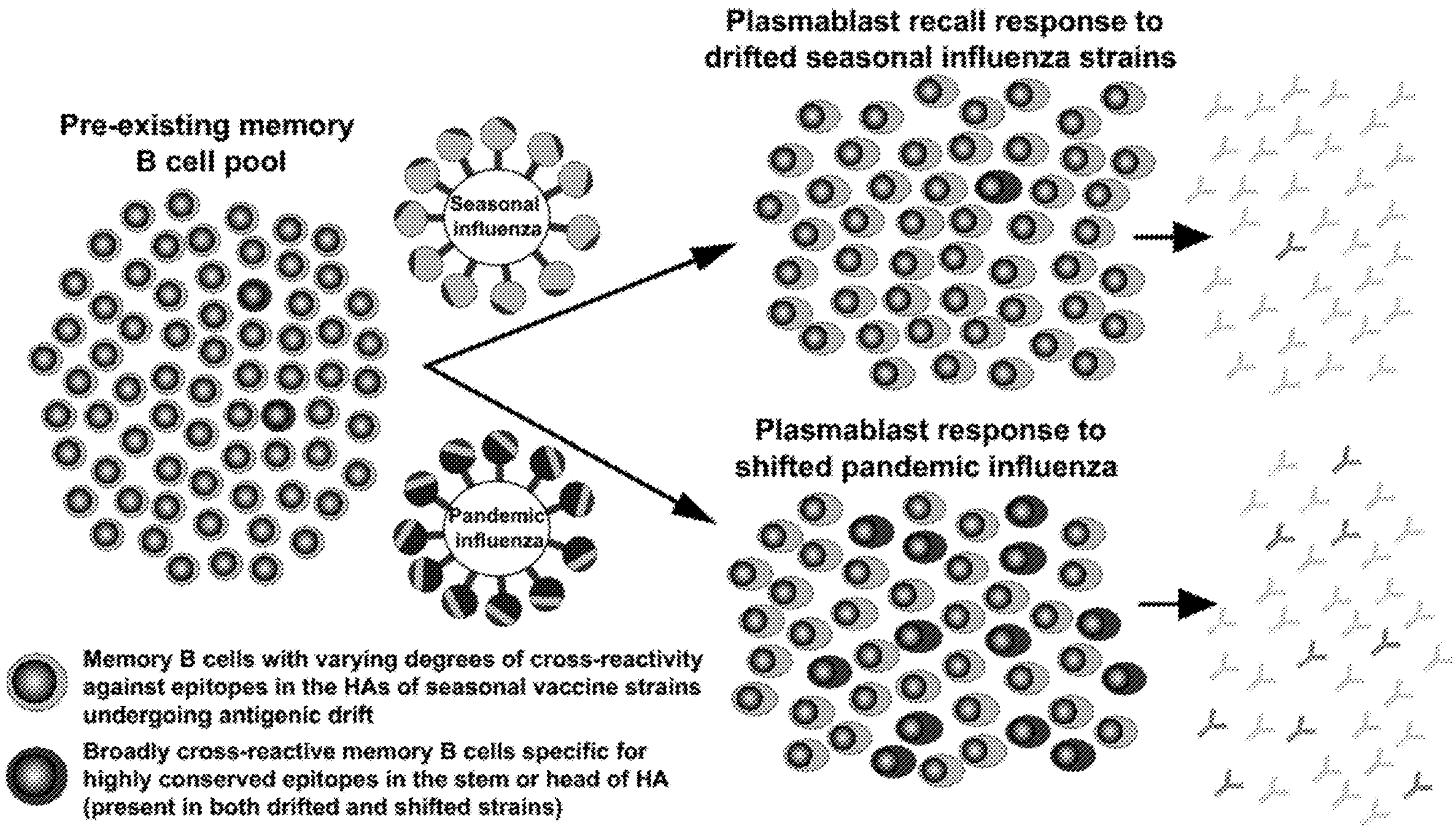
Pre-existing memory B cell pool
Seasonal influenza
Pandemic influenza
Plasmablast recall response to drifted seasonal influenza strains
Plasmablast response to shifted pandemic influenza
Memory B cells with varying degrees of cross-reactivity against epitopes in the HAs of seasonal vaccine strains undergoing antigenic drift
Broadly cross-reactive memory B cells specific for highly conserved epitopes in the stem or head of HA (present in both drifted and shifted strains)

FIG. 6

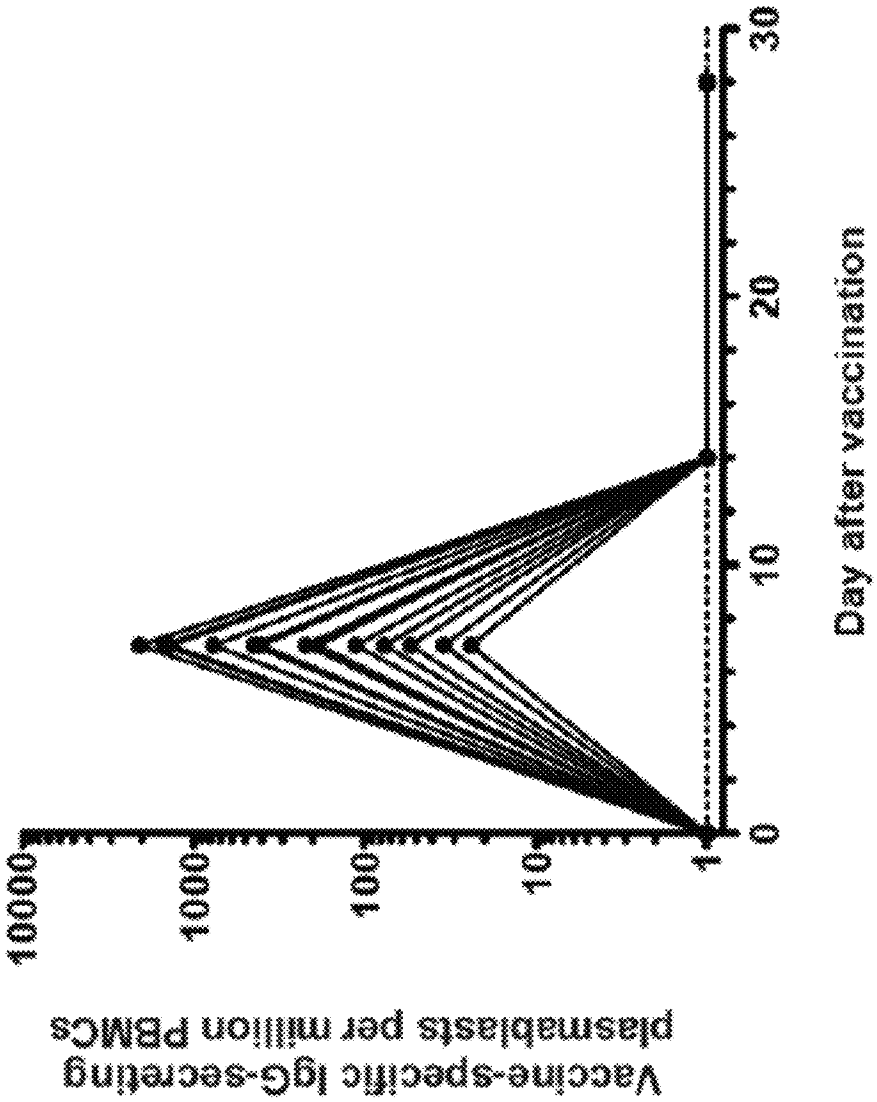
Vaccine-specific IgG-secreting plasmablasts per million PBMCs
10000
1000
100
10
1
0
10
20
30
Day after vaccination

FIG. 7

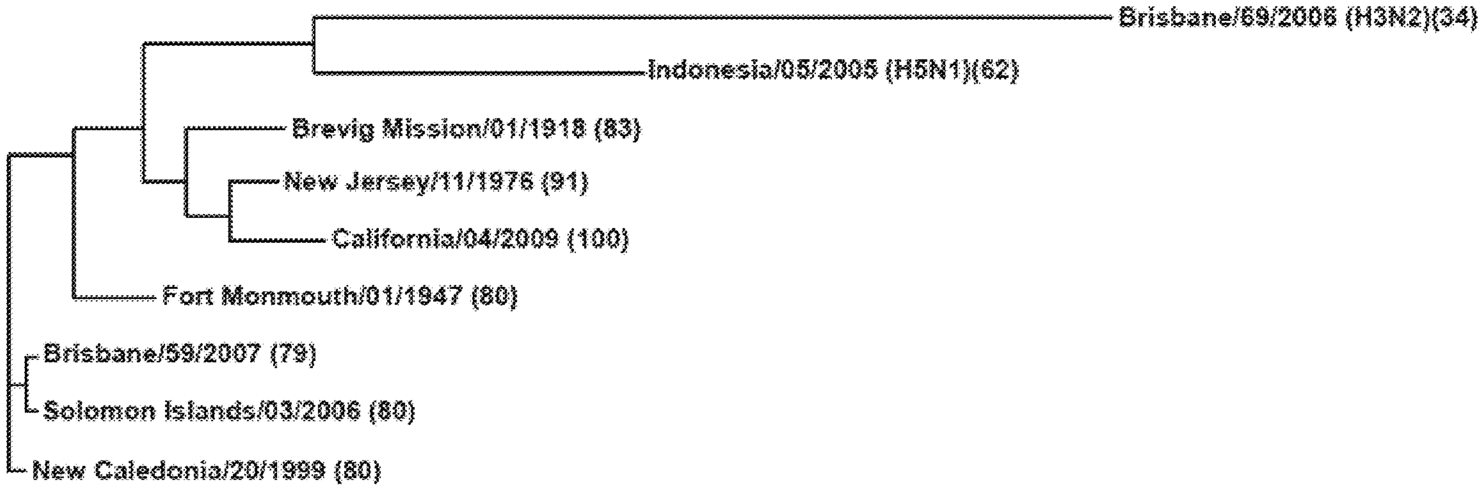
Brisbane/69/2006 (H3N2)(34)
Indonesia/05/2005 (H5N1)(62)
Brevig Mission/01/1918 (83)
New Jersey/11/1976 (91)
California/04/2009 (100)
Fort Monmouth/01/1947 (80)
Brisbane/59/2007 (79)
Solomon Islands/03/2006 (80)
New Caledonia/20/1999 (80)

FIG. 8

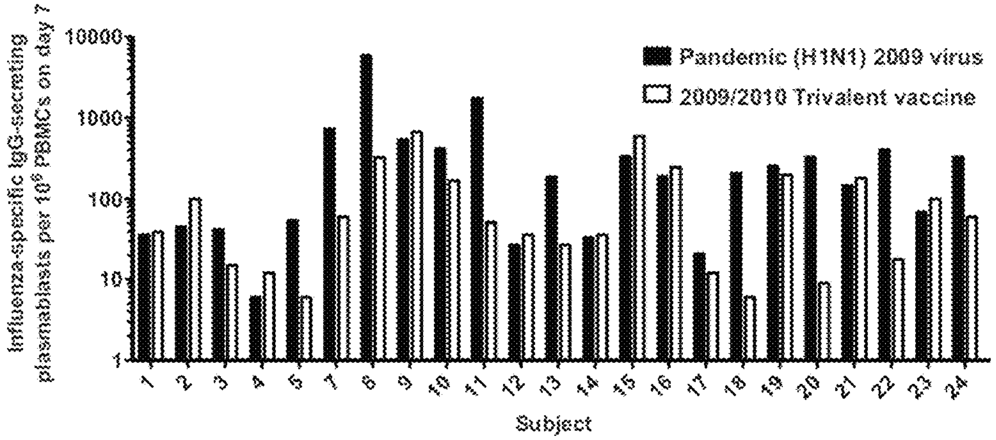

FIG. 9A

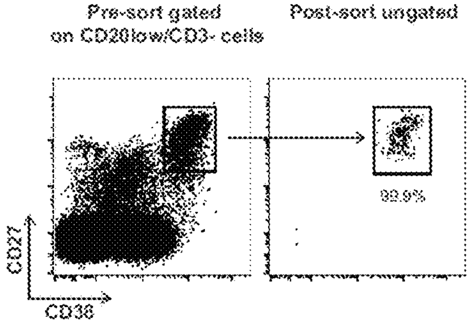

FIG. 9B

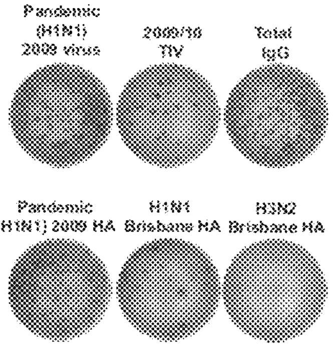

FIG. 9C

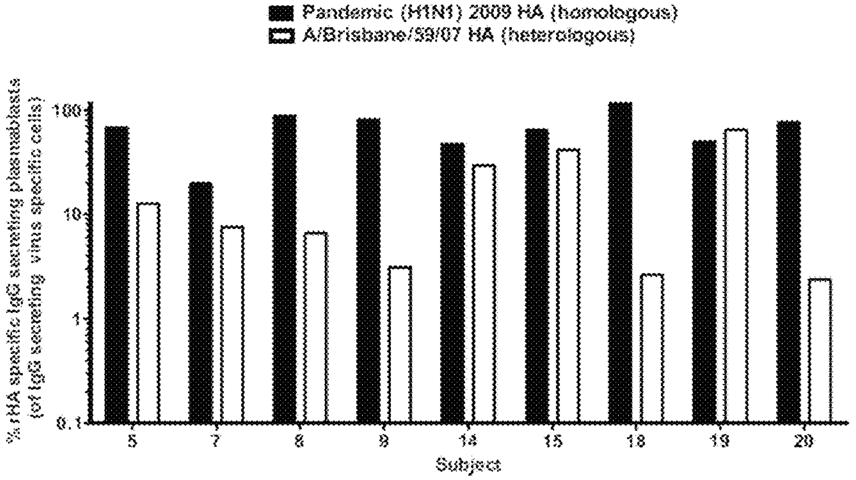

FIG. 9D

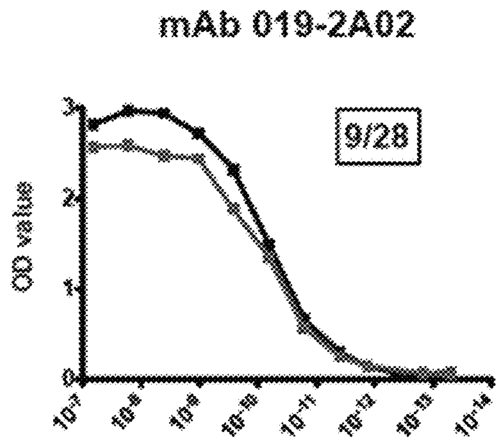

FIG. 10A

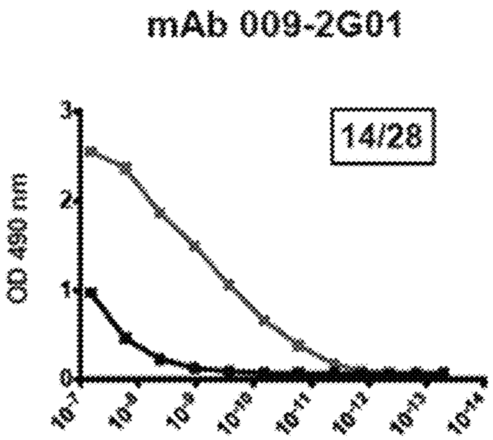

FIG. 10B

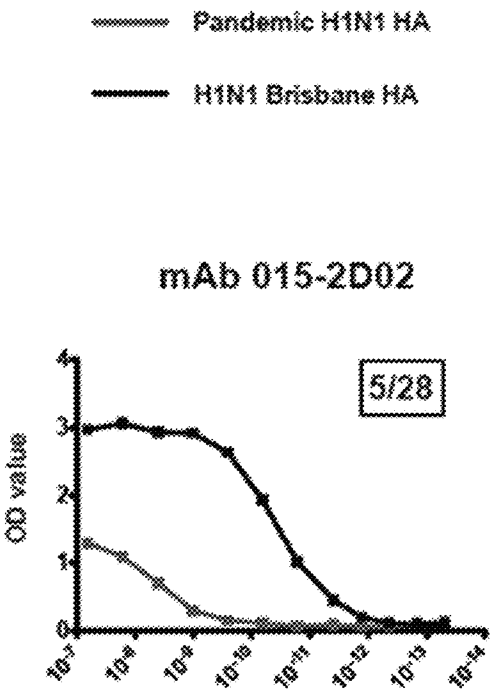

FIG. 10C

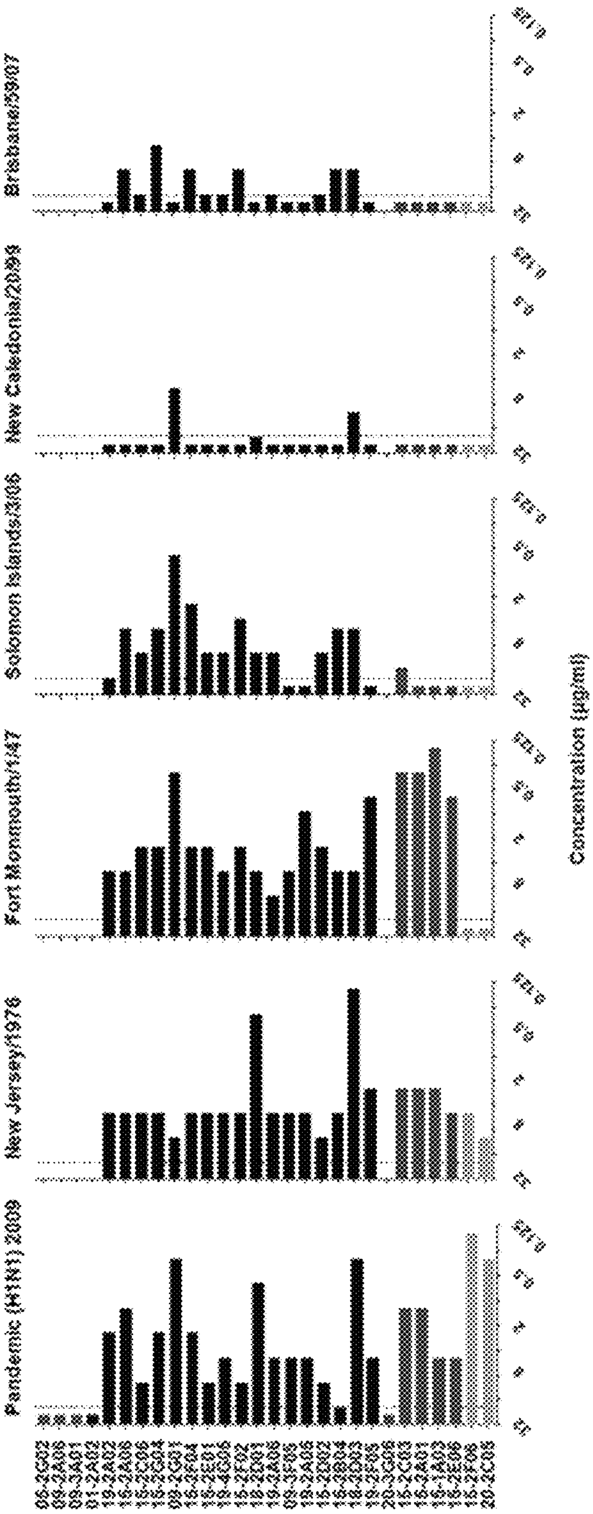
Pandemic (H1N1) 2009
New Jersey/1976
Fort Monmouth/1/47
Solomon Islands/3/06
New Caledonia/20/99
Brisbane/59/07
Concentration (μg/ml)
0.125
0.5
05-2G02
09-3A06
09-3A01
01-2A02
19-2A02
15-3A05
15-2C06
15-2G04
09-2G01
15-2F04
15-3E01
18-4G05
15-2F02
18-2D01
19-3A06
09-3F06
18-2A06
15-2D02
15-3B04
18-2D03
19-2F05
20-3G06
15-2C03
15-3A01
15-1A03
15-2E06
15-2F08
20-2C05

FIG. 11

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
2	005-2G02H	QVQLVQSGPEVKKPGASIKVSCRASGYTFSNYGITWVRQAPGQGLEWMGWISAYNGHTNSAQKFQGRVTMTTDTSTSTAYMEVRSLRSDDTAVYYCAR (SEQ ID NO: 1)	QVQLVQSGPEVKKPGASIKVSCRAS (SEQ ID NO: 2)	GYTFSNYG (SEQ ID NO: 3)	ITWVRQAPGQGLEWMGW (SEQ ID NO: 4)	ISAYNGHT (SEQ ID NO: 5)	NSAQKFQGRVTMTTDTSTSTAYMEVRSLRSDDTAVYYC (SEQ ID NO: 6)	ARDRRDLLTGSLGDY (SEQ ID NO: 7)	caggtgcagctggtgcagtctggacctgaggtgaagaagcctggggcctcaattaaggtctcctgcagggcttcaggatacaccttttccaattatggaatcacctgggtgcgacaggcccctggacaagggcttgagtggatgggctggatcagcgcttacaatggtcacacaaattctgcacagaagttccaggggagagtcaccatgaccacagacacatccacgagcacggcctacatggaggtgaggagcctcagatctgacgacacggccgtatattactgtgcgagagacagaagggatcttttgactggttcgttgggggactactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 8)	QVQLVQSGPEVKKPGASIKVSCRASGYTFSNYGITWVRQAPGQGLEWMGWISAYNGHTNSAQKFQGRVTMTTDTSTSTAYMEVRSLRSDDTAVYYCARDRRDLLTGSLGDYWGQGTLVTVSS (SEQ ID NO: 9)	WGQGTLVTVSS (SEQ ID NO: 10)
3	005-2G02L	DVVMTQSPLSLPVTLGQPASISCRSSRGLLYIDGNTYLNWFQQRPGQSPRRLIHNVSNRDSGVPDRFSGSGSRTDFTLKISRVEAEDVGVYYCMQGTYW (SEQ ID NO: 11)	DVVMTQSPLSLPVTLGQPASISCRSS (SEQ ID NO: 12)	RGLLYIDGNTY (SEQ ID NO: 13)	LNWFQQRPGQSPRRLIH (SEQ ID NO: 14)	NVS (SEQ ID NO: 15)	NRDSGVPDRFSGSGSRTDFTLKISRVEAEDVGVYYC (SEQ ID NO: 16)	MQGTYWPFT (SEQ ID NO: 17)	gatgttgtgatgactcagtctccactctccctgcccgtcacccttggacagccggcctccatctcctgcaggtctagtcgaggcctcctttatattgatggaaacacctacttgaattggtttcaacagaggccaggccaatctccaaggcgcctaattcataacgtttctaaccgggactctggggtcccagacagattcagcggcagtgggtcacgcactgatttcacactgaaaatcagcagggtggaggctgaagatgttggggtttattactgcatgcaaggtacatactggccgttcactttcggccaggggaccaaggtggaaatcaaac (SEQ ID NO: 18)	DVVMTQSPLSLPVTLGQPASISCRSSRGLLYIDGNTYLNWFQQRPGQSPRRLIHNVSNRDSGVPDRFSGSGSRTDFTLKISRVEAEDVGVYYCMQGTYWPFTFGQGTKVEIK (SEQ ID NO: 19)	FGQGTKVEIK (SEQ ID NO: 20)

FIG. 12

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
4	009-2A06H	QVQLVQSGAEVKRPGSSVTVSCKASGGSFTSFVISWVRQAPGQGLEWMGGVIPIFATPKYAQKFQGRLTITADKSTNTAYMELTSLRSEDTAMYYCA (SEQ ID NO: 21)	QVQLVQSGAEVKRPGSSVTVSCKAS (SEQ ID NO: 22)	GGSFTSFV (SEQ ID NO: 23)	ISWVRQAPGQGLEWMGG (SEQ ID NO: 24)	VIPIFATP (SEQ ID NO: 25)	KYAQKFQGRLTITADKSTNTAYMELTSLRSEDTAMYYC (SEQ ID NO: 26)	ASPDLTMVFVPHTGPLDF (SEQ ID NO: 27)	caggtgcagctggtgcagtctggggctgaggtgaagaggccggggtcctcggtgacggtctcctgcaaggcttctggaggctccttcaccagctttgttatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggagggtcatccctattttgctacaccaaagtacgcacagaagttccagggcagactcaccattaccgcggacaagtccacaaatacagcctacatggagctgaccagcctgagatctgaggacacggccatgtattactgtgcgagtccggacttgactatggtattcgtgccgcacaccggaccccttgacttctggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 28)	QVQLVQSGAEVKRPGSSVTVSCKASGGSFTSFVISWVRQAPGQGLEWMGGVIPIFATPKYAQKFQGRLTITADKSTNTAYMELTSLRSEDTAMYYCASPDLTMVFVPHTGPLDFWGQGTLVTVSS (SEQ ID NO: 29)	WGQGTLVTVSS (SEQ ID NO: 30)
5	009-2A06L	DIQMTQSPSTLSASVGDRVTITCRASQSIDNWLAWYQQKPGKAPNLLIYKASSLRSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYDTY (SEQ ID NO: 31)	DIQMTQSPSTLSASVGDRVTITCRAS (SEQ ID NO: 32)	QSIDNW (SEQ ID NO: 33)	LAWYQQKPGKAPNLLIY (SEQ ID NO: 34)	KAS (SEQ ID NO: 35)	SLRSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYC (SEQ ID NO: 36)	QHYDTYSGT (SEQ ID NO: 37)	gacatccagatgacccagtctccgtccaccctgtctgcatctgtcggagacagagtcaccatcacttgccgggccagtcagagcattgataactggttggcctggtatcagcagaaaccagggaaagcccccaacctcctgatctataaggcgtctagtttacgaagtggggtcccatcaaggttcagcggcagtggatctggcacagagttcactctcaccatcagcagcctgcagcctgatgattttgctacttattactgccaacattatgatacttattcggggacgttcggccaagggaccaaggtggaaatcaaac (SEQ ID NO: 38)	DIQMTQSPSTLSASVGDRVTITCRASQSIDNWLAWYQQKPGKAPNLLIYKASSLRSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYDTYSGTFGQGTKVEIK (SEQ ID NO: 39)	FGQGTKVEIK (SEQ ID NO: 40)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
6	009-3A01H	RLQLQESGPGLVKPSETLSLTCTVSGGSITSNTYYWGWIRQPPGKGLESIGSISFSGRTYYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYCAR (SEQ ID NO: 41)	RLQLQESGPGLVKPSETLSLTCTVS (SEQ ID NO: 42)	GGSITSNTYY (SEQ ID NO: 43)	WGWIRQPPGKGLESIGS (SEQ ID NO: 44)	ISFSGRT (SEQ ID NO: 45)	YYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYC (SEQ ID NO: 46)	ARQLTGMVYAILLPSYFDF (SEQ ID NO: 47)	cggctgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctggtggctccatcaccagtaacacttactactggggctggatccgccagccccca gggaaggggctggagtcgattgggagtatctcttttagtgggagaacctactacagcccgtccctcaagagtcgagtcaccatgtcagtagacacgtccaagaaccagttctccctgaagctgagctctgtgaccgccgcggacacggccttttattactgtgcgagacagttaacagggatggtttatgctattctcttaccgtcctactttgacttctggggccagggcaccctggtcaccgtctcctcag (SEQ ID NO: 48)	RLQLQESGPGLVKPSETLSLTCTVSGGSITSNTYYWGWIRQPPGKGLESIGSISFSGRTYYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYCARQLTGMVYAILLPSYFDFWGQGTLVTVSS (SEQ ID NO: 49)	WGQGTLVTVSS (SEQ ID NO: 50)
7	009-3A01L	DIQMTQSPSTLSASVGDRVTITCRASQSIGSWLAWYQQKPGKAPKLLIYKASTLESGVPSRFSGSGSGTEFTLTISSLQPDDLATYYCQQHNSY (SEQ ID NO: 51)	DIQMTQSPSTLSASVGDRVTITCRAS (SEQ ID NO: 52)	QSIGSW (SEQ ID NO: 53)	LAWYQQKPGKAPKLLIY (SEQ ID NO: 54)	KAS (SEQ ID NO: 55)	TLESGVPSRFSGSGSGTEFTLTISSLQPDDLATYYC (SEQ ID NO: 56)	QQHNSYSGA (SEQ ID NO: 57)	caggtgcagctggtgcagtctggggctgaggtgaagaggccggggtcctcggtgacggtctcctgcaaggcttctggaggctccttcaccagctttgttatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggagggggtcatccctatttttgctacacccaaagtacgcacagaagttccagggcagactcaccattaccgcggacaagtccacaaatacagcctacatggagctgaccagcctgagatctgaggacacggccatgtattactgtgcgagtccggacttgactatggtattcgtgccgcacaccggacccacttgacttctggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 58)	QVQLVQSGAEVKRPGSSVTVSCKASGGSFTSFVISWVRQAPGQGLEWMGGVIPIFATPKYAQKFQGRLTITADKSTNTAYMELTSLRSEDTAMYYCASPDLTMVFVPHTGPLDFWGQGTLVTVSS (SEQ ID NO: 59)	FGQGTKVEIK (SEQ ID NO: 60)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
8	005-1C01H	QVQLVESGAEVKKPGSSVRVSCKLSGGTFSTHGINWVRQAPGQGLEWMGGIIPIFGSAKYAQKFQDRVTITADESTRTAYMEVTRLRSEDTATIYCA (SEQ ID NO: 61)	QVQLVESGAEVKKPGSSVRVSCKLS (SEQ ID NO: 62)	GGTFSTHG (SEQ ID NO: 63)	INWVRQAPGQGLEWMGG (SEQ ID NO: 64)	IIPIFGSA (SEQ ID NO: 65)	KYAQKFQDRVTITADESTRTAYMEVTRLRSEDTATIYC (SEQ ID NO: 66)	AGGSDDHAWGSFY (SEQ ID NO: 67)	caggtgcagctggtggagtctggggctgaggtgaagaagcctgggtcctcggtgagggtctcctgcaaactttctggaggcaccttcagcacccatggtatcaactgggtgcgacaggcccccggacaagggcttgagtggatgggagggatcatccctattttggttcagcaaagtatgcacagaagttccaggacagagtcacgattaccgcggacgaatccacgaggacagcctacatggaggtgacccgcctgagatctgaggacacggccacgatttattgtgcgggggggagcgatgatcacgcttgggggagtttttactggggccagggaaccccggtcaccgtttcctcagcctccaccaagggcccatcggtcttccccctggcaccctcctccaggagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgtcg (SEQ ID NO: 68)	QVQLVESGAEVKKPGSSVRVSCKLSGGTFSTHGINWVRQAPGQGLEWMGGIIPIFGSAKYAQKFQDRVTITADESTRTAYMEVTRLRSEDTATIYCAGGSDDHAWGSFYWGQGTPVTVSS (SEQ ID NO: 69)	WGQGTPVTVSS (SEQ ID NO: 70)
9	005-1C01L	DIVMTQTPLSLPVTPGEPASISCRSSQSLXDSDDGNTSLDWYLQKAGQSPQLLIYTLSYRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQRIAF (SEQ ID NO: 71)	DIVMTQTPLSLPVTPGEPASISCRSS (SEQ ID NO: 72)	QSLXDSDDGNTS (SEQ ID NO: 73)	LDWYLQKAGQSPQLLIY (SEQ ID NO: 74)	TLS (SEQ ID NO: 75)	YRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC (SEQ ID NO: 76)	MQRIAFPFT (SEQ ID NO: 77)	gatattgtgatgacccagactccactctccctgcccgtcacccctggagagccggcctccatctcctgcaggtctagtcagagcctcinggatagtgatgatggaaacacctctttggactggtacctgcagaaggcagggcagtctccacagctcctgatctatacgctttcctatcgggcctctggagtcccagacaggttcagtggcagtgggtcaggcactgatttcacactgaaaatcagcagggtggaggctgaggatgttggagtttattattgcatgcaacgtatagcatttccgttcactttggccaggggaccaagctggagatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaa (SEQ ID NO: 78)	DIVMTQTPLSLPVTPGEPASISCRSSQSLXDSDDGNTSLDWYLQKAGQSPQLLIYTLSYRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQRIAFPFTFGQGTKLEIK (SEQ ID NO: 79)	FGQGTKLEIK (SEQ ID NO: 80)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
10	005-1D03H	QVQLVQSGAEVKKPGESLKISCRAYEYTFTAFCVGWVRQMPGTGLEWMGIICPGDSDLKYSPSFQGQVTISADKSITTAYLQWSSLKASDTATYYCAR (SEQ ID NO: 81)	QVQLVQSGAEVKKPGESLKISCRAY (SEQ ID NO: 82)	EYTFTAFC (SEQ ID NO: 83)	VGWVRQMPGTGLEWMGI (SEQ ID NO: 84)	ICPGDSDL (SEQ ID NO: 85)	KYSPSFQGQVTISADKSITTAYLQWSSLKASDTATYYC (SEQ ID NO: 86)	RHVASHWGDYYGMDL (SEQ ID NO: 87)	caggtgcagctggtgcagtctggggcagaggtgaaaaagcccggggagtctctgaagatctcctgtagggcttatgaatacaccttcaccgccttctgcgtcggctgggtgcgccagatgcccggcacaggcctggagtggatggggatcatctgtcctggtgactctgatctcaaatacagtccgtccttccaaggccaggtcaccatctcagccgacaagtccatcaccaccgcctacctgcagtggagcagcctgaaggcctcggacaccgccacatattactgtgcgagacatgtggcaagtcactggggcgactattacggtatggacctctggggccaaggaccctcggtcagcgtctcgtcagcacccaccaaggctccggatgtgttccccatcatatcagggtgcagacacacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtga (SEQ ID NO: 88)	QVQLVQSGAEVKKPGESLKISCRAYEYTFTAFCVGWVRQMPGTGLEWMGIICPGDSDLKYSPSFQGQVTISADKSITTAYLQWSSLKASDTATYYCARHVASHWGDYYGMDLWGQGPRSASRQHPPRLRMCSPSYQGADTPLGAQRPWAAWSRTTSPNR (SEQ ID NO: 89)	WGQGTSVSVSS (SEQ ID NO: 90)
11	005-1D03L	EIVLTQSPGTLSVSPGERVTLSCRASQSVTRNLAWYQQRPGQAPRLLIYSASTRAIGIPVRFSGRGSGTDFTLSISSLQSEDSAVYYCQQYNDW (SEQ ID NO: 91)	EIVLTQSPGTLSVSPGERVTLSCRAS (SEQ ID NO: 92)	QSVTRN (SEQ ID NO: 93)	LAWYQQRPGQAPRLLIY (SEQ ID NO: 94)	SAS (SEQ ID NO: 95)	TRAIGIPVRFSGRGSGTDFTLSISSLQSEDSAVYYC (SEQ ID NO: 96)	QQYNDWLGGT (SEQ ID NO: 97)	gaaattgtgttgacgcagtctccaggcaccctgtctgtgtctccaggagaaagagtcacactctcctgcagggccagccagagtgttaccagaaacttagcctggtaccaacagagacctggccaggctcccaggctcctcatctatagtgcatccaccagggccattggtatcccagtcaggttcagtggccgggggtctgggacagacttcactctcagcatcagcagcctgcagtctgaagattctgcagtttattattgtcagcagtataatgactggctcggggggaccttcggccaggggaccaaagtggaaattaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccag (SEQ ID NO: 98)	EIVLTQSPGTLSVSPGERVTLSCRASQSVTRNLAWYQQRPGQAPRLLIYSASTRAIGIPVRFSGRGSGTDFTLSISSLQSEDSAVYYCQQYNDWLGGTFGQGTKVEIK (SEQ ID NO: 99)	FGQGTKVEIK (SEQ ID NO: 100)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
12	005-1D06H	QVQLQQSGPGLVKPSQTLSLRCTISGDSVTSATYYWTWIRQRPGKGLEWIGNIFKGGNTNYNPSLKSRVAISVDTSTNQFSLTLRSVTAADAAVYFCAR (SEQ ID NO: 101)	QVQLQQSGPGLVKPSQTLSLRCTIS (SEQ ID NO: 102)	GDSVTSATYY (SEQ ID NO: 103)	WTWIRQRPGKGLEWIGN (SEQ ID NO: 104)	IFKGGNT (SEQ ID NO: 105)	NYNPSLKSRVAISVDTSTNQFSLTLRSVTAADAAVYFC (SEQ ID NO: 106)	ARGLEGITVGAYYFDF (SEQ ID NO: 107)	caggtacagctgcagcagtcaggtccaggactggtgaagccttcacagaccctgtccctcagatgcactatttcgggtgactccgtcaccagtgcgacttactactggacctggatccgccagcgcccagggaagggcctggagtggattgggaacatctttaaaggtgggaacaccaactacaacccgtccctgaagagtcgagttgccatatcagtggacacgtctacgaaccagttctccctgactctgaggtctgtgacggccgcggacgcggccgtgtattttgtgcgagaggccttgagggcataacagtgggcgcctactattttgacttctggggccagggagcccttgtcaccgtctcctcagcctccaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccgg (SEQ ID NO: 108)	QVQLQQSGPGLVKPSQTLSLRCTISGDSVTSATYYWTWIRQRPGKGLEWIGNIFKGGNTNYNPSLKSRVAISVDTSTNQFSLTLRSVTAADAAVYFCARGLEGITVGAYYFDFWGQGALVTVSS (SEQ ID NO: 109)	WGQGALVTVSS (SEQ ID NO: 110)
13	005-1D06L	AIQLTQSPSSVSASVGDRVTITCRASQEINYALAWYLQKPGKPPKVLIYNASTMKNGVPSRFGGNGSGPDFTLTINNLQPEDFGTYYCQQFNSF (SEQ ID NO: 111)	AIQLTQSPSSVSASVGDRVTITCRAS (SEQ ID NO: 112)	QEINYA (SEQ ID NO: 113)	LAWYLQKPGKPPKVLIY (SEQ ID NO: 114)	NAS (SEQ ID NO: 115)	TMKNGVPSRFGGNGSGPDFTLTINNLQPEDFGTYYC (SEQ ID NO: 116)	QQFNSFPLT (SEQ ID NO: 117)	gccatccagttgacccagtctccatcctccgtgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcaggaaattaactatgctttagcctggtatctgcaaaaaccaggaaaacctccaaaggtcctgatctataatgcctccaccatgaaaaatggggtcccatcaaggttcggcggcaatggatctgggccagatttcactctcaccatcaacaacctgcagcctgaagactttggaacttattactgtcaacagtttaatagtttcccgctcactttcggcggggggaccagggtggacattagacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaaca (SEQ ID NO: 118)	AIQLTQSPSSVSASVGDRVTITCRASQEINYALAWYLQKPGKPPKVLIYNASTMKNGVPSRFGGNGSGPDFTLTINNLQPEDFGTYYCQQFNSFPLTFGGGTRVDIR (SEQ ID NO: 119)	FGGGTRVDIR (SEQ ID NO: 120)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
14	005-1F02H	QVQLQESGPGLVKPSQTLSLTCTISGDSVSSATYYWTWIRQRPGKGLEWIGNIFNSGSTNYNPSLKSRVAISVDTSRNQFSLTLNSLTAADTAVYFCAR (SEQ ID NO: 121)	QVQLQESGPGLVKPSQTLSLTCTIS (SEQ ID NO: 122)	GDSVSSATYY (SEQ ID NO: 123)	WTWIRQRPGKGLEWIGN (SEQ ID NO: 124)	IFNSGST (SEQ ID NO: 125)	NYNPSLKSRVAISVDTSRNQFSLTLNSLTAADTAVYFC (SEQ ID NO: 126)	ARGLEGITVGVYYCDF (SEQ ID NO: 127)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcacagaccctgtccctcacctgcactatctcaggtgactccgtcagcagtgcgacttactactggacctggatccgccagcgcccagggaagggcctggagtggattgggaacatctttaacagtgggagtaccaactacaacccgtccctcaagagtcgagttgccatatcagtggacacgtctaggaaccagttctccctgactctgaattctctgactgccgcggacacggccgtgtattttttgtgcgagaggccttgagggcataacagtgggggtctactattgtgacttctggggccagggaaccctggtcaccgtctcctcagcctccaccaagggcccatcggtcttccccctggcaccctcctccaggagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggt (SEQ ID NO: 128)	QVQLQESGPGLVKPSQTLSLTCTISGDSVSSATYYWTWIRQRPGKGLEWIGNIFNSGSTNYNPSLKSRVAISVDTSRNQFSLTLNSLTAADTAVYFCARGLEGITVGVYYCDFWGQGTLVTVSS (SEQ ID NO: 129)	WGQGTLVTVSS (SEQ ID NO: 130)
15	005-1F02L	AIQMTQSPSSVSASVGDRVTITCRASQEINYALAWYLQKPGKPPKVLIYNASTLKNGVPSRFGGDGSGPDFTLTISNLQPEDFGTYYCQQFNSY (SEQ ID NO: 131)	AIQMTQSPSSVSASVGDRVTITCRAS (SEQ ID NO: 132)	QEINYA (SEQ ID NO: 133)	LAWYLQKPGKPPKVLIY (SEQ ID NO: 134)	NAS (SEQ ID NO: 135)	TLKNGVPSRFGGDGSGPDFTLTISNLQPEDFGTYYC (SEQ ID NO: 136)	QQFNSYPLT (SEQ ID NO: 137)	gccatccagatgacccagtctccatcctccgtgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcaggaaattaactatgcttttagcctggtatctgcaaaaaccagggaaaacctccaaaggtcctgatctataatgcctccaccttgaaaaatggggtcccatcaaggttcggcggcgatggatctgggccagatttcactctcaccatcagcaacctgcagcctgaagactttggaacttattactgtcaacagtttaatagttacccgctcactttcggcggggggaccaaggtggacattagacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggaga (SEQ ID NO: 138)	AIQMTQSPSSVSASVGDRVTITCRASQEINYALAWYLQKPGKPPKVLIYNASTLKNGVPSRFGGDGSGPDFTLTISNLQPEDFGTYYCQQFNSYPLTFGGGTKVDIR (SEQ ID NO: 139)	FGGGTKVDIR (SEQ ID NO: 140)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
16	009-2A04H	QVQLVQSGAEVKKPGSSVKVSCKASGGTFNTYIINWVRQAPGQGLEWMGRINPSFGSVNYAQRFQGRVTITADNSXXXXXXELNSLRSEDTAVYYCA (SEQ ID NO: 141)	QVQLVQSGAEVKKPGSSVKVSCKAS (SEQ ID NO: 142)	GGTFNTYI (SEQ ID NO: 143)	INWVRQAPGQGLEWMGR (SEQ ID NO: 144)	INPSFGSV (SEQ ID NO: 145)	NYAQRFQGRVTITADNSXXXXXXELNSLRSEDTAVYYC (SEQ ID NO: 146)	ASPAYNSGFALH (SEQ ID NO: 147)	caggtgcagctggtgcagtctggggctgaagtgaagaagcctgggtcgtcggtgaaggtctcctgtaaggcttctggaggcaccttcaacacctatattataaattgggtgcgacaggcccctggacaagggcttgagtggatgggaaggatcaaccctagctttggttcagtaaactacgcacagaggtttcagggcagagtcacgatcaccgcggacaactccannnnnnnnnnnnnnnnntggagttgaacagcctgagatctgaggacacggccgtgtattactgtgcgagccccgcatacaattctggtttcgcgttacttcactggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtgg (SEQ ID NO: 148)	QVQLVQSGAEVKKPGSSVKVSCKASGGTFNTYIINWVRQAPGQGLEWMGRINPSFGSVNYAQRFQGRVTITADNSXXXXXXELNSLRSEDTAVYYCASPAYNSGFALLHWGQGTLVTVSS (SEQ ID NO: 149)	WGQGTLVTVSS (SEQ ID NO: 150)
17	009-2A04L	DIVMTQSPDSLGVSLGERATINCKSSQSVLYTSNNKNYLAWFQQKPGQPPKLLIYWASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYS (SEQ ID NO: 151)	DIVMTQSPDSLGVSLGERATINCKSS (SEQ ID NO: 152)	QSVLYTSNNKNY (SEQ ID NO: 153)	LAWFQQKPGQPPKLLIY (SEQ ID NO: 154)	WAS (SEQ ID NO: 155)	TRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC (SEQ ID NO: 156)	QQYYSNSMYT (SEQ ID NO: 157)	gacatcgtgatgacccagtctccagactccctgggtgtgtctctgggcgagagggccaccatcaactgcaagtccagccagagtgttttatacacctccaacaataagaactacttagcttggttccagcagaaaccaggacagcctcctaagctgctcatttactgggcatctacccgggaatccggagtccctgaccgattcagtggcagcgggtctgggacagatttcactctcaccatcagcagcctgcaggctgaagatgtggcagtttattactgtcaacaatattatagtaattccatgtacacttttggccaggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccct (SEQ ID NO: 158)	DIVMTQSPDSLGVSLGERATINCKSSQSVLYTSNNKNYLAWFQQKPGQPPKLLIYWASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSNSMYTFGQGTKVEIK (SEQ ID NO: 159)	FGQGTKVEIK (SEQ ID NO: 160)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
18	009-2G01H	QVQLQESGPGLVKPSETLSLTCSVSGGSISSYYWTWIRQPPGKGLEWIGNIYYSGSTYYSPSLKSRVTISIDTSKNQFSLKLNSVTTADTAVYYCA (SEQ ID NO: 161)	QVQLQESGPGLVKPSETLSLTCSVS (SEQ ID NO: 162)	GGSISSYY (SEQ ID NO: 163)	WTWIRQPPGKGLEWIGN (SEQ ID NO: 164)	IYYSGST (SEQ ID NO: 165)	YYSPSLKSRVTISIDTSKNQFSLKLNSVTTADTAVYYC (SEQ ID NO: 166)	ARDCSGFEDMDSFYYFMDV (SEQ ID NO: 167)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcagtgtctctggtggctccatcagtagttactactggacctggatccgacagcccccagggaagggggctggagtggattgggaacatctattacagtgggagcacgtactacagcccctccctcaagagtcgagtcaccatatcaatagacacgtccaagaaccaattctccctgaaactgaactctgtgaccactgcggacacggccgtttattactgtgcgagggactgtagtggcttcgaagacatggactccttctactacttcatggacgtctggggcaaaggggccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaa (SEQ ID NO: 168)	QVQLQESGPGLVKPSETLSLTCSVSGGSISSYYWTWIRQPPGKGLEWIGNIYYSGSTYYSPSLKSRVTISIDTSKNQFSLKLNSVTTADTAVYYCARDCSGFEDMDSFYYFMDVWGKGATVTVSS (SEQ ID NO: 169)	WGKGATVTVSS (SEQ ID NO: 170)
19	009-2G01L	EIVLTQSPATLSLSPGERATLSCRASQRLTSSLSWYQQKPGQAPRLLIYAASNRATGVPARFSGSGSGTDFTLTISSLEPEDFAVYYCQYRSHWP (SEQ ID NO: 171)	EIVLTQSPATLSLSPGERATLSCRAS (SEQ ID NO: 172)	QRLTSS (SEQ ID NO: 173)	LSWYQQKPGQAPRLLIY (SEQ ID NO: 174)	AAS (SEQ ID NO: 175)	NRATGVPARFSGSGSGTDFTLTISSLEPEDFAVYYC (SEQ ID NO: 176)	QYRSHWPPAVT (SEQ ID NO: 177)	gaaattgtgttgacacagtctccggccaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagcgtcttaccagctccttatcctggtaccaacaaaagcctggccaggctcccaggctcctcatttatgctgcatccaacagggccactggcgtcccagccaggttcagtggcagtgggtctgggacagacttcactctcaccatcagcagcctggagcctgaagattttgcggtttattactgtcagtaccgaagccactggcctccggcggtcactttcggcggagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactc (SEQ ID NO: 178)	EIVLTQSPATLSLSPGERATLSCRASQRLTSSLSWYQQKPGQAPRLLIYAASNRATGVPARFSGSGSGTDFTLTISSLEPEDFAVYYCQYRSHWPPAVTFGGGTKVEIK (SEQ ID NO: 179)	FGGGTKVEIK (SEQ ID NO: 180)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
20	009-3A01H	RLQLQESGPGLVKPSETLSLTCTVSGGSITSNTYYWGWIRQPPGKGLESIGSISFSGRTYYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYCAR (SEQ ID NO: 181)	RLQLQESGPGLVKPSETLSLTCTVS (SEQ ID NO: 182)	GGSITSNTYY (SEQ ID NO: 183)	WGWIRQPPGKGLESIGS (SEQ ID NO: 184)	ISFSGRT (SEQ ID NO: 185)	YYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYC (SEQ ID NO: 186)	ARQLTGMVYAILLPSYFDF (SEQ ID NO: 187)	cggctgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctggtggctccatcaccagtaacacttactactggggctggatccgccagccccccagggaaggggctggagtcgattgggagtatctcttttagtgggagaacctactacagcccgtccctcaagagtcgagtcaccatgtcagtagacacgtccaagaaccagttctccctgaagctgagctctgtgaccgccgcggacacggccttttattactgtgcgagacagttaacagggatggtttatgctattctcttaccgtcctactttgacttctggggccagggcaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccc (SEQ ID NO: 188)	RLQLQESGPGLVKPSETLSLTCTVSGGSITSNTYYWGWIRQPPGKGLESIGSISFSGRTYYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYCARQLTGMVYAILLPSYFDFWGQGTLVTVSS (SEQ ID NO: 189)	WGQGTLVTVSS (SEQ ID NO: 190)
21	009-3A01L	DIQMTQSPSTLSASVGDRVTITCRASQSIGSWLAWYQQKPGKAPKLLIYKASTLESGVPSRFSGSGSGTEFTLTISSLQPDDLATYYCQQHNSY (SEQ ID NO: 191)	DIQMTQSPSTLSASVGDRVTITCRAS (SEQ ID NO: 192)	QSIGSW (SEQ ID NO: 193)	LAWYQQKPGKAPKLLIY (SEQ ID NO: 194)	KAS (SEQ ID NO: 195)	TLESGVPSRFSGSGSGTEFTLTISSLQPDDLATYYC (SEQ ID NO: 196)	QQHNSYSGA (SEQ ID NO: 197)	gacatccagatgacccagtctccttccacgctgtctgcatctgtaggagacagagtcaccatcacttgccgggccagtcagagtattggtagctggttggcctggtatcagcagaaaccagggaaagcccctaagctcctaatctataaggcgtctactttagaaagtggggtcccatcaaggttcagcggcagtggatctgggacagaattcactctcaccatcagcagcctgcagcctgatgatcttgcaacttattactgccaacagcataatagttattcgggggcgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggag (SEQ ID NO: 198)	DIQMTQSPSTLSASVGDRVTITCRASQSIGSWLAWYQQKPGKAPKLLIYKASTLESGVPSRFSGSGSGTEFTLTISSLQPDDLATYYCQQHNSYSGAFGQGTKVEIK (SEQ ID NO: 199)	FGQGTKVEIK (SEQ ID NO: 200)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
22	009-3A02H	EVQLLESGGGLVQPGGSLRLSCEASGFTFISYAMSWVRQAPGKGLEWVSVISGSGGARYYADSVKGRFTISRDNSKNTLYLEMNNVRAEDTAVYFCAK (SEQ ID NO: 201)	EVQLLESGGGLVQPGGSLRLSCEAS (SEQ ID NO: 202)	GFTFISYA (SEQ ID NO: 203)	MSWVRQAPGKGLEWVSV (SEQ ID NO: 204)	ISGSGGAR (SEQ ID NO: 205)	YYADSVKGRFTISRDNSKNTLYLEMNNVRAEDTAVYFC (SEQ ID NO: 206)	AKDRILPYDTDAFDI (SEQ ID NO: 207)	gaggtgcagctgttggagtctgggggaggcttggtgcagccgggggggtccctgagactctcctgtgaagcctctggattcacctttatcagttatgccatgagttgggtccgccaggctccagggaaggggctggagtgggtctcagttattagtgggagcggtggtgccagatactacgcagactccgtgaagggccggttcaccatctccagagacaattccaagaacaccctatatctggaaatgaacaacgtgagagccgaggacacggccgtatattttgtgcgaaagatcgaattctcccatatgacaccgatgcctttgacatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacg (SEQ ID NO: 208)	EVQLLESGGGLVQPGGSLRLSCEASGFTFISYAMSWVRQAPGKGLEWVSVISGSGGARYYADSVKGRFTISRDNSKNTLYLEMNNVRAEDTAVYFCAKDRILPYDTDAFDIWGQGTMVTVSS (SEQ ID NO: 209)	WGQGTMVTVSS (SEQ ID NO: 210)
23	009-3A02L	DIQMTQSPSTLSASVGDRVTITCRASESVSVSLAWYQQKPGKAPKLLIYKASTLESGVPPRFSGSGSGTEFTLTISSLQPNDFATYYCQEYHTS (SEQ ID NO: 211)	DIQMTQSPSTLSASVGDRVTITCRAS (SEQ ID NO: 212)	ESVSVS (SEQ ID NO: 213)	LAWYQQKPGKAPKLLIY (SEQ ID NO: 214)	KAS (SEQ ID NO: 215)	TLESGVPPRFSGSGSGTEFTLTISSLQPNDFATYYC (SEQ ID NO: 216)	QEYHTSSRVT (SEQ ID NO: 217)	gacatccagatgacccagtctccttccaccctgtctgcgtctgtgggagacagagtcaccatcacttgccgggccagtgagagtgttagtgtctcgttggcctggtatcagcagaaaccgggcaaagcccctaaactcctaatctataaggcgtctacttagaaagtggcgtcccacccaggttcagcggcagtggatctgggacagaattcactctcaccattagcagcctgcagcctaatgactttgcgacttattactgccaagaatatcacacttcttcgcgggtcactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccag (SEQ ID NO: 218)	DIQMTQSPSTLSASVGDRVTITCRASESVSVSLAWYQQKPGKAPKLLIYKASTLESGVPPRFSGSGSGTEFTLTISSLQPNDFATYYCQEYHTSSRVTFGPGTKVDIK (SEQ ID NO: 219)	FGPGTKVDIK (SEQ ID NO: 220)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
24	009-3D04H	EVQLLESGGGLVQPGASLRLSCAASGFSFKDYALSWVRQAPGKGLEWVSHISGSGLSTYYADSVKGRFTISRDNSKNTVYLQMNSLRAEDTAVYFCAK (SEQ ID NO: 221)	EVQLLESGGGLVQPGASLRLSCAAS (SEQ ID NO: 222)	GFSFKDYA (SEQ ID NO: 223)	LSWVRQAPGKGLEWVSH (SEQ ID NO: 224)	ISGSGLST (SEQ ID NO: 225)	YYADSVKGRFTISRDNSKNTVYLQMNSLRAEDTAVYFC (SEQ ID NO: 226)	AKDRVVGRPWEYSLDF (SEQ ID NO: 227)	gaggtgcagctgttggagtctgggggaggcctggtgcagcctggggcgtccctgagactctcctgtgcagcctctggattcagctttaaggactatgccctgagctgggtccgccaggctccagggaaggggctggagtgggtctcacatattagtggtagtggtcttagtacatactacgcagactccgtcaagggccggttcaccatctccagagacaattccaagaacacggtgtatttgcaaatgaacagcctgagagccgaggacacggccgtgtatttctgtgcgaaagatcgggtagtaggtcgcccctgggagtactcccttgacttctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtg (SEQ ID NO: 228)	EVQLLESGGGLVQPGASLRLSCAASGFSFKDYALSWVRQAPGKGLEWVSHISGSGLSTYYADSVKGRFTISRDNSKNTVYLQMNSLRAEDTAVYFCAKDRVVGRPWEYSLDFWGQGTLVTVSS (SEQ ID NO: 229)	WGQGTLVTVSS (SEQ ID NO: 230)
25	009-3D04L	EIVMTQSPATVSVSPGERATLSCRASQSVNSDLVWYQQKPGQAPRLLIYGASIRATGIPARFSGSGSGTEFTLTISSIQSEDFAVYYCQQYNNWP (SEQ ID NO: 231)	EIVMTQSPATVSVSPGERATLSCRAS (SEQ ID NO: 232)	QSVNSD (SEQ ID NO: 233)	LVWYQQKPGQAPRLLIY (SEQ ID NO: 234)	GAS (SEQ ID NO: 235)	IRATGIPARFSGSGSGTEFTLTISSIQSEDFAVYYC (SEQ ID NO: 236)	QQYNNWPPLT (SEQ ID NO: 237)	gaaatagtgatgacgcagtctccagccaccgtgtctgtgtctccaggggaaagagccaccctctcttgcagggccagtcagagtgttaacagcgacctcgtatggtaccagcagaaacctggccaggctcccagactcctcatttatggagcgtccattagggccactggtatcccagccaggttcagtggcagtgggtctgggacagagttcactctcaccatcagcagcattcagtctgaagattttgcagtttattactgtcagcagtataataactggcctccgctcactttcggcggagggaccaaggtggaaatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccag (SEQ ID NO: 238)	EIVMTQSPATVSVSPGERATLSCRASQSVNSDLVWYQQKPGQAPRLLIYGASIRATGIPARFSGSGSGTEFTLTISSIQSEDFAVYYCQQYNNWPPLTFGGGTKVEIK (SEQ ID NO: 239)	FGGGTKVEIK (SEQ ID NO: 240)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
26	009-3E06H	EVQLVESGGGLVQPGGSLRLSCAASGFSVSSNFMSWVRQTPGKGLEWVSVLYSGGATFYADSVKGRFTISRDNSKNTLYLQMDSLRVEDTGVYYCA (SEQ ID NO: 241)	EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 242)	GFSVSSNF (SEQ ID NO: 243)	MSWVRQTPGKGLEWVSV (SEQ ID NO: 244)	LYSGGAT (SEQ ID NO: 245)	FYADSVKGRFTISRDNSKNTLYLQMDSLRVEDTGVYYC (SEQ ID NO: 246)	ASRHYNYDDDY (SEQ ID NO: 247)	gaggtgcagctggtggagtctgggggaggcttggtccagcctggggggtccctgagactctcctgtgcagcctctggattcagcgtcagtagcaacttcatgagttgggtccgccagactccagggaaggggctggagtgggtctcagttctttatagcggtggtgccacattctacgcagactccgtgaagggcagattcaccatctccagagacaattcgaagaacacgctgtatcttcaaatggacagcctgagagtcgaggacacgggtgtgtattactgtgcgagcagacactacaattacgacgatgactacggggccagggaacactggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactca (SEQ ID NO: 248)	EVQLVESGGGLVQPGGSLRLSCAASGFSVSSNFMSWVRQTPGKGLEWVSVLYSGGATFYADSVKGRFTISRDNSKNTLYLQMDSLRVEDTGVYYCASRHYNYDDDYGGQGTLVTVSS (SEQ ID NO: 249)	GGQGTLVTVSS (SEQ ID NO: 250)
27	009-3E06L	DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSDGNTYLNWFQQRPGQSLRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHW (SEQ ID NO: 251)	DVVMTQSPLSLPVTLGQPASISCRSS (SEQ ID NO: 252)	QSLVHSDGNTY (SEQ ID NO: 253)	LNWFQQRPGQSLRRLIY (SEQ ID NO: 254)	KVS (SEQ ID NO: 255)	NRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC (SEQ ID NO: 256)	MQGTHWPT (SEQ ID NO: 257)	gatgttgtgatgactcagtctccactctccctgcccgtcacccttggacagccggcctccatctcctgcaggtctagtcaaagcctcgtacacagtgatggaaacacctacttgaattggtttcagcagaggccaggccaatctctaaggcgcctaatttataaggtttctaaccgggactctggggtcccagacagattcagcggcagtgggtcaggcactgacttcacactgaaaatcagcagggtggaggctgaggatgttggggtttattactgcatgcaaggtacacactggcccaccttcggccaagggacacgactggagattaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggt (SEQ ID NO: 258)	DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSDGNTYLNWFQQRPGQSLRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPTFGQGTRLEIK (SEQ ID NO: 259)	FGQGTRLEIK (SEQ ID NO: 260)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
38	009-3F05H	EVQLVESGGTVVQPGGSLRLSCVASEYTFRNYWMSWVRQAPGKGLEWVGNINQDGSEKYYVDSVKGRFTISRDNAENSLFLQMNSLRVADTAVYYCAR (SEQ ID NO: 261)	EVQLVESGGTVVQPGGSLRLSCVAS (SEQ ID NO: 262)	EYTFRNYW (SEQ ID NO: 263)	MSWVRQAPGKGLEWVGN (SEQ ID NO: 264)	INQDGSEK (SEQ ID NO: 265)	YYVDSVKGRFTISRDNAENSLFLQMNSLRVADTAVYYC (SEQ ID NO: 266)	ARAGSYGDYRPINNWFDP (SEQ ID NO: 267)	gaggtgcagctggtggagtctgggggaaccgtggtccagccgggggggtccctgagactctcctgtgtagcctctgaatatacctttcaggaattattggatgagctgggtccgccaggctccagggaaggggctggagtgggtgggcaacataaatcaagatggaagtgagaagtactatgtggactctgtgaagggccgattcaccatctccagagacaacgccgagaactccctatttctgcaaatgaacagcctgagagtcgcggacacggctgttattactgtgcgagagcggggagttacggtgactacaggccgataaacaactggttcgacccctgggccggggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgagctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggac (SEQ ID NO: 268)	EVQLVESGGTVVQPGGSLRLSCVASEYTFRNYWMSWVRQAPGKGLEWVGNINQDGSEKYYVDSVKGRFTISRDNAENSLFLQMNSLRVADTAVYYCARAGSYGDYRPINNWFDPWGRGTLVTVSS (SEQ ID NO: 269)	WGRGTLVTVSS (SEQ ID NO: 270)
39	009-3F05L	DIQMTQSPSTLSASVGGRVTITCRASQSISFSLAWYQQKPGKAPELVIYQTSNLKSGVPSRFSGSGSGTQFTLTISSLQPEDFATYYCQHYSNY (SEQ ID NO: 271)	DIQMTQSPSTLSASVGGRVTITCRAS (SEQ ID NO: 272)	QSISFS (SEQ ID NO: 273)	LAWYQQKPGKAPELVIY (SEQ ID NO: 274)	QTS (SEQ ID NO: 275)	NLKSGVPSRFSGSGSGTQFTLTISSLQPEDFATYYC (SEQ ID NO: 276)	QHYSNYSYT (SEQ ID NO: 277)	gacatccagatgacccagtctccttccaccctgtctgcatctgtaggggcagagtcaccatcacttgccgggccagtcagagtattagtttctcgttggcctggtatcagcagaaaccagggaaagcccctgaactcgtcatctatcagacgtctaatttaaaaagtggggtcccatcaagattcagcggcagtggctctgggacacaattcactctcaccatcagcagcctgcagcctgaagattttgcaacctattactgccaacactattctaattactcgtacactttggccaggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagag (SEQ ID NO: 278)	DIQMTQSPSTLSASVGGRVTITCRASQSISFSLAWYQQKPGKAPELVIYQTSNLKSGVPSRFSGSGSGTQFTLTISSLQPEDFATYYCQHYSNYSYTFGQGTKVEIK (SEQ ID NO: 279)	FGQGTKVEIK (SEQ ID NO: 280)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
30	009-3G01H	QVQLVESGGGVVQPGRSLRLSCAASGFTFRIYAMHWVRQAPGKGLEWVAVISNEGTNKYYADSVKGRFTISRDNSKNTLYLQMNSLRPEDAAVYYCAR (SEQ ID NO: 281)	QVQLVESGGGVVQPGRSLRLSCAAS (SEQ ID NO: 282)	GFTFRIYA (SEQ ID NO: 283)	MHWVRQAPGKGLEWVAV (SEQ ID NO: 284)	ISNEGTNK (SEQ ID NO: 285)	YYADSVKGRFTISRDNSKNTLYLQMNSLRPEDAAVYYC (SEQ ID NO: 286)	ARDPSNPPHWGNFDS (SEQ ID NO: 287)	caggtgcagctggtggagtctgggggtggcgtggtccagcctgggaggtccctgagactctcctgtgcagcctctggattcaccttcagaatctatgctatgcactgggtccgccaggctccaggcaaggggctggagtgggtggcagttatatcaaatgaaggaactaataaatactacgcagactccgtgaagggccgattcaccatttccagagacaattccaagaacacgttgtatttgcaaatgaatagcctgagacctgaggacgcggctgtgtattactgtgcgagagatccctctaatcccccgcactgggggaactttgactcttggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacg (SEQ ID NO: 288)	QVQLVESGGGVVQPGRSLRLSCAASGFTFRIYAMHWVRQAPGKGLEWVAVISNEGTNKYYADSVKGRFTISRDNSKNTLYLQMNSLRPEDAAVYYCARDPSNPPHWGNFDSWGQGTLVTVSS (SEQ ID NO: 289)	WGQGTLVTVSS (SEQ ID NO: 290)
31	009-3G01L	EIVLTQSPGTLSLSPGERATLSCRASESVSSYLAWYQKKPGQAPRLLIYDASHRATGIPARFSGSGSGTDFTLTISSLESEDFGVYYCQQRSNWP (SEQ ID NO: 291)	EIVLTQSPGTLSLSPGERATLSCRAS (SEQ ID NO: 292)	ESVSSY (SEQ ID NO: 293)	LAWYQKKPGQAPRLLIY (SEQ ID NO: 294)	DAS (SEQ ID NO: 295)	HRATGIPARFSGSGSGTDFTLTISSLESEDFGVYYC (SEQ ID NO: 296)	QQRSNWPPIT (SEQ ID NO: 297)	gaaattgtgttgacacagtctccaggcaccctgtctctgtctccaggggaaagagccaccctctcctgcagggccagtgagagtgttagcagctacttagcctggtaccaaaagaaacctggccaggctcccaggctcctcatctatgatgcatcccacagggccactggcatcccagccaggttcagtggcagtgggtctgggacagacttcactctcaccatcagcagcctagagtctgaagattttggagtttattactgtcagcagcgtagcaactggcctccgatcaccttcggccaagggacacgactggagattaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccag (SEQ ID NO: 298)	EIVLTQSPGTLSLSPGERATLSCRASESVSSYLAWYQKKPGQAPRLLIYDASHRATGIPARFSGSGSGTDFTLTISSLESEDFGVYYCQQRSNWPPITFGQGTRLEIK (SEQ ID NO: 299)	FGQGTRLEIK (SEQ ID NO: 300)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
32	009-3G03H	EVQLLESGGGLIQPGGSLRLSCAASAFTFNKYAMNWVRQAPGKGLEWVSHISGSGLSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK (SEQ ID NO: 301)	EVQLLESGGGLIQPGGSLRLSCAAS (SEQ ID NO: 302)	AFTFNKYA (SEQ ID NO: 303)	MNWVRQAPGKGLEWVSH (SEQ ID NO: 304)	ISGSGLST (SEQ ID NO: 305)	YYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC (SEQ ID NO: 306)	AKDLAVTPPAQGYLDR (SEQ ID NO: 307)	gaggtgcagctgttggagtctgggggaggcttgatacagccgggggggtccctgagactctcctgtgcagcctctgcattcacatttaacaaatatgccatgaactgggtccgccaggctccagggaaggggctggagtgggtctcgcatattagtggcagtggtcttagcacatactacgcagactccgtgaagggccggttcaccatctccagagacaattccaagaacacgctgtatctgcaaatgaacagcctgagagccgaggacacggccgtctactactgtgcgaaagatctcgccgttacaccacctgcccagggttacttggaccgctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtga (SEQ ID NO: 308)	EVQLLESGGGLIQPGGSLRLSCAASAFTFNKYAMNWVRQAPGKGLEWVSHISGSGLSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDLAVTPPAQGYLDRWGQGTLVTVSS (SEQ ID NO: 309)	WGQGTLVTVSS (SEQ ID NO: 310)
33	009-3G03L	EIVLTQSPATLSLSPGERATLSCRASQSVNNYLAWYQEKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWP (SEQ ID NO: 311)	EIVLTQSPATLSLSPGERATLSCRAS (SEQ ID NO: 312)	QSVNNY (SEQ ID NO: 313)	LAWYQEKPGQAPRLLIY (SEQ ID NO: 314)	DAS (SEQ ID NO: 315)	NRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYC (SEQ ID NO: 316)	QQRSNWPPIT (SEQ ID NO: 317)	gaaattgtgttgacacagtctccagccaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgttaacaactacttagcctggtaccaagagaagcctggccaggctcccaggctcctcatctatgatgcatccaacagggccactggcatcccagccaggttcagtggcagtgggtctgggacagacttcactctcaccatcagcagcctagaacctgaagattttgcagtttattactgtcagcagcgtagcaactggcctccgatcaccttcggccaagggacacgactggagattaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccagga (SEQ ID NO: 318)	EIVLTQSPATLSLSPGERATLSCRASQSVNNYLAWYQEKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPITFGQGTRLEIK (SEQ ID NO: 319)	FGQGTRLEIK (SEQ ID NO: 320)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
34	015-1A01H	QVQLVQSGAEVRKPGSSVKVSCTTSGGTFGSYGFNWVRQAPGQGLEWMGRIFPLLGTANYAQRFQGRVTITADKSTTTAYMELSRLTSEDTAVYYCAR (SEQ ID NO: 321)	QVQLVQSGAEVRKPGSSVKVSCTTS (SEQ ID NO: 322)	GGTFGSYG (SEQ ID NO: 323)	FNWVRQAPGQGLEWMGR (SEQ ID NO: 324)	IFPLLGTA (SEQ ID NO: 325)	NYAQRFQGRVTITADKSTTTAYMELSRLTSEDTAVYYC (SEQ ID NO: 326)	ARDDYMTVDRDYYYMDV (SEQ ID NO: 327)	caggtccagctggtgcagtctggggctgaggtgaggaagcctgggtcctcggtgaaggtctcctgtacgacctctggaggcaccttcggcagttatggttttaattgggtgcgacaggcccctggacaagggcttgagtggatgggaaggatcttccctctcctggggactgcaaactatgcacagcgcttccagggcagagtcacgattaccgcggacaaatccacgaccacagcctacatggagctgagcaggctgacatctgaggacacggccgtgtattattgtgcgagagatgactatatgacagtggaccgagactactactacatggacgtctggggcaaagggacctcggtcaccgtctcctcagcctccaccaagggcccatcggtcttccccctggcaccctcctccaggagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctac (SEQ ID NO: 328)	QVQLVQSGAEVRKPGSSVKVSCTTSGGTFGSYGFNWVRQAPGQGLEWMGRIFPLLGTANYAQRFQGRVTITADKSTTTAYMELSRLTSEDTAVYYCARDDYMTVDRDYYYMDVWGKGTSVTVSS (SEQ ID NO: 329)	WGKGTSVTVSS (SEQ ID NO: 330)
35	015-1A01L	EIVLTQSPATLSVSPGERATLSCRASQSISTNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTVSSLQSEDFAVYYCQQYNNWP (SEQ ID NO: 331)	EIVLTQSPATLSVSPGERATLSCRAS (SEQ ID NO: 332)	QSISTN (SEQ ID NO: 333)	LAWYQQKPGQAPRLLIY (SEQ ID NO: 334)	GAS (SEQ ID NO: 335)	TRATGIPARFSGSGSGTEFTLTVSSLQSEDFAVYYC (SEQ ID NO: 336)	QQYNNWPPLFS (SEQ ID NO: 337)	gaaattgtgctgacacagtctccagccaccctgtctgtgtctccaggggaaagagccaccctctcctgcagggccagtcagagtattagcaccaacttagcctggtaccagcaaaaacctggccaggctcccaggctcctcatctatggtgcgtcgaccagggccactggtatcccagccaggttcagtggcagtgggtctgggacagagttcactctcaccgtcagcagcctgcagtctgaagactttgcagtttattactgtcagcagtataataattggcctccctattcagtttcggccctgggaccaaagtggatatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactccc (SEQ ID NO: 338)	EIVLTQSPATLSVSPGERATLSCRASQSISTNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTVSSLQSEDFAVYYCQQYNNWPPLFSFGPGTKVDIK (SEQ ID NO: 339)	FGPGTKVDIK (SEQ ID NO: 340)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
36	015-1A03H	EVQLVESGRGLVHPGGSLRLSCAASGFTFSSYSMSWVRQAPGKGLEWLATINKEGSENHHVDYAKGRFTISRDNAKNTLYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 341)	EVQLVESGRGLVHPGGSLRLSCAAS (SEQ ID NO: 342)	GFTFSSYS (SEQ ID NO: 343)	MSWVRQAPGKGLEWLAT (SEQ ID NO: 344)	INKEGSEN (SEQ ID NO: 345)	HHVDYAKGRFTISRDNAKNTLYLQMNSLRAEDTAVYYC (SEQ ID NO: 346)	ARVSREEWATVDDPHDYYYMDV (SEQ ID NO: 347)	gaggtgcagctggtggagtctgggagaggcttggtccaccctggggggtccctgagactctcctgtgcagcctctggattcacctttagtagttattcgatgagttgggtccgccaggctccagggaaggggctggagtggctggccaccataaacaaagagggaagtgaaaaccaccatgtggactacgcgaagggccggttcactatctccagagacaatgccaagaataccctgtatctacaaatgaatagtctgagagccgaggacacggctgtgtattattgtgcgagagtctccagggaagagtgggcgacagttgacgaccctcacgactactactacatggacgtatggggccaagggaccacggtcaccgtctcctcagcctccaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctaca (SEQ ID NO: 348)	EVQLVESGRGLVHPGGSLRLSCAASGFTFSSYSMSWVRQAPGKGLEWLATINKEGSENHHVDYAKGRFTISRDNAKNTLYLQMNSLRAEDTAVYYCARVSREEWATVDDPHDYYYMDVWGQGTTVTVSS (SEQ ID NO: 349)	WGQGTTVTVSS (SEQ ID NO: 350)
37	015-1A03L	DIQMTQSPSSLSASVGDRVTITCRASQRISNYLNWYQQNPGRAPKLLIYKAYNLERGVPSRFSGSGSGTDFTLTISTLQPEDFGTYYCQQNYNP (SEQ ID NO: 351)	DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 352)	QRISNY (SEQ ID NO: 353)	LNWYQQNPGRAPKLLIY (SEQ ID NO: 354)	KAY (SEQ ID NO: 355)	NLERGVPSRFSGSGSGTDFTLTISTLQPEDFGTYYC (SEQ ID NO: 356)	QQNYNPLFT (SEQ ID NO: 357)	gacatccagatgacccagtctccatcctccctgtctgcatctgtgggagacagagtcaccatcacttgccgggcaagtcagaggattagcaactacttaaattggtatcagcagaacccagggcagagcccctaaactcctgatctataaagcatacaatttagaaaggggagtcccgtcaaggttcagtggcagtggatctgggacagatttcactctcaccatcagcactctgcaacctgaagattttggtacttactactgtcaacagaattacaatcccctgttcactttcggcggggggaccaaggtagagatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggaga (SEQ ID NO: 358)	DIQMTQSPSSLSASVGDRVTITCRASQRISNYLNWYQQNPGRAPKLLIYKAYNLERGVPSRFSGSGSGTDFTLTISTLQPEDFGTYYCQQNYNPLFTFGGGTKVEIK (SEQ ID NO: 359)	FGGGTKVEIK (SEQ ID NO: 360)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
38	015-1A04H	EVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGPQWVANIKKEGGEKQEMDHVKGRFTISRDNAKNTLYLQMNSLRVEDTAVYYCVR (SEQ ID NO: 361)	EVQLVQSGGGLVQPGGSLRLSCAAS (SEQ ID NO: 362)	GFTFSSYA (SEQ ID NO: 363)	MSWVRQAPGKGPQWVAN (SEQ ID NO: 364)	IKKEGGEK (SEQ ID NO: 365)	QEMDHVKGRFTISRDNAKNTLYLQMNSLRVEDTAVYYC (SEQ ID NO: 366)	VRVSREEWATVDDPHDYYYMDV (SEQ ID NO: 367)	gaggtgcagctggtgcagtctgggggaggcttggtccagccgggggggtccctgagactctcctgtgcagcctctggattcacgtttagtagttacgcgatgagttgggtccgccaggctccagggaaggggccgcagtgggtggccaatataaagaaagaaggcggtgaaaagcaggaaatggaccatgtgaagggccggttcactatctccagagacaacgccaagaatacactgtatctgcaaatgaatagtctgagagtcgaggacacggctgtgtattactgtgtgagagtctccagggaagagtgggcgacagttgacgaccctcacgactactactacatggacgtctggggccaagggt (SEQ ID NO: 368)	EVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGPQWVANIKKEGGEKQEMDHVKGRFTISRDNAKNTLYLQMNSLRVEDTAVYYCVRVSREEWATVDDPHDYYYMDVWGQG (SEQ ID NO: 369)	WGQG (SEQ ID NO: 370)
39	015-1A04L	DIQMTQSPSSLSASVGDRVTITCRASQRISNYLNWYQQKPGKAPKLLIYNANILENGVPSRFSGGGSGTDFTLSISGLQPEDFGTYYCQQSYNS (SEQ ID NO: 371)	DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 372)	QRISNY (SEQ ID NO: 373)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 374)	NAN (SEQ ID NO: 375)	ILENGVPSRFSGGGSGTDFTLSISGLQPEDFGTYYC (SEQ ID NO: 376)	QQSYNSLFT (SEQ ID NO: 377)	gacatccagatgacgcagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgtcgggcaagtcagaggattagcaactacttaaattggtatcagcaaaaaccagggaaagcccctaaactcctgatctataacgcaaacattttagagaatggggtcccatcaaggttcagtggcggtgggtctgggacagatttcactctctccatcagcggtctgcaacctgaagattttggtacttactactgtcaacagagttacaattccctgttcactttcggcgggggggaccaaggtagagatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagag (SEQ ID NO: 378)	DIQMTQSPSSLSASVGDRVTITCRASQRISNYLNWYQQKPGKAPKLLIYNANILENGVPSRFSGGGSGTDFTLSISGLQPEDFGTYYCQQSYNSLFTFGGGTKVEIK (SEQ ID NO: 379)	FGGGTKVEIK (SEQ ID NO: 380)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
40	015-2A01H	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMTWVRQAPGKGLEWVANIEKEGSEKDHVGYVKGRFTISRDNAKSTLYLQMNSLSAEDTAVYYCAR (SEQ ID NO: 381)	EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 382)	GFTFSSYS (SEQ ID NO: 383)	MTWVRQAPGKGLEWVAN (SEQ ID NO: 384)	IEKEGSEK (SEQ ID NO: 385)	DHVGYVKGRFTISRDNAKSTLYLQMNSLSAEDTAVYYC (SEQ ID NO: 386)	ARVSREEWATVDDPHDYYYMDV (SEQ ID NO: 387)	gaggtgcagctggtggagtctgggggaggcttggtccagcctggggggtccctgaggctctcctgtgcagcctctggattcacctttagtagttattcgatgacctgggtccgccaggctccagggaaggggctggagtgggtggccaatatagagaaagaaggaagtgagaaagaccatgtgggctatgtgaagggccgattcactatctccagagacaacgccaagagtacactgtatctgcaaatgaatagtctgagcgccgaggacacggctgtgtattactgtgcgagagtctccagggaagagtgggcgacagttgacgaccctcacgactactactacatggacgtctggggccaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaagg (SEQ ID NO: 388)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMTWVRQAPGKGLEWVANIEKEGSEKDHVGYVKGRFTISRDNAKSTLYLQMNSLSAEDTAVYYCARVSREEWATVDDPHDYYYMDVWGQGTTVTVSS (SEQ ID NO: 389)	WGQGTTVTVSS (SEQ ID NO: 390)
41	015-2A01L	DIQMTQSPFSLSASVGDRVTITCRAGQRISNYLNWYQQKPGKAPKLLIYNANTLQGGVPLRFSGSGSGTDFTLTISSLQPEDSGTYYCQQSYN (SEQ ID NO: 391)	DIQMTQSPFSLSASVGDRVTITCRAG (SEQ ID NO: 392)	QRISNY (SEQ ID NO: 393)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 394)	NAN (SEQ ID NO: 395)	TLQGGVPLRFSGSGSGTDFTLTISSLQPEDSGTYYC (SEQ ID NO: 396)	QQSYNRLFT (SEQ ID NO: 397)	gacatccagatgacccagtctccgttctccctgtctgcatctgtgggagacagagtcaccatcacttgccgggcaggtcagaggattagcaactacttaaattggtatcagcagaagccaggcaaagcccctaaactgctgatctataacgcaaacactttacaaggtggggtcccattaaggttcagtggcagtggatctgggacagatttcactctcaccatcagcagtctgcaacctgaagattctggtacttactactgtcaacagagttacaataggctgttcacttcggcgggggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgaga (SEQ ID NO: 398)	DIQMTQSPFSLSASVGDRVTITCRAGQRISNYLNWYQQKPGKAPKLLIYNANTLQGGVPLRFSGSGSGTDFTLTISSLQPEDSGTYYCQQSYNRLFTFGGGTKVEIK (SEQ ID NO: 399)	FGGGTKVEIK (SEQ ID NO: 400)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
42	015-2A06H	QVQLVQSGAEVKKPGTSVKVSCKASGYIFSGSYIQWVRQAPGQGLEWMGRINPKTGNTNYAQKFQGRVTMTRDMSISTAYMELTRLSSDDTAVYYCAR (SEQ ID NO: 401)	QVQLVQSGAEVKKPGTSVKVSCKAS (SEQ ID NO: 402)	GYIFSGSY (SEQ ID NO: 403)	IQWVRQAPGQGLEWMGR (SEQ ID NO: 404)	INPKTGNT (SEQ ID NO: 405)	NYAQKFQGRVTMTRDMSISTAYMELTRLSSDDTAVYYC (SEQ ID NO: 406)	ARDFDYGDYRGSAFDI (SEQ ID NO: 407)	caggtgcagctggtgcagtctggggctgaggtaaagaagcctgggacctcagtgaaagtctcctgcaaggcttctggatacatcttctccggctcctatatccagtgggtacgacaggcccctgggcaagggcttgagtggatgggaaggatcaaccctaagactggtaatacaaattatgcacagaagtttcagggcagggtcaccatgaccagggacatgtccatcagcacagcctacatggagctgactaggctgagctctgacgacacggccgtgtattactgtgcgagagactttgattacggtgactaccgcggctctgcttttgatatctggggccaagggcaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtg (SEQ ID NO: 408)	QVQLVQSGAEVKKPGTSVKVSCKASGYIFSGSYIQWVRQAPGQGLEWMGRINPKTGNTNYAQKFQGRVTMTRDMSISTAYMELTRLSSDDTAVYYCARDFDYGDYRGSAFDIWGQGAMVTVSS (SEQ ID NO: 409)	WGQGAMVTVSS (SEQ ID NO: 410)
43	015-2A06L	DIQMTQSPSSLSASVGDRVTITCQPSQDFSNYLNWYQQKPGKAPKLLIYDTSNLETGVPSRFSGSGAGTHFTLTINSLQPEDIATYYCQQ (SEQ ID NO: 411)	DIQMTQSPSSLSASVGDRVTITCQPS (SEQ ID NO: 412)	QDFSNY (SEQ ID NO: 413)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 414)	DTS (SEQ ID NO: 415)	NLETGVPSRFSGSGAGTHFTLTINSLQPEDIATYYC (SEQ ID NO: 416)	QQLNT (SEQ ID NO: 417)	gacatccagatgacccagtctccatcctccctgtctgcatctgttggtgacagagtcaccatcacttgccagccgagtcaggactttagcaactatttaaattggtatcagcagaaaccagggaaagcccctaagctcctgatctacgatacatccaatttggaaacaggggtcccatcaagattcagtggaagtggggctgggacacattttactctcaccatcaacagcctgcagcctgaagacattgcaacatattactgtcaacagttaaatacctttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 418)	DIQMTQSPSSLSASVGDRVTITCQPSQDFSNYLNWYQQKPGKAPKLLIYDTSNLETGVPSRFSGSGAGTHFTLTINSLQPEDIATYYCQQLNTFGPGTKVDIK (SEQ ID NO: 419)	FGPGTKVDIK (SEQ ID NO: 420)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
44	015-2B04H	QVQLVQSGAEVKRPGASVKVSCKAAGFTLNNLYIHWVRQAPGQGLEWMGRINPNSGITKYADKFRGRVTLTRDTSVNTAYMEVARLRSDDTAVYYCAR (SEQ ID NO: 421)	QVQLVQSGAEVKRPGASVKVSCKAA (SEQ ID NO: 422)	GFTLNNLY (SEQ ID NO: 423)	IHWVRQAPGQGLEWMGR (SEQ ID NO: 424)	INPNSGIT (SEQ ID NO: 425)	KYADKFRGRVTLTRDTSVNTAYMEVARLRSDDTAVYYC (SEQ ID NO: 426)	ARDIDTGDYRGADVLQM (SEQ ID NO: 427)	caggtgcagctggtgcagtctggggctgaggtgaagaggcccggggcctcagtgaaggtctcctgcaaggctgcgggattcacgttgaacaacctctacatacactgggtgcgacaggcccctggacagggacttgagtggatgggacggatcaaccctaacagtggaatcacaaagtatgcagacaagtttcggggcagggtcacgttgaccagggacacgtccgtcaacactgcctatatggaggtggcgcggctgcgatctgacgacacggccgtctattattgtgcgcgagacattgacaccggtgactaccgcggcgctgatgttctccaaatgtggggtcaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacc (SEQ ID NO: 428)	QVQLVQSGAEVKRPGASVKVSCKAAGFTLNNLYIHWVRQAPGQGLEWMGRINPNSGITKYADKFRGRVTLTRDTSVNTAYMEVARLRSDDTAVYYCARDIDTGDYRGADVLQMWGQGTMVTVSS (SEQ ID NO: 429)	WGQGTMVTVSS (SEQ ID NO: 430)
45	015-2B04L	DIQMTQSPSSLSASVGDRVTITCQASQDFSNYLNWYQQKPGRAPKLLIYDASKLATGVPSRFSGHKSGADYTFTITSLQPEDIATYYCQQ (SEQ ID NO: 431)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 432)	QDFSNY (SEQ ID NO: 433)	LNWYQQKPGRAPKLLIY (SEQ ID NO: 434)	DAS (SEQ ID NO: 435)	KLATGVPSRFSGHKSGADYTFTITSLQPEDIATYYC (SEQ ID NO: 436)	QQLYT (SEQ ID NO: 437)	gacatccagatgacccagtctccatcctccctgtctgcatctgtgggagacagagtcaccatcacttgccaggcgagtcaagacttcagtaattatctaaattggtatcaacagaaacctgggagagcccctaagctcctcatctacgatgcttccaatttggcaacaggggtcccatcgaggttcagtggacataaatctggggcagattataccttcaccatcaccagcctgcagcctgaagatattgcaacatattactgtcaacagttgtatactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagca (SEQ ID NO: 438)	DIQMTQSPSSLSASVGDRVTITCQASQDFSNYLNWYQQKPGRAPKLLIYDASKLATGVPSRFSGHKSGADYTFTITSLQPEDIATYYCQQLYTFGPGTKVDIK (SEQ ID NO: 439)	FGPGTKVDIK (SEQ ID NO: 440)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
46	015-2C03H	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMSWVRQAPGKGLEWVANINKEGSEKNHVDFVKGRFTISRDNAKNTLSLQMNSLRAEDSAVYYCAR (SEQ ID NO: 441)	EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 442)	GFTFSSYS (SEQ ID NO: 443)	MSWVRQAPGKGLEWVAN (SEQ ID NO: 444)	INKEGSEK (SEQ ID NO: 445)	NHVDFVKGRFTISRDNAKNTLSLQMNSLRAEDSAVYYC (SEQ ID NO: 446)	ARVSREEWATVDDPHDYYYMDV (SEQ ID NO: 447)	gaggtgcagctggtggagtctgggggaggcttggtccagcctggggggtccctgagactctcctgtgcagcctctggattcacctttagtagttattcgatgagctgggtccgccaggctccagggaaggggctggagtgggtggccaatataaataaagaaggaagtgaaaagaaccatgtggactttgtgaagggccggttcactatctccagagacaacgccaagaatacactgtcgctgcaaatgaatagtctgagagccgaagattcggctgtgtattactgtgcgagagtctccagggaagagtgggcgacagttgacgaccctcacgactactactacatggacgtctggggccaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaagg (SEQ ID NO: 448)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMSWVRQAPGKGLEWVANINKEGSEKNHVDFVKGRFTISRDNAKNTLSLQMNSLRAEDSAVYYCARVSREEWATVDDPHDYYYMDVWGQGTTVTVSS (SEQ ID NO: 449)	WGQGTTVTVSS (SEQ ID NO: 450)
47	015-2C03L	DIQMTQSPSSLSASVGDRVTITCRASQRISNYLNWYQQRPGEAPKLLIYNAYTLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYIT (SEQ ID NO: 451)	DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 452)	QRISNY (SEQ ID NO: 453)	LNWYQQRPGEAPKLLIY (SEQ ID NO: 454)	NAY (SEQ ID NO: 455)	TLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 456)	QQSYITLFT (SEQ ID NO: 457)	gacatccagatgacccagtctccgtcctccctgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcagaggattagcaactacttgaattggtatcagcagagaccaggcgaagcccctaaactcctgatctataacgcatacactttagaaagtggggtcccatcaaggttcagtggcagtggatctgggacagatttcactctcaccatcagcagtctgcaacctgaggattttgctacttactactgtcaacagagttacattaccctgttcactttcggcgggggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaa (SEQ ID NO: 458)	DIQMTQSPSSLSASVGDRVTITCRASQRISNYLNWYQQRPGEAPKLLIYNAYTLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYITLFTFGGGTKVEIK (SEQ ID NO: 459)	FGGGTKVEIK (SEQ ID NO: 460)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
48	015-2C04H	EVQLLESGGALLQPGGSLRLSCAASGFTFSSYAMSWVRQPPGKGLQWVSIMSGRGDTMQYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCAR (SEQ ID NO: 461)	EVQLLESGGALLQPGGSLRLSCAAS (SEQ ID NO: 462)	GFTFSSYA (SEQ ID NO: 463)	MSWVRQPPGKGLQWVSI (SEQ ID NO: 464)	MSGRGDTM (SEQ ID NO: 465)	QYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYC (SEQ ID NO: 466)	AREEFTDTEMTITQGDFGY (SEQ ID NO: 467)	gaggtgcagctgttggagtctgggggagccttgctacagccggggggtccctgagactctcctgtgcagcctctggattcacctttagcagctatgccatgagctgggtccgccagcctccagggaagggtctgcagtgggtctcaattatgagtggtagggtgataccatgcagtacgcagactccgtgaagggccggttcaccatctccagagacaattccaagaacacactttatctgcaaatgaacagcctgagagccgaggacacggccatttattactgtgcgagagaggagtttaccgacacagagatgactataacccaaggggactttggctactggggccagggcaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttcccc (SEQ ID NO: 468)	EVQLLESGGALLQPGGSLRLSCAASGFTFSSYAMSWVRQPPGKGLQWVSIMSGRGDTMQYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCAREEFTDTEMTITQGDFGYWGQGTLVTVSS (SEQ ID NO: 469)	WGQGTLVTVSS (SEQ ID NO: 470)
49	015-2C04L	DIQMTQSPSSLSASVGDRVTITCRASQSISVYLNWYQQKPGKAPKLLIYGASNLQSGVPSRFSGSGSETDFTLTISSLQPEDFATYYCQRSYIT (SEQ ID NO: 471)	DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 472)	QSISVY (SEQ ID NO: 473)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 474)	GAS (SEQ ID NO: 475)	NLQSGVPSRFSGSGSETDFTLTISSLQPEDFATYYC (SEQ ID NO: 476)	QRSYITPFT (SEQ ID NO: 477)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcagagcattagtgtctatttaaattggtatcaacaaaaaccagggaaagcccctaagctcctgatctatggtgcatccaatttgcaaagtgggtgtcccatcaaggttcagtggcagtggatccgagacagatttcactctcaccatcagcagtctgcaacctgaagattttgcaacttactactgtcaacgcagttacatcactccattcactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagag (SEQ ID NO: 478)	DIQMTQSPSSLSASVGDRVTITCRASQSISVYLNWYQQKPGKAPKLLIYGASNLQSGVPSRFSGSGSETDFTLTISSLQPEDFATYYCQRSYITPFTFGPGTKVDIK (SEQ ID NO: 479)	FGPGTKVDIK (SEQ ID NO: 480)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
50	015-2C06H	QVQLVQSGSEVRKPGASVKVSCKASGFTFTDCFIHWVRQAPGQGLEWMGRINPSRGTTKYAEKFRGRVSMTRDMAINTAYMDMSRLQSDDTAVYYCAR (SEQ ID NO: 481)	QVQLVQSGSEVRKPGASVKVSCKAS (SEQ ID NO: 482)	GFTFTDCF (SEQ ID NO: 483)	IHWVRQAPGQGLEWMGR (SEQ ID NO: 484)	INPSRGTT (SEQ ID NO: 485)	KYAEKFRGRVSMTRDMAINTAYMDMSRLQSDDTAVYYC (SEQ ID NO: 486)	ARDIDSGDYRAADVFQI (SEQ ID NO: 487)	caggtgcagctggtgcagtctgggtctgaggtgaggaagcctggggcctcagtgaaggtctcctgcaaggcttctggattcacattcaccgactgctttatacactgggtgcgacaggcccctggacagggacttgagtggatgggtcggatcaatcctagtagaggaaccacaaaatatgcagagaaatttcggggccgggtctcgatgacccgggacatggccatcaacacagcctacatggacatgagcaggctgcaatctgacgacacggccgtgtattactgtgcgagagacattgactccggtgactaccgcgccgctgatgttttccagatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacc (SEQ ID NO: 488)	QVQLVQSGSEVRKPGASVKVSCKASGFTFTDCFIHWVRQAPGQGLEWMGRINPSRGTTKYAEKFRGRVSMTRDMAINTAYMDMSRLQSDDTAVYYCARDIDSGDYRAADVFQIWGQGTMVTVSS (SEQ ID NO: 489)	WGQGTMVTVSS (SEQ ID NO: 490)
51	015-2C06L	DIQMTQSPSSLSASLGDRVTITCQASQDFSNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTEYTLTISSLQPEDSATYYCQQ (SEQ ID NO: 491)	DIQMTQSPSSLSASLGDRVTITCQAS (SEQ ID NO: 492)	QDFSNY (SEQ ID NO: 493)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 494)	DAS (SEQ ID NO: 495)	NLETGVPSRFSGSGSGTEYTLTISSLQPEDSATYYC (SEQ ID NO: 496)	QQLTT (SEQ ID NO: 497)	gacatccagatgacccagtctccatcctccctgtctgcgtctctaggagacagagtcaccatcacttgccaggcgagtcaggactttagcaactatttaaattggtatcagcagaaaccagggaaagcccctaagctcctgatctacgatgcatccaatttggaaacaggggtcccatcaagattcagtggaagtggatctgggacagaatatactttaaccatcagcagcctgcagcctgaagattctgcaacatattactgtcaacagttgactacgttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 498)	DIQMTQSPSSLSASLGDRVTITCQASQDFSNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTEYTLTISSLQPEDSATYYCQQLTTFGPGTKVDIK (SEQ ID NO: 499)	FGPGTKVDIK (SEQ ID NO: 500)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
52	015-2D02H	QVQLVQSGAEVKKPGASVKVSCKASGFRFSDLYIHWVRQAPGQGLEWMGRINPTRGTTKYAEKFLGRVSMTRDTAISTAYLDVTRLQSDDTALYYCAR (SEQ ID NO: 501)	QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO: 502)	GFRFSDLY (SEQ ID NO: 503)	IHWVRQAPGQGLEWMGR (SEQ ID NO: 504)	INPTRGTT (SEQ ID NO: 505)	KYAEKFLGRVSMTRDTAISTAYLDVTRLQSDDTALYYC (SEQ ID NO: 506)	ARDIDSGDYRAADVFQI (SEQ ID NO: 507)	caggtgcagctggtgcagtctggggctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggattcaggttcagcgacttgtatatacactgggtgcgacaggcccctggacaggggcttgagtggatgggtcggatcaatcctaccagaggaaccacaaaatatgcagagaaatttctgggccgggtctcgatgaccagggacacggccatcagcacagcctatttggacgtgaccaggctgcaatctgacgacacggccctttattactgtgcgcgagacattgactccggtgactaccgcgccgctgatgtttttcagatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacc (SEQ ID NO: 508)	QVQLVQSGAEVKKPGASVKVSCKASGFRFSDLYIHWVRQAPGQGLEWMGRINPTRGTTKYAEKFLGRVSMTRDTAISTAYLDVTRLQSDDTALYYCARDIDSGDYRAADVFQIWGQGTMVTVSS (SEQ ID NO: 509)	WGQGTMVTVSS (SEQ ID NO: 510)
53	015-2D02L	DIQMTQSPSSLSASVGDRVTITCQASQDFSNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQQ (SEQ ID NO: 511)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 512)	QDFSNY (SEQ ID NO: 513)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 514)	DAS (SEQ ID NO: 515)	NLETGVPSRFSGSGSGTEYTLTISSLQPEDFATYYC (SEQ ID NO: 516)	QQLAT (SEQ ID NO: 517)	gacatccagatgacccagtctccatcctccctgtctgcgtctgtaggagacagagtcaccatcacttgccaggcgagtcaggactttagcaactatttaaattggtatcagcagaaaccagggaaagcccctaagctcctgatctacgatgcatccaatttggaaacaggggtcccatcaaggttcagtggaagtggatctgggacagaatatactttaaccatcagcagcctgcagcctgaagattttgcaacatattactgtcaacagttggctactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 518)	DIQMTQSPSSLSASVGDRVTITCQASQDFSNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQQLATFGPGTKVDIK (SEQ ID NO: 519)	FGPGTKVDIK (SEQ ID NO: 520)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
54	015-2E01H	QVQLVQSGSEVRKPGASVKVSCKASGFTFTDCFIHWVRQAPGQGPEWMGRINPSRGTTKYAEKFRGRVSMTRDTAINTAYMDVSRLQSDDTAVYYCAR (SEQ ID NO: 521)	QVQLVQSGSEVRKPGASVKVSCKAS (SEQ ID NO: 522)	GFTFTDCF (SEQ ID NO: 523)	IHWVRQAPGQGPEWMGR (SEQ ID NO: 524)	INPSRGTT (SEQ ID NO: 525)	KYAEKFRGRVSMTRDTAINTAYMDVSRLQSDDTAVYYC (SEQ ID NO: 526)	ARDIDSGDYRAADVFQI (SEQ ID NO: 527)	caggtgcagctggtgcagtctgggtctgaggtgaggaagcctggggcctcagtgaaggtctcctgcaaggcttctggattcacattcaccgactgctttatacactgggtgcgacaggcccctggacaggggcctgagtggatgggtcggatcaatcctagtaggaaccacaaaatatgcagagaaatttcggggccgggtctcgatgacccgggacacggccatcaacacagcctacatggacgtgagcaggctgcaatctgacgacacggccgtgtattactgtgcgagagacattgactccggtgactaccgcgccgctgatgtttttcagatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactct (SEQ ID NO: 528)	QVQLVQSGSEVRKPGASVKVSCKASGFTFTDCFIHWVRQAPGQGPEWMGRINPSRGTTKYAEKFRGRVSMTRDTAINTAYMDVSRLQSDDTAVYYCARDIDSGDYRAADVFQIWGQGTMVTVSS (SEQ ID NO: 529)	WGQGTMVTVSS (SEQ ID NO: 530)
55	015-2E01L	DIQMTQSPSSLSASLGDRVTITCQASQDFSNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTEYTLTISSLQPEDSATYYCQQ (SEQ ID NO: 531)	DIQMTQSPSSLSASLGDRVTITCQAS (SEQ ID NO: 532)	QDFSNY (SEQ ID NO: 533)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 534)	DAS (SEQ ID NO: 535)	NLETGVPSRFSGSGSGTEYTLTISSLQPEDSATYYC (SEQ ID NO: 536)	QQLTT (SEQ ID NO: 537)	gacatccagatgacccagtctccatcctccctgtctgcgtctctaggagacagagtcaccatcacttgccaggcgagtcaggactttagcaactatttaaattggtatcagcagaaaccagggaaagcccctaagctcctgatctacgatgcatccaatttggaaacaggggtcccatcaagattcagtggaagtggatctgggacagaatatactttaaccatcagcagcctgcagcctgaagattctgcaacatattactgtcaacagttgactacgttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 538)	DIQMTQSPSSLSASLGDRVTITCQASQDFSNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTEYTLTISSLQPEDSATYYCQQLTTFGPGTKVDIK (SEQ ID NO: 539)	FGPGTKVDIK (SEQ ID NO: 540)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
56	015-2E06H	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMSWVRQAPGKGLEWVANMNKEGGEKNHVDYVKGRFTISRDNAKSTLYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 541)	EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 542)	GFTFSSYS (SEQ ID NO: 543)	MSWVRQAPGKGLEWVAN (SEQ ID NO: 544)	MNKEGGEK (SEQ ID NO: 545)	NHVDYVKGRFTISRDNAKSTLYLQMNSLRAEDTAVYYC (SEQ ID NO: 546)	ARVSREEWATVDDPHDYYYMDV (SEQ ID NO: 547)	gaggtgcagctggtggagtctgggggaggcttggtccagcctggggggtccctgagactctcctgcgcagcctctggattcacctttagtagttattcgatgagctgggtccgccaggctccagggaaggggctggagtgggtggccaatatgaacaaagagggaggtgaaaaaaaccatgtggactatgtgaagggccgattcactatctccagagacaacgccaagagtacactgtatctgcaaatgaatagtctgagagccgaggacacggcggtgtattactgtgcgagagtctccagggaagagtgggcgacagttgacgaccctcacgactactattacatggacgtctggggccaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaagg (SEQ ID NO: 548)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMSWVRQAPGKGLEWVANMNKEGGEKNHVDYVKGRFTISRDNAKSTLYLQMNSLRAEDTAVYYCARVSREEWATVDDPHDYYYMDVWGQGTTVTVSS (SEQ ID NO: 549)	WGQGTTVTVSS (SEQ ID NO: 550)
57	015-2E06L	DIQMTQSPSSLSASVGGGVTITCRASQRISNYLNWYHQQPGKAPKLLIYNAYTLQSGVPSRFSGTGSGTDFTLTISSLQPEDFGTFYCQQSYNS (SEQ ID NO: 551)	DIQMTQSPSSLSASVGGGVTITCRAS (SEQ ID NO: 552)	QRISNY (SEQ ID NO: 553)	LNWYHQQPGKAPKLLIY (SEQ ID NO: 554)	NAY (SEQ ID NO: 555)	TLQSGVPSRFSGTGSGTDFTLTISSLQPEDFGTFYC (SEQ ID NO: 556)	QQSYNSLFT (SEQ ID NO: 557)	gacatccagatgacccagtctccatcctccctgtctgcatctgtgggaggcggagtcaccatcacttgccgggcaagtcagaggattagcaactacttaaattggtatcaccaacaaccaggcaaagcccctaaactcctgatctataacgcatacactttacagagtggggtcccatcaaggttcagtggcactggatctgggacagatttcactctcaccatcagcagtctgcaacctgaagattttggtactttctactgtcaacagagttacaatagcctgttcactttcggcggggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggag (SEQ ID NO: 558)	DIQMTQSPSSLSASVGGGVTITCRASQRISNYLNWYHQQPGKAPKLLIYNAYTLQSGVPSRFSGTGSGTDFTLTISSLQPEDFGTFYCQQSYNSLFTFGGGTKVEIK (SEQ ID NO: 559)	FGGGTKVEIK (SEQ ID NO: 560)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
58	015-2F01H	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYAISWVRQAPGQGLEWMGWISTYNGNSYYAQKLQDRVTMTTDTSTNTAYMELRSLRSDDTAVYFCAR (SEQ ID NO: 561)	QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO: 562)	GYTFTSYA (SEQ ID NO: 563)	ISWVRQAPGQGLEWMGW (SEQ ID NO: 564)	ISTYNGNS (SEQ ID NO: 565)	YYAQKLQDRVTMTTDTSTNTAYMELRSLRSDDTAVYFC (SEQ ID NO: 566)	AREGYDHLWGTYRFEAIDYYYTDV (SEQ ID NO: 567)	caggtgcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggttacacctttaccagttatgctatcagctgggtgcgacaggcccctggacaagggcttgagtggatgggatggatcagcacttacaatggtaactcatactatgcacagaaactccaagacagagtcaccatgaccacagacacatccacgaacacagcctacatggagctgaggagcctgagatctgacgacacggccgtctattttgtgcgagagagggatatgatcaccttggggggacttatcgctttgaggcgatagactactactacacggacgtctggggccaaggaaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtc (SEQ ID NO: 568)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYAISWVRQAPGQGLEWMGWISTYNGNSYYAQKLQDRVTMTTDTSTNTAYMELRSLRSDDTAVYFCAREGYDHLWGTYRFEAIDYYYTDVWGQGTTVTVSS (SEQ ID NO: 569)	WGQGTTVTVSS (SEQ ID NO: 570)
59	015-2F01L	EIVLTQSPGTLSLSPGERATLSCRASQSLSSXYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTITRLEPEDSAVYYCHQYGSS (SEQ ID NO: 571)	EIVLTQSPGTLSLSPGERATLSCRAS (SEQ ID NO: 572)	QSLSSXY (SEQ ID NO: 573)	LAWYQQKPGQAPRLLIY (SEQ ID NO: 574)	GAS (SEQ ID NO: 575)	SRATGIPDRFSGSGSGTDFTLTITRLEPEDSAVYYC (SEQ ID NO: 576)	HQYGSSTGT (SEQ ID NO: 577)	gaaattgtgttgacgcagtctccaggcaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtcttagcagcnnntacttagcctggtaccagcagaaacctggccaggctcccaggctcctcatctatggtgcatccagcagggccaccggcatcccagacaggttcagtggcagtgggtctgggacagacttcactctcaccatcaccagactggagcctgaagattctgcagtgtattattgtcaccagtatggtagctcaacgggaacgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacga (SEQ ID NO: 578)	EIVLTQSPGTLSLSPGERATLSCRASQSLSSXYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTITRLEPEDSAVYYCHQYGSSTGTFGQGTKVEIK (SEQ ID NO: 579)	FGQGTKVEIK (SEQ ID NO: 580)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
60	015-2F02H	QVQLVQSGAEVKRPGASVNVSCRASGFSFSDTYIHWVRQAPGQGLEWMGRLNPKRGTTKYAGHFQGRLTLTRDASINTAYMELSRLGTGDTAVYYCAR (SEQ ID NO: 581)	QVQLVQSGAEVKRPGASVNVSCRAS (SEQ ID NO: 582)	GFSFSDTY (SEQ ID NO: 583)	IHWVRQAPGQGLEWMGR (SEQ ID NO: 584)	LNPKRGTT (SEQ ID NO: 585)	KYAGHFQGRLTLTRDASINTAYMELSRLGTGDTAVYYC (SEQ ID NO: 586)	ARDIDFGDYRAADVFHI (SEQ ID NO: 587)	caggtgcagctggtgcagtctggggctgaggtgaagaggcctggggcctcagtgaacgtctcctgcagggcttctggattcagtttcagcgacacctatatacactgggtgcgacaggctcctgggcaggggctagagtggatgggacgactcaatcctaagagaggaaccacaaaatatgcagggcactttcagggcaggctcacgttgaccagggacgcgtccatcaacacagcctacatggagttgagcaggctggggactggcgacacggccgtctattactgcgcgcgagacattgacttcggtgactaccgcgccgctgatgttttcatatatggggccaggggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactc (SEQ ID NO: 588)	QVQLVQSGAEVKRPGASVNVSCRASGFSFSDTYIHWVRQAPGQGLEWMGRLNPKRGTTKYAGHFQGRLTLTRDASINTAYMELSRLGTGDTAVYYCARDIDFGDYRAADVFHIWGQGTMVTVSS (SEQ ID NO: 589)	WGQGTMVTVSS (SEQ ID NO: 590)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
61	015-2F02L	DIQMTQSPSSLSASVGDRVTITCQASQDFSNFLNWYQQRPGKAPKLLIYDASNLETGVPSRFSGRKSGAHYTLTISSLQAEDIATYYCQQ (SEQ ID NO: 591)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 592)	QDFSNF (SEQ ID NO: 593)	LNWYQQRPGKAPKLLIY (SEQ ID NO: 594)	DAS (SEQ ID NO: 595)	NLETGVPSRFSGRKSGAHYTLTISSLQAEDIATYC (SEQ ID NO: 596)	QQLDT (SEQ ID NO: 597)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccaggcgagtcaggactttagtaattttcttaattggtatcaacagagacctgggaaagcccctaaactcctgatctacgatgcatccaatttggagacaggggtcccatcaaggttcagtggaagaaaatctggggcacactatactctcaccatcagcagcctgcaggctgaagatattgcaacatattattgtcaacagttggatactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtctacg (SEQ ID NO: 598)	DIQMTQSPSSLSASVGDRVTITCQASQDFSNFLNWYQQRPGKAPKLLIYDASNLETGVPSRFSGRKSGAHYTLTISSLQAEDIATYYCQQLDTFGPGTKVDIK (SEQ ID NO: 599)	FGPGTKVDIK (SEQ ID NO: 600)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
62	015-2F04H	QVQLVQSGAEVKKPGTSVKVSCKASGYIFSGSYIQWVRQAPGQGLEWMGRINPKTGGTNYPQKFQGRVTMTRDMSISTAYMELSRLISDDTAVYYCAR (SEQ ID NO: 601)	QVQLVQSGAEVKKPGTSVKVSCKAS (SEQ ID NO: 602)	GYIFSGSY (SEQ ID NO: 603)	IQWVRQAPGQGLEWMGR (SEQ ID NO: 604)	INPKTGGT (SEQ ID NO: 605)	NYPQKFQGRVTMTRDMSISTAYMELSRLISDDTAVYYC (SEQ ID NO: 606)	ARDFDYGDYRGSAFDI (SEQ ID NO: 607)	caggtgcagctggtgcagtctggggctgaggtaaagaagcctgggacctcagtgaaagtctcctgcaaggcttctggatacatcttctccggctcctatattcaatgggtacgacaggcccctggacaagggcttgagtggatgggaaggatcaaccctaagactggtggcacaaattatccacagaagtttcagggcagggtcaccatgaccagggacatgtccatcagcacagcctatatggagctgagtaggctgatctctgacgacacggccgtgtattactgtgcgagagacttcgattacggtgactaccgcggctctgcttttgatatctggggccaagggggcaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactcc (SEQ ID NO: 608)	QVQLVQSGAEVKKPGTSVKVSCKASGYIFSGSYIQWVRQAPGQGLEWMGRINPKTGGTNYPQKFQGRVTMTRDMSISTAYMELSRLISDDTAVYYCARDFDYGDYRGSAFDIWGQGAMVTVSS (SEQ ID NO: 609)	WGQGAMVTVSS (SEQ ID NO: 610)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
63	015-2F04L	DIQMTQSPSSLSASVGDRVTITCQTSQDFSNYLNWYQQKPGKAPKLLIHDTSKLETGVPSRFSGGGAGTYFTLTINGLQPEDIATYWCQQ (SEQ ID NO: 611)	DIQMTQSPSSLSASVGDRVTITCQTS (SEQ ID NO: 612)	QDFSNY (SEQ ID NO: 613)	LNWYQQKPGKAPKLLIH (SEQ ID NO: 614)	DTS (SEQ ID NO: 615)	KLETGVPSRFSGGGAGTYFTLTINGLQPEDIATYWC (SEQ ID NO: 616)	QQLNT (SEQ ID NO: 617)	gacatccagatgacccagtctccatcctccctgtctgcatctgttggtgacagagtcaccatcacttgccagacgagtcaggactttagcaattatttaaattggtatcagcagaaaccagggaaagcccctaaactcctgatccacgatacatccaagttggaaacaggggtcccatcaagattcagtggaggtggggccgggacatattttactctcaccatcaacggcctgcagcctgaagacattgcaacatattggtgtcaacagttgaataccttcggtcctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtctac (SEQ ID NO: 618)	DIQMTQSPSSLSASVGDRVTITCQTSQDFSNYLNWYQQKPGKAPKLLIHDTSKLETGVPSRFSGGGAGTYFTLTINGLQPEDIATYWCQQLNTFGPGTKVDIK (SEQ ID NO: 619)	FGPGTKVDIK (SEQ ID NO: 620)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
64	015-2F06H	EVQLLESGGDLVQPGGSLRLSCAASGFIFRSYAMSWVRQAPGKGLEWVSMISGSSEDTHYADSVKGRFTISRDNSKNTVYLRMNNLRAEDTAFYYCAR (SEQ ID NO: 621)	EVQLLESGGDLVQPGGSLRLSCAAS (SEQ ID NO: 622)	GFIFRSYA (SEQ ID NO: 623)	MSWVRQAPGKGLEWVSM (SEQ ID NO: 624)	ISGSSEDT (SEQ ID NO: 625)	HYADSVKGRFTISRDNSKNTVYLRMNNLRAEDTAFYYC (SEQ ID NO: 626)	AREEFTDTEMTINQGDFAY (SEQ ID NO: 627)	gaggtgcagctgttggagtctgggggagacttggtacagccgggggggtccctgagactctcctgtgcagcctctggattcatctttagaagttatgccatgagctgggtccgccaggctccagggaagggtctggagtgggtctcaatgattagtggtagcagtgaagatacacactacgcagactccgtgaagggccggttcaccatctccagagacaattccaagaacaccgtttatctgcgcatgaataatctgagagccgaggacacggccttttattactgtgcgagagaggagtttaccgacacagagatgactataaaccaaggggactttgcctactggggccacggcaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcagg (SEQ ID NO: 628)	EVQLLESGGDLVQPGGSLRLSCAASGFIFRSYAMSWVRQAPGKGLEWVSMISGSSEDTHYADSVKGRFTISRDNSKNTVYLRMNNLRAEDTAFYYCAREEFTDTEMTINQGDFAYWGHGTLVTVSS (SEQ ID NO: 629)	WGHGTLVTVSS (SEQ ID NO: 630)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
65	015-2F06L	DIQMTQSPSSLSASVGDTVTITCRASQSISVYLNWYQQKPGKAPKLLIYGASILQSGVPSRFSGIGSGTDFTLTISSLQPEDFATYYCQRSFIT (SEQ ID NO: 631)	DIQMTQSPSSLSASVGDTVTITCRAS (SEQ ID NO: 632)	QSISVY (SEQ ID NO: 633)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 634)	GAS (SEQ ID NO: 635)	ILQSGVPSRFSGIGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 636)	QRSFITPFT (SEQ ID NO: 637)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacacagtcaccatcacttgccgggcaagtcagagcattagtgtctatttaaattggtatcaacaaaaaccagggaaagcccctaagctcctgatctatggtgcatccattttgcaaagtggggtcccgtcaaggttcagtggcattggatccgggacagatttcactctcaccatcagcagtctgcaacctgaagatttcgcaacttactactgtcaacggagtttcatcactccattcactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaaca (SEQ ID NO: 638)	DIQMTQSPSSLSASVGDTVTITCRASQSISVYLNWYQQKPGKAPKLLIYGASILQSGVPSRFSGIGSGTDFTLTISSLQPEDFATYYCQRSFITPFTFGPGTKVDIK (SEQ ID NO: 639)	FGPGTKVDIK (SEQ ID NO: 640)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
66	015-2G04H	QVQLVQSGAEVKKPGTSVKVSCKASGYVFSDSYIQWVRQAPGQGLEWMGRINPKTGGTNFAQKFQGRVTMTRDMSISTAYMDLSRLISDDTAVYYCAR (SEQ ID NO: 641)	QVQLVQSGAEVKKPGTSVKVSCKAS (SEQ ID NO: 642)	GYVFSDSY (SEQ ID NO: 643)	IQWVRQAPGQGLEWMGR (SEQ ID NO: 644)	INPKTGGT (SEQ ID NO: 645)	NFAQKFQGRVTMTRDMSISTAYMDLSRLISDDTAVYYC (SEQ ID NO: 646)	ARDFDYGDYRGSAFDI (SEQ ID NO: 647)	caggtgcagctggtgcagtctggggctgaggtaaagaagcctgggacctcagtgaaagtctcctgcaaggcttctggatacgtcttctccgactcctatattcaatgggtacgacaggcccctggacaagggcttgagtggatgggaaggatcaaccctaagactggtggcacaaatttgcacagaagtttcagggcagggtcaccatgaccagggacatgtccatcagcacagcctatatggacctgagtaggctgatctctgacgacacggccgtatattactgtgcgagagacttcgattacggtgactaccgcggctctgcttttgatatctggggccaagggggcaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccggtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctact (SEQ ID NO: 648)	QVQLVQSGAEVKKPGTSVKVSCKASGYVFSDSYIQWVRQAPGQGLEWMGRINPKTGGTNFAQKFQGRVTMTRDMSISTAYMDLSRLISDDTAVYYCARDFDYGDYRGSAFDIWGQGAMVTVSS (SEQ ID NO: 649)	WGQGAMVTVSS (SEQ ID NO: 650)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
67	015-2G04L	DIQMTQSPSSLSASVGDRVTITCQTSQDFSNYLNWYQQKPGKAPKLLIHDTSKLETGVPSRFSGGGAGTYFTLTINGLQPEDIATYWCQQ (SEQ ID NO: 651)	DIQMTQSPSSLSASVGDRVTITCQTS (SEQ ID NO: 652)	QDFSNY (SEQ ID NO: 653)	LNWYQQKPGKAPKLLIH (SEQ ID NO: 654)	DTS (SEQ ID NO: 655)	KLETGVPSRFSGGGAGTYFTLTINGLQPEDIATYWC (SEQ ID NO: 656)	QQLNT (SEQ ID NO: 657)	gacatccagatgacccagtctccatcctccctgtctgcatctgttggtgacagagtcaccatcacttgccagacgagtcaggactttagcaattatttaaattggtatcagcagaaaccagggaaagcccctaaactcctgatccacgatacatccaagttggaaacaggggtcccatcaagattcagtggaggtggggccgggacatattttactctcaccatcaacggcctgcagcctgaagacattgcaacatattggtgtcaacagttgaataccttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtctac (SEQ ID NO: 658)	DIQMTQSPSSLSASVGDRVTITCQTSQDFSNYLNWYQQKPGKAPKLLIHDTSKLETGVPSRFSGGGAGTYFTLTINGLQPEDIATYWCQQLNTFGPGTKVDIK (SEQ ID NO: 659)	FGPGTKVDIK (SEQ ID NO: 660)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
68	018-1B01H	QVQLVESGGGLVQPGRSLRLSCVASGFNFFNYPMHWVRQAPGKGLEWVAVITYDGSDKYYADSVKGRFTISRDNSKDTLYLEMNNLRSEDTALYYCAR (SEQ ID NO: 661)	QVQLVESGGGLVQPGRSLRLSCVAS (SEQ ID NO: 662)	GFNFFNYP (SEQ ID NO: 663)	MHWVRQAPGKGLEWVAV (SEQ ID NO: 664)	ITYDGSDK (SEQ ID NO: 665)	YYADSVKGRFTISRDNSKDTLYLEMNNLRSEDTALYYC (SEQ ID NO: 666)	ARDQELVVLYYFDF (SEQ ID NO: 667)	caggtgcagctggtggagtctgggggaggcttggtccagcctgggaggtccctgagactctcctgtgtagcctctggattcaacttctttaattatcccatgcactgggtccgccaggctccaggcaaggggctggagtgggtggctgtcataacatatgatggaagtgataaatactatgcagactccgtgaagggccgattcaccatttccagagacaactccaaggacacactgtatttggagatgaacaacctgagatcggaggacacggctctttattattgcgcgagagatcaggaactggtggtcctttattattttgacttctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccctcagc (SEQ ID NO: 668)	QVQLVESGGGLVQPGRSLRLSCVASGFNFFNYPMHWVRQAPGKGLEWVAVITYDGSDKYYADSVKGRFTISRDNSKDTLYLEMNNLRSEDTALYYCARDQELVVLYYFDFWGQGTLVTVSS (SEQ ID NO: 669)	WGQGTLVTVSS (SEQ ID NO: 670)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
69	018-1801L	SYELTQPPSVSVAPGQTARLTCGGNNIGSKNVHWYQQRPGQAPVLVVYDTSDRPSGIPERFSGSSSENTATLTISGVQGGDEADYSCQVYDNSVDH (SEQ ID NO: 671)	SYELTQPPSVSVAPGQTARLTCGGN (SEQ ID NO: 672)	NIGSKN (SEQ ID NO: 673)	VHWYQQRPGQAPVLVVY (SEQ ID NO: 674)	DTS (SEQ ID NO: 675)	DRPSGIPERFSGSSSENTATLTISGVQGGDEADYSC (SEQ ID NO: 676)	QVYDNSVDHAV (SEQ ID NO: 677)	tcctatgagctgacacagccaccctcggtgtcagtggccccaggccagacggccaggttgacctgtgggggaaacaacattggaagtaaaaatgtgcactggtatcagcagaggccaggccaggcccctgttctggtcgtctatgatactagcgaccggccctcagggatccctgagcgattctctggctccagctctgagaacacggccaccctgaccatcagcggggtccaaggcggagatgaggccgactactcctgtcaggtttatgataatagtgttgatcatgcggtcttcggcggagggaccaagctgaccgtcctaggtcagcccaaggctgccccctcggtcactctgttcccgccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaaggcgggagtggagaccaccacaccctccaaacaaagcaacaacaagtacgcggccagcagctatctgagcctgacgcctgagcagtgg (SEQ ID NO: 678)	SYELTQPPSVSVAPGQTARLTCGGNNIGSKNVHWYQQRPGQAPVLVVYDTSDRPSGIPERFSGSSSENTATLTISGVQGGDEADYSCQVYDNSVDHAVFGGGTKLTVL (SEQ ID NO: 679)	FGGGTKLTVL (SEQ ID NO: 680)
70	018-1803H	EVQLLESGGGLVQPGGSLRLSCAASGFPFSSFAMSWVRQSPGKGLQWVSSISGGGDATSYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK (SEQ ID NO: 681)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 682)	GFPFSSFA (SEQ ID NO: 683)	MSWVRQSPGKGLQWVSS (SEQ ID NO: 684)	ISGGGDAT (SEQ ID NO: 685)	SYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC (SEQ ID NO: 686)	AKEPYRDYLGNWPDP (SEQ ID NO: 687)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcggcctctggattcccctttagcagctttgccatgagctgggtccgccagtctccagggaaggggctacaatgggtctcgtctattagtggaggtggagatgccacatcctacgcagactccgtgaagggccgattcaccatctccagggacaattccaagaacacgctatatctgcagatgaacagcctgagagccgaggacacggccgtgtattactgtgcgaaagagccataccgtgactacctggggaactggcccgaccccctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacg (SEQ ID NO: 688)	EVQLLESGGGLVQPGGSLRLSCAASGFPFSSFAMSWVRQSPGKGLQWVSSISGGGDATSYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKEPYRDYLGNWPDPWGQGTLVTVSS (SEQ ID NO: 689)	WGQGTLVTVSS (SEQ ID NO: 690)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
71	018-1803L	DIVMTQSPDSLAVSLGERATVNCRASQSVLYNSNNKNYLTWYQQKPGQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCHQHYTIP (SEQ ID NO: 691)	DIVMTQSPDSLAVSLGERATVNCRAS (SEQ ID NO: 692)	QSVLYNSNNKNY (SEQ ID NO: 693)	LTWYQQKPGQSPKLLIY (SEQ ID NO: 694)	WAS (SEQ ID NO: 695)	TRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC (SEQ ID NO: 696)	HQHYTIPPT (SEQ ID NO: 697)	gacatcgtgatgacccagtctccagactccctggctgtgtctctgggcgagagggccaccgtcaactgcagggccagccagagtgtgttatacaactccaataataagaactacttaacttggtaccagcagaaaccagggcagtctcctaagttgctcatttactgggcatctacccgggaatccggggtccctgaccgattcagtggcagcgggtctgggacagacttcactctcaccatcagcagcctgcaggctgaagatgtggcagtttattactgtcaccaacattatactattccccccactttcggccctgggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagc (SEQ ID NO: 698)	DIVMTQSPDSLAVSLGERATVNCRASQSVLYNSNNKNYLTWYQQKPGQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCHQHYTIPPTFGPGTKVEIK (SEQ ID NO: 699)	FGPGTKVEIK (SEQ ID NO: 700)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
72	018-1C01H	QVQLVQSGAEVKKPGSSVKVSCKPSGDTSSTYAITWVRQAPGQGLEWMGQIIPLTGKDIYAQNFQGRVSITADESTNTVYMDLTGLTSDDTAVYFCAR (SEQ ID NO: 701)	QVQLVQSGAEVKKPGSSVKVSCKPS (SEQ ID NO: 702)	GDTSSTYA (SEQ ID NO: 703)	ITWVRQAPGQGLEWMGQ (SEQ ID NO: 704)	IIPLTGKD (SEQ ID NO: 705)	IYAQNFQGRVSITADESTNTVYMDLTGLTSDDTAVYFC (SEQ ID NO: 706)	ARRQVATYWFDP (SEQ ID NO: 707)	caggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtcaaggtctcctgcaagccttctggagacacctccagcacctatgctatcacctgggtgcgacaggcccctggacaagggcttgagtggatgggacagatcatccctctcaccggaaaagacatctacgcacagaacttccagggcagagtctcgattaccgcggacgaatccacgaacacagtctacatggacctgaccggcctgacatctgatgacacggccgtctattctgtgcgagaagacaggtggctacatattggtttgaccccctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccctcagcagcgtgg (SEQ ID NO: 708)	QVQLVQSGAEVKKPGSSVKVSCKPSGDTSSTYAITWVRQAPGQGLEWMGQIIPLTGKDIYAQNFQGRVSITADESTNTVYMDLTGLTSDDTAVYFCARRQVATYWFDPWGQGTLVTVSS (SEQ ID NO: 709)	WGQGTLVTVSS (SEQ ID NO: 710)
73	018-1C01L	SYELTQPPSVSVAPGQTATCTCGGDDIGSKTVHWYQQRPGQAPVLVISDDSARPSGIPARFSGSNSRNTATLTISSVEAGDEADYFCQVWDSNSGH (SEQ ID NO: 711)	SYELTQPPSVSVAPGQTATCTCGGD (SEQ ID NO: 712)	DIGSKT (SEQ ID NO: 713)	VHWYQQRPGQAPVLVIS (SEQ ID NO: 714)	DDS (SEQ ID NO: 715)	ARPSGIPARFSGSNSRNTATLTISSVEAGDEADYFC (SEQ ID NO: 716)	QVWDSNSGHFV (SEQ ID NO: 717)	tcctatgagctgacacagcctccttcggtgtcagtggccccgggacagacggccacctgtacctgtgggggagacgacattggatccaaaactgtgcactggtaccagcagaggccaggccaggcccctgttctggtcatcagtgatgatagtgcccggccctcagggatccctgcacgattctctggctccaattctaggaacacggccaccctgaccatcagcagtgtcgaagccggggatgaggccgactatttctgtcaggtgtgggacagtaacagtggtcatttgtcttcggatctgggaccaaggtcaccgtcctaagtcagcccaaggccaaccccactgtcactctgttcccgccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaaggcggga (SEQ ID NO: 718)	SYELTQPPSVSVAPGQTATCTCGGDDIGSKTVHWYQQRPGQAPVLVISDDSARPSGIPARFSGSNSRNTATLTISSVEAGDEADYFCQVWDSNSGHFVFGSGTKVTVL (SEQ ID NO: 719)	FGSGTKVTVL (SEQ ID NO: 720)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
74	018-1D04H	EVQLLESGGGLVQPGGSLRLSCVASGFTFSNYPMVWVRQAPGKGLEWVSIIGGSYGGSYYADSVKGRFTISRDNSKNTLYLQMDNLRVEDTAVYYCA (SEQ ID NO: 721)	EVQLLESGGGLVQPGGSLRLSCVAS (SEQ ID NO: 722)	GFTFSNYP (SEQ ID NO: 723)	MVWVRQAPGKGLEWVSI (SEQ ID NO: 724)	IGGSYGGS (SEQ ID NO: 725)	YYADSVKGRFTISRDNSKNTLYLQMDNLRVEDTAVYYC (SEQ ID NO: 726)	ATSPATSGWWAY (SEQ ID NO: 727)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcgtgtgtagcctctggattcacttttagcaactatcccatggtctgggtccgccaggctccagggaaggggctggagtgggtctcaattattggtggtagttatgggggctcatattacgcagactccgtgaagggccggttcaccatctccagagacaattccaagaacaccctgtatctccaaatggacaacctgagagtcgaggacacggccgtctattactgtgcgacaagccccgcaaccagtggctggtggtgggcctactggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcg (SEQ ID NO: 728)	EVQLLESGGGLVQPGGSLRLSCVASGFTFSNYPMVWVRQAPGKGLEWVSIIGGSYGGSYYADSVKGRFTISRDNSKNTLYLQMDNLRVEDTAVYYCATSPATSGWWWAYWGQGTLVTVSS (SEQ ID NO: 729)	WGQGTLVTVSS (SEQ ID NO: 730)
75	018-1D04L	EIVLTQSPAILSLSPGERATLSCRASQSVGRNYLAWYQXKPGQAPRVLIYGASSRATGTPDRFSGXGSGTDFTLTISRLEPEDFAVYYCHQYDIPP (SEQ ID NO: 731)	EIVLTQSPAILSLSPGERATLSCRAS (SEQ ID NO: 732)	QSVGRNY (SEQ ID NO: 733)	LAWYQXKPGQAPRVLIY (SEQ ID NO: 734)	GAS (SEQ ID NO: 735)	SRATGTPDRFSGXGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 736)	HQYDIPPQT (SEQ ID NO: 737)	gaaattgtgttgacgcagtctccagccatcctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgttggcagaaattacttagcctggtaccagnagaaacctggccaggctcccagggtcctcatttatggtgcatccagcagggccactggcaccccagacaggttcagtggcngtgggtctgggacagacttcactctcaccatcagcagactggagcctgaagattttgcggtgtattactgtcatcagtatgatatcccacctcagacttttggccaggggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacga (SEQ ID NO: 738)	EIVLTQSPAILSLSPGERATLSCRASQSVGRNYLAWYQXKPGQAPRVLIYGASSRATGTPDRFSGXGSGTDFTLTISRLEPEDFAVYYCHQYDIPPQTFGQGTKVEIK (SEQ ID NO: 739)	FGQGTKVEIK (SEQ ID NO: 740)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
76	018-2B05H	EVQLLESGGGLVQPGGSLRLSCAASGFTLGDYSMTWVRQAPGKGLEWVSSIRKSGGDTFYTDSVKGRFTISRDTPKNTLFLQMNSLRGEDTAVYFCA (SEQ ID NO: 741)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 742)	GFTLGDYS (SEQ ID NO: 743)	MTWVRQAPGKGLEWVSS (SEQ ID NO: 744)	IRKSGGDT (SEQ ID NO: 745)	FYTDSVKGRFTISRDTPKNTLFLQMNSLRGEDTAVYFC (SEQ ID NO: 746)	ARPTPYGTTWFGRVDS (SEQ ID NO: 747)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcagcctctggattcaccttgggagactattccatgacctgggtccgccaggctccagggaaggggctggagtgggtctcaagtattaggaaaagtggcggtgacacattctacacagactccgtgaagggccggttcaccatctccagagacactcccaagaacacactgtttctgcaaatgaacagcctgagaggcgaggacacggccgtatattctgtgcgagaccaacccccgtatggcaccacttggtttgggcgggttgactcctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccc (SEQ ID NO: 748)	EVQLLESGGGLVQPGGSLRLSCAASGFTLGDYSMTWVRQAPGKGLEWVSSIRKSGGDTFYTDSVKGRFTISRDTPKNTLFLQMNSLRGEDTAVYFCARPTPYGTTWFGRVDSWGQGTLVTVSS (SEQ ID NO: 749)	WGQGTLVTVSS (SEQ ID NO: 750)
77	018-2B05L	DIQMTQSPSSLSASLGDRVTITCRTSQSISNYLNWYQQKPGKAPKLLIYATSSLHSGVPSRFSGSGSGTDFTLTISSLQPEDFASYYCQQTYRT (SEQ ID NO: 751)	DIQMTQSPSSLSASLGDRVTITCRTS (SEQ ID NO: 752)	QSISNY (SEQ ID NO: 753)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 754)	ATS (SEQ ID NO: 755)	SLHSGVPSRFSGSGSGTDFTLTISSLQPEDFASYYC (SEQ ID NO: 756)	QQTYRTPIT (SEQ ID NO: 757)	gacatccagatgacccagtctccatcctccctgtctgcatctcttggagacagagtcaccatcacttgccggacaagtcaaagcattagtaactacttgaattggtatcagcagaaaccagggaaagcccctaaactcctgatctatgctacatccagcttgcatagtggggtcccatcaagattcagtggcagtggatctgggacagatttcactctcaccatcagcagtctgcaacctgaagattttgcaagttattactgtcaacagacttacaggaccccaatcactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcanactacgagaaac (SEQ ID NO: 758)	DIQMTQSPSSLSASLGDRVTITCRTSQSISNYLNWYQQKPGKAPKLLIYATSSLHSGVPSRFSGSGSGTDFTLTISSLQPEDFASYYCQQTYRTPITFGPGTKVDIK (SEQ ID NO: 759)	FGPGTKVDIK (SEQ ID NO: 760)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
78	018-2D01H	EVQLVQSGAEVKKPGESLRISCKASGYSFTSSWINWVRQKAGKGLEWMGRLNPSDSYPNYSPSFQGHVTISADNSVTTAYLQWSSLKASDTAIYYCTR (SEQ ID NO: 761)	EVQLVQSGAEVKKPGESLRISCKAS (SEQ ID NO: 762)	GYSFTSSW (SEQ ID NO: 763)	INWVRQKAGKGLEWMGR (SEQ ID NO: 764)	LNPSDSYP (SEQ ID NO: 765)	NYSPSFQGHVTISADNSVTTAYLQWSSLKASDTAIYYC (SEQ ID NO: 766)	TRDSFYDVDLSSFYMDV (SEQ ID NO: 767)	gaagtgcagctggtgcagtctggagcagaggtgaaaaagcccggggagtctctgaggatctcctgtaaggcttctggatacagctttaccagttcctggatcaactgggtgcgccagaaggccgggaaaggcctggagtggatggggaggcttaatcctagtgactcttaccccaactacagcccgtccttccaaggccacgtcaccatctcagctgacaactccgtcaccactgcctacctgcagtggagcagcctgaaggcctcggacaccgccatatattactgtacaagagattcctttacgatgtggacctgtcctccttctacatggacgtctggggcaaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctg (SEQ ID NO: 768)	EVQLVQSGAEVKKPGESLRISCKASGYSFTSSWINWVRQKAGKGLEWMGRLNPSDSYPNYSPSFQGHVTISADNSVTTAYLQWSSLKASDTAIYYCTRDSFYDVDLSSFYMDVWGKGTTVTVSS (SEQ ID NO: 769)	WGKGTTVTVSS (SEQ ID NO: 770)
79	018-2D01L	EIVLTQSPGTLSLSPGERATLSCRASQSLSNSYLAWYQQKPGQAPRLLIYGASNRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVFYCQQYGSS (SEQ ID NO: 771)	EIVLTQSPGTLSLSPGERATLSCRAS (SEQ ID NO: 772)	QSLSNSY (SEQ ID NO: 773)	LAWYQQKPGQAPRLLIY (SEQ ID NO: 774)	GAS (SEQ ID NO: 775)	NRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVFYC (SEQ ID NO: 776)	QQYGSSRHT (SEQ ID NO: 777)	gaaattgtgttgacgcagtctccaggcaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtcttagcaacagctacttagcctggtatcagcagaaacctggccaggctcccaggctcctcatctatggtgcatccaacagggccactggcatcccagacaggttcagtggcagtgggtctgggacagacttcactctcaccatcagcagactggagcctgaagattttgcggtgttttactgtcagcaatatggttcgtcacggcacactttggccaggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccag (SEQ ID NO: 778)	EIVLTQSPGTLSLSPGERATLSCRASQSLSNSYLAWYQQKPGQAPRLLIYGASNRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVFYCQQYGSSRHTFGQGTKVEIK (SEQ ID NO: 779)	FGQGTKVEIK (SEQ ID NO: 780)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
80	018-2D03H	QVQLVQSGGEVKKPGASVKVSCKASGYTFTSHGISWVRQAPGQGLEWLGWISVYNGDTNYAQKVQDRLTVTTDTSTSTVYMELRSLRSDDTAVYYCAR (SEQ ID NO: 781)	QVQLVQSGGEVKKPGASVKVSCKAS (SEQ ID NO: 782)	GYTFTSHG (SEQ ID NO: 783)	ISWVRQAPGQGLEWLGW (SEQ ID NO: 784)	ISVYNGDT (SEQ ID NO: 785)	NYAQKVQDRLTVTTDTSTSTVYMELRSLRSDDTAVYYC (SEQ ID NO: 786)	ARDRIDYVVYDAFDI (SEQ ID NO: 787)	caggtgcagctggtgcagtctggaggtgaggtgaagaagcctggggcctcagtgaaggtctcctgcaaggcttctggttacacctttaccagtcatggtattagttgggtgcgacaggcccctggacaagggcttgagtggttgggatggatcagcgtttacaatggtgacacaaactatgcacagaaggtccaagacagactcaccgtgaccacagacacgtccacgagcacagtttacatggagctgaggagcctgagatctgacgacacggccgtgtattactgtgcgagagatagaattgactatgtggtgtatgatgcttttgatatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacg (SEQ ID NO: 788)	QVQLVQSGGEVKKPGASVKVSCKASGYTFTSHGISWVRQAPGQGLEWLGWISVYNGDTNYAQKVQDRLTVTTDTSTSTVYMELRSLRSDDTAVYYCARDRIDYVVYDAFDIWGQGTMVTVSS (SEQ ID NO: 769)	WGQGTMVTVSS (SEQ ID NO: 790)
81	018-2D03L	DIQMTQSPSTLSASVGDRVTITCRASQRISGWLAWYQQKPGKAPKLLIHRASILESGVSSRFSGSGSGTEFTLTISSLQPDDSATYYCQLYDD (SEQ ID NO: 791)	DIQMTQSPSTLSASVGDRVTITCRAS (SEQ ID NO: 792)	QRISGW (SEQ ID NO: 793)	LAWYQQKPGKAPKLLIH (SEQ ID NO: 794)	RAS (SEQ ID NO: 795)	ILESGVSSRFSGSGSGTEFTLTISSLQPDDSATYYC (SEQ ID NO: 796)	QLYDDFRT (SEQ ID NO: 797)	gacatccagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgccgggccagtcagaggattagtggctggttggcctggtatcagcagaaaccagggaaagcccctaaactcttgatccatagggcatcaatttagagagtggggtctcatcaaggttcagcggcagtggatctgggacagaattcactctgaccatcagcagcctgcagcctgatgattctgcaacttattactgtcaactgtatgatgatttccggacgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagt (SEQ ID NO: 798)	DIQMTQSPSTLSASVGDRVTITCRASQRISGWLAWYQQKPGKAPKLLIHRASILESGVSSRFSGSGSGTEFTLTISSLQPDDSATYYCQLYDDFRTFGQGTKVEIK (SEQ ID NO: 799)	FGQGTKVEIK (SEQ ID NO: 800)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
82	018-2E03H	EVQLVESGGGLVQPGGSLTLSCAASGFTFRSYWMHWVRQVPGKGPVWLSRINNDGSSSRYADSVKGRFFITRDSAKNTVFLQLNSLRVEDTAIYYCAR (SEQ ID NO: 801)	EVQLVESGGGLVQPGGSLTLSCAAS (SEQ ID NO: 802)	GFTFRSYW (SEQ ID NO: 803)	MHWVRQVPGKGPVWLSR (SEQ ID NO: 804)	INNDGSSS (SEQ ID NO: 805)	RYADSVKGRFFITRDSAKNTVFLQLNSLRVEDTAIYYC (SEQ ID NO: 806)	ARGDLVSTANFDY (SEQ ID NO: 807)	gaggtgcagctggtggagtccgggggaggcttagttcagccgggggggtccctgacactgtcctgtgcagcctctggattcaccttcaggagctactggatgcactgggtccgccaagttccaggcaaggggccggtgtggctctcacgtattaacaatgatggcagtagctcgaggtacgcggactccgtgaagggccgcttcttcatcaccagagatagcgccaagaacacggtgttcctccaactgaacagtctcagagtcgaggacacggccatttattactgtgcaagaggagatttagtctctacggccaactttgactactggggccggggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcg (SEQ ID NO: 808)	EVQLVESGGGLVQPGGSLTLSCAASGFTFRSYWMHWVRQVPGKGPVWLSRINNDGSSSRYADSVKGRFFITRDSAKNTVFLQLNSLRVEDTAIYYCARGDLVSTANFDYWGRGTLVTVSS (SEQ ID NO: 809)	WGRGTLVTVSS (SEQ ID NO: 810)
83	018-2E03L	EIVLTQSPGTLSLSPGERATLSCRASQRVDRSYLAWYRQKPGQAPSLLISGTSTRAPGIADRFIGSGSGTDFTLTISGLEPEDFAVYYCQQYEN (SEQ ID NO: 811)	EIVLTQSPGTLSLSPGERATLSCRAS (SEQ ID NO: 812)	QRVDRSY (SEQ ID NO: 813)	LAWYRQKPGQAPSLLIS (SEQ ID NO: 814)	GTS (SEQ ID NO: 815)	TRAPGIADRFIGSGSGTDFTLTISGLEPEDFAVYYC (SEQ ID NO: 816)	QQYENSQHGSSPPYT (SEQ ID NO: 817)	gaaattgtgttgacgcagtctccaggcaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagagttgacaggagctacttagcctggtaccgccaaaaacctggccaggctcccagcctcctcatctccgggacatccaccagggcccctggcatcgccgacagattcattggcagtgggtctgggacagacttcactctcaccatcagcggactggagcctgaagattttgcagtatattactgtcagcagtatgaaaattcgcaacatggaagttcacccccgtacacttttggccaggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgc (SEQ ID NO: 818)	EIVLTQSPGTLSLSPGERATLSCRASQRVDRSYLAWYRQKPGQAPSLLISGTSTRAPGIADRFIGSGSGTDFTLTISGLEPEDFAVYYCQQYENSQHGSSPPYTFGQGTKVEIK (SEQ ID NO: 819)	FGQGTKVEIK (SEQ ID NO: 820)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
84	019-1B04H	EVQLVESGGKVVQPGGSLRLSCAASGFTFSSSWMHWVRQAPGQGLVWVSRINSAGSSKSYADSVKGRFTISRDNAKNTLYLQMNSLRGEDTAVYYCAR (SEQ ID NO: 821)	EVQLVESGGKVVQPGGSLRLSCAAS (SEQ ID NO: 822)	GFTFSSSW (SEQ ID NO: 823)	MHWVRQAPGQGLVWVSR (SEQ ID NO: 824)	INSAGSSK (SEQ ID NO: 825)	SYADSVKGRFTISRDNAKNTLYLQMNSLRGEDTAVYYC (SEQ ID NO: 826)	ARDHDYGDYRGNAFDM (SEQ ID NO: 827)	gaggtgcagctggtggagtccgggggaaaggtcgttcagccgggggggtccctgagactctcctgtgcagcctctggattcaccttcagtagttcctggatgcactgggtccgccaagctccagggcaggggctggtgtgggtctcacgtattaacagtgctgggagtagcaaaagctacgcggactccgtgaagggccgattcaccatctccagagacaacgccaagaacacgctgtatctgcaaatgaacagtctgagaggcgaggacacggctgtgtattactgtgcaagagatcatgactacggtgactacagagggaacgcttttgatatgtggggcctagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgt (SEQ ID NO: 828)	EVQLVESGGKVVQPGGSLRLSCAASGFTFSSSWMHWVRQAPGQGLVWVSRINSAGSSKSYADSVKGRFTISRDNAKNTLYLQMNSLRGEDTAVYYCARDHDYGDYRGNAFDMWGLGTMVTVSS (SEQ ID NO: 829)	WGLGTMVTVSS (SEQ ID NO: 830)
85	019-1B04L	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASKLETGVPSRFSGRQSGTDYTFTISSLQPEDFATYFCQQ (SEQ ID NO: 831)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 832)	QDISNY (SEQ ID NO: 833)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 834)	DAS (SEQ ID NO: 835)	KLETGVPSRFSGRQSGTDYTFTISSLQPEDFATYFC (SEQ ID NO: 836)	QQLHT (SEQ ID NO: 837)	gacatccagatgacccagtctccatcctccctgtctgcatctgtgggagacagagtcaccatcacttgccaggcgagtcaggacattagcaactatttaaattggtatcagcagaaaccagggaaagcccctaagctcctgatctacgatgcatccaaattggaaacaggggtcccatcaaggttcagtggaagacaatctgggacagattatactttcaccatcagcagcctgcagcctgaagattttgcaacatatttctgtcaacagcttcatactttcggcggagggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 838)	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASKLETGVPSRFSGRQSGTDYTFTISSLQPEDFATYFCQQLHTFGGGTKVEIK (SEQ ID NO: 839)	FGGGTKVEIK (SEQ ID NO: 840)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
86	019-2A02H	QVQLVQSGAEVKRPGASLKVSCKASGYSFTTYGITWVRQAPGQGLEWMGWISTYNGYTNYAQRLQGRVTMTTDTSTGTAYLELRSLTYDDTAVYYCAR (SEQ ID NO: 841)	QVQLVQSGAEVKRPGASLKVSCKAS (SEQ ID NO: 842)	GYSFTTYG (SEQ ID NO: 843)	ITWVRQAPGQGLEWMGW (SEQ ID NO: 844)	ISTYNGYT (SEQ ID NO: 845)	NYAQRLQGRVTMTTDTSTGTAYLELRSLTYDDTAVYYC (SEQ ID NO: 846)	ARRGDYGDYRGDAFDI (SEQ ID NO: 847)	caggtgcagctggtgcagtctggagctgaggtgaagaggcctggggcctcactgaaggtctcctgcaaggcctctggttacagctttaccacctacgggatcacctgggtgcgacaggcccctggacaagggcttgagtggatgggatggatcagcacttacaatggttacacaaactatgcacagagactccagggcagagtcaccatgaccacagacacatccactgggacagcctacttggagctgaggagcctgacatatgacgacacggccgtctattattgtgcgagacgtggggactacggtgactaccggggtgatgcatttgatatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgt (SEQ ID NO: 848)	QVQLVQSGAEVKRPGASLKVSCKASGYSFTTYGITWVRQAPGQGLEWMGWISTYNGYTNYAQRLQGRVTMTTDTSTGTAYLELRSLTYDDTAVYYCARRGDYGDYRGDAFDIWGQGTMVTVSS (SEQ ID NO: 849)	WGQGTMVTVSS (SEQ ID NO: 850)
87	019-2A02L	DIQMTQSPSSLSASVGDRVTITCQASQDVSNYLNWYQQKPGKAPKLLIYDTSNLETGVPSRFSGTGSGTDFTFTISSLQPEDVATYFCQQ (SEQ ID NO: 851)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 852)	QDVSNY (SEQ ID NO: 853)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 854)	DTS (SEQ ID NO: 855)	NLETGVPSRFSGTGSGTDFTFTISSLQPEDVATYFC (SEQ ID NO: 856)	QQVFT (SEQ ID NO: 857)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggcgacagagtcaccatcacttgccaggcgagtcaggacgttagcaactatttaaattggtatcagcagaaaccagggaaagcccctaaactcctgatctacgatacatccaatttggaaacaggggtcccatcaaggttcagtggaactggatctgggacagattttactttcaccatcagcagcctgcagcctgaagatgttgcaacatatttctgtcaacaggttttcacttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 858)	DIQMTQSPSSLSASVGDRVTITCQASQDVSNYLNWYQQKPGKAPKLLIYDTSNLETGVPSRFSGTGSGTDFTFTISSLQPEDVATYFCQQVFTFGPGTKVDIK (SEQ ID NO: 859)	FGPGTKVDIK (SEQ ID NO: 860)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
88	019-2A05H	EVQLVESGGGLVKPGGSLRLSCAASGFIFSDYTMNWVRQVPGKGLEWVSSISSYSGYIYYADSVKGRFTLSRDNAKKSLYLQMNNLRAEDTAVYYCAK (SEQ ID NO: 861)	EVQLVESGGGLVKPGGSLRLSCAAS (SEQ ID NO: 862)	GFIFSDYT (SEQ ID NO: 863)	MNWVRQVPGKGLEWVSS (SEQ ID NO: 864)	ISSYSGYI (SEQ ID NO: 865)	YYADSVKGRFTLSRDNAKKSLYLQMNNLRAEDTAVYYC (SEQ ID NO: 866)	AKDRVRDGDNDWDSVDATYWGYGVFDT (SEQ ID NO: 867)	gaggtgcagctggtggagtctgggggaggcctggtcaagcctggggggtccctgagactgtcttgtgcagcctctggattcatattcagtgactataccatgaattgggtccgccaggttccagggaagggcctggagtgggtctcaagtattagtagttacagtggttacatatactacgcagactcagtgaagggccgattcaccctttccagagacaacgccaagaagtcactgtatctgcaaatgaacaacctgagagccgaggacacggctgtctattactgtgcgaaagatagggtgcgagatggcgacaatgactgggattcagtggacgccacttactggggttacggtgttttgatacctcgggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggc (SEQ ID NO: 868)	EVQLVESGGGLVKPGGSLRLSCAASGFIFSDYTMNWVRQVPGKGLEWVSSISSYSGYIYYADSVKGRFTLSRDNAKKSLYLQMNNLRAEDTAVYYCAKDRVRDGDNDWDSVDATYWGYGVFDTSGQGTMVTVSS (SEQ ID NO: 869)	SGQGTMVTVSS (SEQ ID NO: 870)
89	019-2A05L	DIVMTQSPDSLAVSLGERATINCKSSQSVLYGSNNKNYFAWYQQKPGQPPKMLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQHYRIP (SEQ ID NO: 871)	DIVMTQSPDSLAVSLGERATINCKSS (SEQ ID NO: 872)	QSVLYGSNNKNY (SEQ ID NO: 873)	FAWYQQKPGQPPKMLIY (SEQ ID NO: 874)	WAS (SEQ ID NO: 875)	TRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC (SEQ ID NO: 876)	QQHYRIPQT (SEQ ID NO: 877)	gacatcgtgatgacccagtctccagactccctggctgtgtctctgggcgagagggccaccatcaactgcaagtccagccagagtgttttatacggctccaacaataagaactacttcgcttggtaccagcagaaaccaggacagcctcctaagatgctcatttactgggcatctacccgggaatccggggtccctgaccgcttcagtggcagcgggtctgggacagatttcactctcaccatcagcagcctgcaggctgaagatgtggcagtttattactgtcagcaacattatagaattcctcagacgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgag (SEQ ID NO: 878)	DIVMTQSPDSLAVSLGERATINCKSSQSVLYGSNNKNYFAWYQQKPGQPPKMLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQHYRIPQTFGQGTKVEIK (SEQ ID NO: 879)	FGQGTKVEIK (SEQ ID NO: 880)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
90	019-2A06H	EVQLVESGGGLVQPGGSLRLSCAASGFSFSSFWMHWVRQVPGKGLLWVARINNDGTFTTYADSVKGRFTISRDNAKNTLNLHMSNLRVEDSALYFCVR (SEQ ID NO: 881)	EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 882)	GFSFSSFW (SEQ ID NO: 883)	MHWVRQVPGKGLLWVAR (SEQ ID NO: 884)	INNDGTFT (SEQ ID NO: 885)	TYADSVKGRFTISRDNAKNTLNLHMSNLRVEDSALYFC (SEQ ID NO: 886)	VRDNDYGDYRGNAFDI (SEQ ID NO: 887)	gaggtgcagctggtggagtccgggggaggcttagttcagccgggggggtccctgagactctcctgtgcagcctctggattctccttcagtagtttctggatgcactgggtccgccaagttccagggaagggactgctgtgggtcgcacgtattaacaacgatgggactttcacaacctacgcggactctgtgaagggccgattcaccatctccagagacaacgccaagaatacgctgaatctgcacatgagcaatctcagagtcgaggattcggctctgtatttctgtgtaagagataatgactacggcgactacagagggaacgcttttgatatttggggccaggggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtg (SEQ ID NO: 888)	EVQLVESGGGLVQPGGSLRLSCAASGFSFSSFWMHWVRQVPGKGLLWVARINNDGTFTTYADSVKGRFTISRDNAKNTLNLHMSNLRVEDSALYFCVRDNDYGDYRGNAFDIWGQGTMVTVSS (SEQ ID NO: 889)	WGQGTMVTVSS (SEQ ID NO: 890)
91	019-2A06L	DIQMTQSPSSLSASVGDRVTITCQASQDMSNYLNWYQQKSGKAPKLLIYDTSKLEAGVPSRFSGSGFGTHYVLSITSLQPEDIATYYCEQ (SEQ ID NO: 891)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 892)	QDMSNY (SEQ ID NO: 893)	LNWYQQKSGKAPKLLIY (SEQ ID NO: 894)	DTS (SEQ ID NO: 895)	KLEAGVPSRFSGSGFGTHYVLSITSLQPEDIATYYC (SEQ ID NO: 896)	EQLHT (SEQ ID NO: 897)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccaggcgagtcaggacatgagcaactatttaaattggtatcagcaaaaatcagggaaagcccctaagctcctgatttacgatacttccaaattggaagcaggggtcccatcaaggttcagtggcagtggatttgggacacattatgttttaagcatcaccagtctacagcctgaagatattgcaacatattactgtgaacagcttcatactttcggcggagggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtctac (SEQ ID NO: 898)	DIQMTQSPSSLSASVGDRVTITCQASQDMSNYLNWYQQKSGKAPKLLIYDTSKLEAGVPSRFSGSGFGTHYVLSITSLQPEDIATYYCEQLHTFGGGTKVEIK (SEQ ID NO: 899)	FGGGTKVEIK (SEQ ID NO: 900)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
92	019-2F05H	EVQLVESGGGLVKPGGSLRISCSSSGFTFSDYTMNWVRQAPGKGLEWVSSISSRSGYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 901)	EVQLVESGGGLVKPGGSLRISCSSS (SEQ ID NO: 902)	GFTFSDYT (SEQ ID NO: 903)	MNWVRQAPGKGLEWVSS (SEQ ID NO: 904)	ISSRSGYI (SEQ ID NO: 905)	YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYC (SEQ ID NO: 906)	ARDRVRDGDNYWDSVDATYWGYGAFDI (SEQ ID NO: 907)	gaggtgcagctggtggagtctgggggaggcctggtcaagcctggggggtccctaagaatctcatgttcatcctctggattcaccttcagtgactataccatgaattgggtccgccaggctccagggaaggggctggagtgggtctcatccattagtagtagaagtggttatatatactacgcagactcagtgaagggccgattcaccatctccagagacaacgccaagaactcactgtatttgcaaatgaacagcctgagagccgaggacacggctgtctattactgtgcgagagatagggtgcgagatggcgacaattactgggattcagtggacgccacttactggggttacggtgcttttgatatctgcggccacgggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctcaagagcacctctgggggcacagcggccctgggc (SEQ ID NO: 908)	EVQLVESGGGLVKPGGSLRISCSSSGFTFSDYTMNWVRQAPGKGLEWVSSISSRSGYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDRVRDGDNYWDSVDATYWGYGAFDICGHGTMVTVSS (SEQ ID NO: 909)	CGHGTMVTVSS (SEQ ID NO: 910)
93	019-2F05L	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYFAWYQQRPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISGLQAEDVAVYYCQQHFTTP (SEQ ID NO: 911)	DIVMTQSPDSLAVSLGERATINCKSS (SEQ ID NO: 912)	QSVLYSSNNKNY (SEQ ID NO: 913)	FAWYQQRPGQPPKLLIY (SEQ ID NO: 914)	WAS (SEQ ID NO: 915)	TRESGVPDRFSGSGSGTDFTLTISGLQAEDVAVYYC (SEQ ID NO: 916)	QQHFTTPQT (SEQ ID NO: 917)	gacatcgtgatgacccagtctccagactccctggctgtgtctctgggcgagagggccaccatcaactgcaagtccagccagagtgttttatacagctccaacaataagaactactttgcttggtaccagcagagaccaggacagcctcctaaactgctcatttactgggcatctacccgggaatccggggtccctgaccgattcagtggcagcgggtctgggacagatttcacgctcaccatcagcggcctgcaggctgaagatgtggcagtttattactgtcagcaacattttactactcctcagacgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaa (SEQ ID NO: 918)	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYFAWYQQRPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISGLQAEDVAVYYCQQHFTTPQTFGQGTKVEIK (SEQ ID NO: 919)	FGQGTKVEIK (SEQ ID NO: 920)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
94	019-4A01H	QLQLQESGPGLVKPSETLSLTCSVSGDSITCSSCYWGWIRQPPGKGLEWIGSMYYSGRTNYNPSLKSRVTISVDTSKSQVSLKLRSVTAADAAVYYCAR (SEQ ID NO: 921)	QLQLQESGPGLVKPSETLSLTCSVS (SEQ ID NO: 922)	GDSITCSSCY (SEQ ID NO: 923)	WGWIRQPPGKGLEWIGS (SEQ ID NO: 924)	MYYSGRT (SEQ ID NO: 925)	NYNPSLKSRVTISVDTSKSQVSLKLRSVTAADAAVYYC (SEQ ID NO: 926)	ARLFGELVGYQAFDV (SEQ ID NO: 927)	cagctgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcagtgtctctggtgactccattacttgtagtagttgctactggggctggatccgccagccccccagggaaggggctggagtggattggttctatgtattacagtgggagaaccaactacaatccgtccctcaagagtcgagtcaccatatccgtagacacgtccaagagccaggtgtccctgaagttgcgctctgtgaccgccgcagatgcggctgtctattactgtgcgagactattcggggagttggtcggttatcaggcttttgatgtctggggcctagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtga (SEQ ID NO: 928)	QLQLQESGPGLVKPSETLSLTCSVSGDSITCSSCYWGWIRQPPGKGLEWIGSMYYSGRTNYNPSLKSRVTISVDTSKSQVSLKLRSVTAADAAVYYCARLFGELVGYQAFDVWGLGTMVTVSS (SEQ ID NO: 929)	WGLGTMVTVSS (SEQ ID NO: 930)
95	019-4A01L	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPKLLIYSNIERPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNG (SEQ ID NO: 931)	QSVLTQPPSASGTPGQRVTISCSGS (SEQ ID NO: 932)	SSNIGSNT (SEQ ID NO: 933)	VNWYQQLPGTAPKLLIY (SEQ ID NO: 934)	SNI (SEQ ID NO: 935)	ERPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYC (SEQ ID NO: 936)	AAWDDSLNGYV (SEQ ID NO: 937)	cagtctgtgctgacgcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggaagcagctccaacatcggaagtaatactgtgaactggtaccagcagctcccaggaacggcccccaaactcctcatctatagtaatattgagcggccctcaggggtccctgaccgattctctggctccaagtctggcacctcagcgtccctggccatcagtgggctccagtctgaggatgaggctgattattactgtgcagcctgggatgacagcctgaatggttatgtcttcggaactgggaccaaggtcaccgtcctaggtcagcccaaggccaaccccactgtcactctgttcccgccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaaggc (SEQ ID NO: 938)	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPKLLIYSNIERPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLNGYVFGTGTKVTVL (SEQ ID NO: 939)	FGTGTKVTVL (SEQ ID NO: 940)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
96	019-4C01H	QVQLQESGPGLVKPSQTLSLTCSVSGDSINSGGFSWTWIRQHPGKGLEWIGSISYNGKIQFNPSLKSRLSMSVDTSKNQFSLKMSSVTGADTAVYFCAR (SEQ ID NO: 941)	QVQLQESGPGLVKPSQTLSLTCSVS (SEQ ID NO: 942)	GDSINSGGFS (SEQ ID NO: 943)	WTWIRQHPGKGLEWIGS (SEQ ID NO: 944)	ISYNGKI (SEQ ID NO: 945)	QFNPSLKSRLSMSVDTSKNQFSLKMSSVTGADTAVYFC (SEQ ID NO: 946)	ARELGDYPYYYAMDV (SEQ ID NO: 947)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcacagaccctgtccctcacctgctctgtctctggtgactccatcaacagtggtggtttctcttggacctggatccgccagcacccagggaagggcctggagtggattggttccatctcttataatggcaaaattcaattcaacccgtccctcaagagtcggctttccatgtcagtggacacgtccaagaaccagttctccctgaaaatgagctcagtaactggcgcagacacggccgtttacttttgtgcgagagaacttggcgactatccctattactacgcaatggacgtctggggccaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgac (SEQ ID NO: 948)	QVQLQESGPGLVKPSQTLSLTCSVSGDSINSGGFSWTWIRQHPGKGLEWIGSISYNGKIQFNPSLKSRLSMSVDTSKNQFSLKMSSVTGADTAVYFCARELGDYPYYYAMDVWGQGTTVTVSS (SEQ ID NO: 949)	WGQGTTVTVSS (SEQ ID NO: 950)
97	019-4C01L	DIQMTQSPSFLSASVGDRVTITCRASQGIASFLAWYQQKPGRAPNLLVYAASSLQTGVPSRFSGGGSGTEFTLTINSLQPEDFATYYCQQVITFP (SEQ ID NO: 951)	DIQMTQSPSFLSASVGDRVTITCRAS (SEQ ID NO: 952)	QGIASF (SEQ ID NO: 953)	LAWYQQKPGRAPNLLVY (SEQ ID NO: 954)	AAS (SEQ ID NO: 955)	SLQTGVPSRFSGGGSGTEFTLTINSLQPEDFATYYC (SEQ ID NO: 956)	QQVITFPRT (SEQ ID NO: 957)	gacatccagatgacccagtctccatccttcctgtctgcatctgtgggagacagagtcaccatcacttgccgggccagtcagggcattgccagttttttagcctggtatcagcaaaaaccagggagagcccctaacctcctggtctatgctgcgtcctctttgcaaactggggtcccatcaaggttcagcggcggtggatctgggacagagttcactctcacaatcaacagcctacagcctgaagattttgccacttattactgtcaacaggtcattactttccctcggacgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgagaaa (SEQ ID NO: 958)	DIQMTQSPSFLSASVGDRVTITCRASQGIASFLAWYQQKPGRAPNLLVYAASSLQTGVPSRFSGGGSGTEFTLTINSLQPEDFATYYCQQVITFPRTFGQGTKVEIK (SEQ ID NO: 959)	FGQGTKVEIK (SEQ ID NO: 960)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
98	019-4C02H	QLQLQESGPGLVKPSETLSLTCAVSGGSMRSSSYYWGWIRQPPGKGLEWIGGMYYSGSTYYSPSLKRRVTISVDTSENHFSLKLTSVTAADTAVYYCAR (SEQ ID NO: 961)	QLQLQESGPGLVKPSETLSLTCAVS (SEQ ID NO: 962)	GGSMRSSSYY (SEQ ID NO: 963)	WGWIRQPPGKGLEWIGG (SEQ ID NO: 964)	MYYSGST (SEQ ID NO: 965)	YYSPSLKRRVTISVDTSENHFSLKLTSVTAADTAVYYC (SEQ ID NO: 966)	ARRWFGELDYYGSDV (SEQ ID NO: 967)	cagctgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcgctgtctctggggggctccatgaggagtagtagttactactggggctggatccgccagcccccagggaaggggactggagtggattggggtatgtattatagtgggagcacctactacagcccgtccctcaagaggcgagtcaccatatccgtagacacgtccgagaaccacttctccctgaagttgacctctgtgaccgccgcagacacggctgtctattactgtgcgagacgatggttcggggagctagactactacggttcggacgtctggggccaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgt (SEQ ID NO: 968)	QLQLQESGPGLVKPSETLSLTCAVSGGSMRSSSYYWGWIRQPPGKGLEWIGGMYYSGSTYYSPSLKRRVTISVDTSENHFSLKLTSVTAADTAVYYCARRWFGELDYYGSDVWGQGTTVTVSS (SEQ ID NO: 969)	WGQGTTVTVSS (SEQ ID NO: 970)
99	019-4C02L	QLVLTQSPSASASLGTSVKLTCTLSSGXSSSPIAWHXQQPEKGPRFLMKVNXDGSHYKEDGIPDRFSGSXSGSERYLTISNLQSEDEADYYCQTWGTDX (SEQ ID NO: 971)	QLVLTQSPSASASLGTSVKLTCTLS (SEQ ID NO: 972)	SGXSSSP (SEQ ID NO: 973)	IAWHXQQPEKGPRFLMK (SEQ ID NO: 974)	VNXDGSH (SEQ ID NO: 975)	YKEDGIPDRFSGSXSGSERYLTISNLQSEDEADYYC (SEQ ID NO: 976)	QTWGTDXQV (SEQ ID NO: 977)	cagcttgtgctgactcaatcgccctctgcctctgcctccctgggaacctcggtcaagctcacctgcactctgagcagcgggnacagcagctccccatcgcatggcatcngcagcagccggagaagggccctcggttcttgatgaaggttaacantgatggcagtcactacaaagaggacgggatccctgatcgcttctcgggctccnagtctgggtctgagcgctacctcaccatctccaacctccagtccgaggatgaggctgattattactgtcagacctggggcactgacnttcaggtattcggcggagggaccaagctgaccgtcctgggtcagcccaaggctgccccctcggtcactctgttcccgccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaa (SEQ ID NO: 978)	QLVLTQSPSASASLGTSVKLTCTLSSGXSSSPIAWHXQQPEKGPRFLMKVNXDGSHYKEDGIPDRFSGSXSGSERYLTISNLQSEDEADYYCQTWGTDXQVFGGGTKLTVL (SEQ ID NO: 979)	FGGGTKLTVL (SEQ ID NO: 980)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
100	019-4C05H	QVQLQESRPGLVKPSETLSLSCTVSGGSMRSYYWSWIRQSPGKGLEWIGYVYYSGGTEYNPSLKSRVIISVDTSKNQFSLNLSSVSAADTAVYYCAR (SEQ ID NO: 981)	QVQLQESRPGLVKPSETLSLSCTVS (SEQ ID NO: 982)	GGSMRSYY (SEQ ID NO: 983)	WSWIRQSPGKGLEWIGY (SEQ ID NO: 984)	VYYSGGT (SEQ ID NO: 985)	EYNPSLKSRVIISVDTSKNQFSLNLSSVSAADTAVYYC (SEQ ID NO: 986)	ARGVSALVSVDYYYYYMDV (SEQ ID NO: 987)	caggtgcagctgcaggagtcgcgtccaggactggtgaagccttcggagaccctgtccctcagctgcactgtctctggtggctccatgagaagttactactggagctggatccggcagtccccaggaaaagggactggagtggattggctatgtctattatagtgggggcaccgagtacaacccctccctcaagagtcgagtaatcatatcagtagacacgtccaagaaccagttctccctgaacctgagctctgtgagcgctgcggacacggccgtttattactgtgcgagaggggtatcagctcttgtttccgtggactactactactactacatggacgtctggggcaaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaac (SEQ ID NO: 988)	QVQLQESRPGLVKPSETLSLSCTVSGGSMRSYYWSWIRQSPGKGLEWIGYVYYSGGTEYNPSLKSRVIISVDTSKNQFSLNLSSVSAADTAVYYCARGVSALVSVDYYYYYMDVWGKGTTVTVSS (SEQ ID NO: 989)	WGKGTTVTVSS (SEQ ID NO: 990)
101	019-4C05L	SYELTQPPSVSVAPGKTAIITCGGNNIGSKSVQWYQRKPGQAPVLVIYYNRDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDRNID (SEQ ID NO: 991)	SYELTQPPSVSVAPGKTAIITCGGN (SEQ ID NO: 992)	NIGSKS (SEQ ID NO: 993)	VQWYQRKPGQAPVLVIY (SEQ ID NO: 994)	YNR (SEQ ID NO: 995)	DRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYC (SEQ ID NO: 996)	QVWDRNIDPH (SEQ ID NO: 997)	tcctatgagctgacacagccaccctcagtgtcagtggccccaggaaagacggccataattacctgtgggggaaacaacattggaagtaagagtgtgcagtggtatcagcggaagccaggccaggcccctgtgttggtcatctattataatagggaccggccctcagggatccctgagcgattctctggctccaactctgggaacacggccaccctgaccatcagcagggtcgaggccggggatgaggccgactattactgtcaggtgtgggataggaacattgatccccacttcggaactgggaccgaggtcaccgtcctaggtcagcccaaggccaaccccactgtcactctgttcccaccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaaggcgggagtgg (SEQ ID NO: 998)	SYELTQPPSVSVAPGKTAIITCGGNNIGSKSVQWYQRKPGQAPVLVIYYNRDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDRNIDPHFGTGTEVTVL (SEQ ID NO: 999)	FGTGTEVTVL (SEQ ID NO: 1000)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
102	019-4D01H	QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWTWIRQSPGKGLEWIGYVYYTGGTEYNSSLKSRVTISVDTSKNQFSLKLNSATAADTAVYYCAR (SEQ ID NO: 1001)	QVQLQESGPGLVKPSETLSLTCTVS (SEQ ID NO: 1002)	GGSISTYY (SEQ ID NO: 1003)	WTWIRQSPGKGLEWIGY (SEQ ID NO: 1004)	VYYTGGT (SEQ ID NO: 1005)	EYNSSLKSRVTISVDTSKNQFSLKLNSATAADTAVYYC (SEQ ID NO: 1006)	ARAVSTLVSVDYYFYYIDV (SEQ ID NO: 1007)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctggtggctccatcagtacttactactggacctggatccgacagtccccagggaagggactggagtggattggttatgtctattacactgggggcaccgagtacaactcctccctcaagagtcgagtcaccatttcagtagacacgtccaagaatcagttctccctgaagttgaactccgccaccgctgcggacacggccgtttattactgtgcgagagcagtttcgactcttgtttcagtggactattacttctactacatagacgtctggggcaaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacc (SEQ ID NO: 1008)	QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWTWIRQSPGKGLEWIGYVYYTGGTEYNSSLKSRVTISVDTSKNQFSLKLNSATAADTAVYYCARAVSTLVSVDYYFYYIDVWGKGTTVTVSS (SEQ ID NO: 1009)	WGKGTTVTVSS (SEQ ID NO: 1010)
103	019-4D01L	SYELTQPPSVSLAPGKTATITCGGNNIGSKSVHWYQQKPGQAPVLVIYHNNNRPTGIPERFSGSNSGNTATLTISRAAAGDEAEYFCQVWDRNND (SEQ ID NO: 1011)	SYELTQPPSVSLAPGKTATITCGGN (SEQ ID NO: 1012)	NIGSKS (SEQ ID NO: 1013)	VHWYQQKPGQAPVLVIY (SEQ ID NO: 1014)	HNN (SEQ ID NO: 1015)	NRPTGIPERFSGSNSGNTATLTISRAAAGDEAEYFC (SEQ ID NO: 1016)	QVWDRNNDPL (SEQ ID NO: 1017)	tcctatgagctgacacagccaccctcagtgtcactggccccaggaaagacggccacgattacctgtgggggaaataacattggaagtaaaagtgtgcactggtatcagcagaagccaggccaggcccctgtcctggtcatctatcataataataatcggccccacagggatccctgagcgattctctggctccaactctgggaacacggccaccctgaccatcagcagggccgcagccggggatgaggccgagtacttctgtcaggtttgggataggaataatgatcccctcttcggaactgggaccaaggtcaccgtcctaagtcagcccaaggccaacccactgtcactctgttcccaccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaaggcgggagtgga (SEQ ID NO: 1018)	SYELTQPPSVSLAPGKTATITCGGNNIGSKSVHWYQQKPGQAPVLVIYHNNNRPTGIPERFSGSNSGNTATLTISRAAAGDEAEYFCQVWDRNNDPLFGTGTKVTVL (SEQ ID NO: 1019)	FGTGTKVTVL (SEQ ID NO: 1020)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
104	019-4D02H	QVQLQESGPGLVKPSETLSLTCTVSGGSIRSYYWSWIRQPPGKGLEWIGYVYYTGGTEYNPSLKSRVIISVDTSKNQFSLNLSSVTAADTAVYYCAR (SEQ ID NO: 1021)	QVQLQESGPGLVKPSETLSLTCTVS (SEQ ID NO: 1022)	GGSIRSYY (SEQ ID NO: 1023)	WSWIRQPPGKGLEWIGY (SEQ ID NO: 1024)	VYYTGGT (SEQ ID NO: 1025)	EYNPSLKSRVIISVDTSKNQFSLNLSSVTAADTAVYYC (SEQ ID NO: 1026)	ARGVSALVSVDYYYYYMDV (SEQ ID NO: 1027)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctggtggctccatcagaagttactactggagttggatccggcagcccccaggaaagggactggagtggattggctatgtctattatactgggggcaccgagtacaatccctccctcaagagtcgagtaatcatatcagtagacacgtccaagaaccagttctccctgaacctgagctctgtgaccgctgcggacacggccgtttattactgtgcgagaggggtatcagctcttgtttccgtggactactactactactacatggacgtctggggcaaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaac (SEQ ID NO: 1028)	QVQLQESGPGLVKPSETLSLTCTVSGGSIRSYYWSWIRQPPGKGLEWIGYVYYTGGTEYNPSLKSRVIISVDTSKNQFSLNLSSVTAADTAVYYCARGVSALVSVDYYYYYMDVWGKGTTVTVSS (SEQ ID NO: 1029)	WGKGTTVTVSS (SEQ ID NO: 1030)
105	019-4D02L	SYELTQPPSVSVAPGKTAIITCGGNNIGSKSVQWYQQKPGQAPVLVIYYNRDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDRNID (SEQ ID NO: 1031)	SYELTQPPSVSVAPGKTAIITCGGN (SEQ ID NO: 1032)	NIGSKS (SEQ ID NO: 1033)	VQWYQQKPGQAPVLVIY (SEQ ID NO: 1034)	YNR (SEQ ID NO: 1035)	DRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYC (SEQ ID NO: 1036)	QVWDRNIDPH (SEQ ID NO: 1037)	tcctatgagctgactcagccaccctcagtgtcagtggccccaggaaagacggccataattacctgtgggggaaacaacattggaagtaagagtgtgcagtggtatcagcagaagccaggccaggcccctgtgttggtcatctattataatagggaccggccctcagggatccctgagcgattctctggctccaactctgggaacacggccaccctgaccatcagcagggtcgaggccggggatgaggccgactattactgtcaggtgtgggataggaatattgatccccacttcggaactgggaccgaggtcaccgtcctaggtcagcccaaggccaaccccactgtcactctgttcccaccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaaggcgggagtgg (SEQ ID NO: 1038)	SYELTQPPSVSVAPGKTAIITCGGNNIGSKSVQWYQQKPGQAPVLVIYYNRDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDRNIDPHFGTGTEVTVL (SEQ ID NO: 1039)	FGTGTEVTVL (SEQ ID NO: 1040)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
106	019-4E01H	QVQLQESGPGLLKPSETLSLTCTVSGGSISKYYWTWIRQPPGKTLEWIGYVHYAFYIGATNYNPSLKSRVTISVDTAKNQVSLRLTSVTAADTA (SEQ ID NO: 1041)	QVQLQESGPGLLKPSETLSLTCTVS (SEQ ID NO: 1042)	GGSISKYY (SEQ ID NO: 1043)	WTWIRQPPGKTLEWIGY (SEQ ID NO: 1044)	VHYAFYI (SEQ ID NO: 1045)	GATNYNPSLKSRVTISVDTAKNQVSLRLTSVTAADTAV (SEQ ID NO: 1046)	YYCVRADGDSEGFGYHYGMDV (SEQ ID NO: 1047)	caggtgcagctgcaggagtcgggcccaggactgctgaagccttcggagaccctgtccctcacctgcactgtctctggtggctccatcagtaaatattactggacctggatccggcagcccccagggaagacactggagtggattggatatgtccattatgcctttatatttggggccaccaattataaccccctcctcaagagtcgagtcaccatatcagtagacacggccaagaaccaggtctcccttaggttgacctctgtgaccgctgcggacacggccgtttattactgtgtgagagcagacggtgactccgagggcttcgggtaccactacggaatggacgtctgggggccgggggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc (SEQ ID NO: 1048)	QVQLQESGPGLLKPSETLSLTCTVSGGSISKYYWTWIRQPPGKTLEWIGYVHYAFYIGATNYNPSLKSRVTISVDTAKNQVSLRLTSVTAADTAVYYCVRADGDSEGFGYHYGMDVWGRGTTVTVSS (SEQ ID NO: 1049)	WGRGTTVTVSS (SEQ ID NO: 1050)
107	019-4E01L	DIQMTQSPSSLSASVGDRVTITCRASQGIGNDLAWYQQKLGTAPKRLIYDASSLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNDYP (SEQ ID NO: 1051)	DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 1052)	QGIGND (SEQ ID NO: 1053)	LAWYQQKLGTAPKRLIY (SEQ ID NO: 1054)	DAS (SEQ ID NO: 1055)	SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYC (SEQ ID NO: 1056)	LQHNDYPLT (SEQ ID NO: 1057)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcagggcattggaaatgacttagcctggtatcaacagaaactagggacagcccctaagcgcctgatttatgatgcatccagtttgcaaagtggggtcccatcgagattcagcggcagtggatctgggacagaattcactctcacaatcagcagcctgcagcctgaagattttgcaacttattactgcctacaacataatgattaccctctgacgttcggccaagggaccaaggtggaaatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggaga (SEQ ID NO: 1058)	DIQMTQSPSSLSASVGDRVTITCRASQGIGNDLAWYQQKLGTAPKRLIYDASSLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNDYPLTFGQGTKVEIK (SEQ ID NO: 1059)	FGQGTKVEIK (SEQ ID NO: 1060)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
108	019-4E03H	QVQLVQSGAEVKKPGSSVKVSCKASGVIFSNYAIGWVRQAPGQGLEWVGGILPIFGTANYAQRFQGRVTITADESTSTTYMELSSLRSDDTAVYYCA (SEQ ID NO: 1061)	QVQLVQSGAEVKKPGSSVKVSCKAS (SEQ ID NO: 1062)	GVIFSNYA (SEQ ID NO: 1063)	IGWVRQAPGQGLEWVGG (SEQ ID NO: 1064)	ILPIFGTA (SEQ ID NO: 1065)	NYAQRFQGRVTITADESTSTTYMELSSLRSDDTAVYYC (SEQ ID NO: 1066)	ARAARLYQQAYDI (SEQ ID NO: 1067)	caggtgcagctggtgcagtctggggctgaggtgaagaagcctgggtcctcggtgaaggtctcctgcaaggcctctggagtcatcttcagcaactatgctatcggctgggtgcgacaggcccctggacaagggcttgaatgggtgggagggatcctccctatttttggtacggcaaactacgcacagaggtttcagggcagggtcacgattaccgcggacgaatccacgagcacaacctacatggagctgagcagcctgagatctgacgacacggccgtatattactgtgcgagggcggcccgactttatcaacaggcttatgatatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctc (SEQ ID NO: 1068)	QVQLVQSGAEVKKPGSSVKVSCKASGVIFSNYAIGWVRQAPGQGLEWVGGILPIFGTANYAQRFQGRVTITADESTSTTYMELSSLRSDDTAVYYCARAARLYQQAYDIWGQGTMVTVSS (SEQ ID NO: 1069)	WGQGTMVTVSS (SEQ ID NO: 1070)
109	019-4E03L	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGEPPKLLISDASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFHSYP (SEQ ID NO: 1071)	AIQLTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 1072)	QGISSA (SEQ ID NO: 1073)	LAWYQQKPGEPPKLLIS (SEQ ID NO: 1074)	DAS (SEQ ID NO: 1075)	SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 1076)	QQFHSYPLFT (SEQ ID NO: 1077)	gccatccagttgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccgggcaagtcagggcattagcagtgctttagcctggtatcagcagaaaccaggtgaacctcctaagctcctaatctctgatgcctccagtttgcaaagtggggtcccatcaaggttcagcggcagtggatctgggacagatttcactctcaccatcagcagcctgcagcctgaagattttgcaacttattactgtcaacagtttcacagttaccctctgttcactttcggccctgggaccaaagtggatatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgaga (SEQ ID NO: 1078)	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGEPPKLLISDASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFHSYPLFTFGPGTKVDIK (SEQ ID NO: 1079)	FGPGTKVDIK (SEQ ID NO: 1080)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
110	019-4F03H	QLQLQESGPGLVKPSETLSLICSVSGDSMSCSSCYWGWIRQPPGKGLEYIGSSHYTGRTSHNPSLKSRVTISVDTSKRQLSLRLSSVTAADTAVYYCAR (SEQ ID NO: 1081)	QLQLQESGPGLVKPSETLSLICSVS (SEQ ID NO: 1082)	GDSMSCSSCY (SEQ ID NO: 1083)	WGWIRQPPGKGLEYIGS (SEQ ID NO: 1084)	SHYTGRT (SEQ ID NO: 1085)	SHNPSLKSRVTISVDTSKRQLSLRLSSVTAADTAVYYC (SEQ ID NO: 1086)	ARLFGELVGYQAFDF (SEQ ID NO: 1087)	cagctgcagctgcaggagtcgggcccaggactggtaaagccttcggagaccctgtccctcatttgcagtgtctctggtgactccatgagctgtagtagttgctactggggctggatccgccagcccccagggaaggggctggaatacattgggagttcccattatactgggcgcacctcccacaacccgtctctcaaaagtcgagtcaccatttccgttgacacgtccaagaggcagctctccctgaggctgagctctgtgaccgccgcagatacggctgtatattactgtgcgagactgttcggggaattagttggttatcaggcttttgatttctggggtctagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtga (SEQ ID NO: 1088)	QLQLQESGPGLVKPSETLSLICSVSGDSMSCSSCYWGWIRQPPGKGLEYIGSSHYTGRTSHNPSLKSRVTISVDTSKRQLSLRLSSVTAADTAVYYCARLFGELVGYQAFDFWGLGTMVTVSS (SEQ ID NO: 1089)	WGLGTMVTVSS (SEQ ID NO: 1090)
111	019-4F03L	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNSVNWYQQLPGTAPKLLIFSNNERPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLDG (SEQ ID NO: 1091)	QSVLTQPPSASGTPGQRVTISCSGS (SEQ ID NO: 1092)	SSNIGSNS (SEQ ID NO: 1093)	VNWYQQLPGTAPKLLIF (SEQ ID NO: 1094)	SNN (SEQ ID NO: 1095)	ERPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYC (SEQ ID NO: 1096)	AAWDDSLDGYV (SEQ ID NO: 1097)	cagtctgtgctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggaagcagctccaacatcggaagtaattctgttaactggtaccagcaactcccaggaacggcccccaaactcctcatctttagtaataatgagcggccctcaggggtccctgaccgattctctggctccaagtctggcacctcagcctccctggccatcagtggactccagtctgaggatgaggctgattactactgtgcagcatgggatgacagcctggatggttatgtcttcggaagtgggaccaaggtcaccgtcctaggtcagcccaaggccaaccccactgtcactctgttcccgccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaagg (SEQ ID NO: 1098)	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNSVNWYQQLPGTAPKLLIFSNNERPSGVPDRFSGSKSGTSASLAISGLQSEDEADYYCAAWDDSLDGYVFGSGTKVTVL (SEQ ID NO: 1099)	FGSGTKVTVL (SEQ ID NO: 1100)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
112	019-4G01H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGIHWARRVPGKGLEWVALISYDGYNKYYADSVKGRFIISRDNSRNRVDLQMNSLRAEDAAVYYCA (SEQ ID NO: 1101)	QVQLVESGGGVVQPGRSLRLSCAAS (SEQ ID NO: 1102)	GFTFSSYG (SEQ ID NO: 1103)	IHWARRVPGKGLEWVAL (SEQ ID NO: 1104)	ISYDGYNK (SEQ ID NO: 1105)	YYADSVKGRFIISRDNSRNRVDLQMNSLRAEDAAVYYC (SEQ ID NO: 1106)	AKIFSWQQLDYYYYAMDV (SEQ ID NO: 1107)	caggtgcagctggtggagtctgggggaggcgtggtccagcctgggaggtccctgagactctcctgtgcagcctctggattcaccttcagttcctatggcatccactgggcccgccgggttccaggcaagggactggagtgggtggcacttatatcatatgatggatataataaatattatgcagactccgtgaagggccgattcatcatctccagagacaactccaggaacagagttgatctgcaaatgaacagcctgagagctgaggacgcggctgtgtattactgtgcgaaaatcttttcttggcagcagctcgactactattattacgctatggacgtctggggccaagggaccacggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaa (SEQ ID NO: 1108)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGIHWARRVPGKGLEWVALISYDGYNKYYADSVKGRFIISRDNSRNRVDLQMNSLRAEDAAVYYCAKIFSWQQLDYYYYAMDVWGQGTTVTVSS (SEQ ID NO: 1109)	WGQGTTVTVSS (SEQ ID NO: 1110)
113	019-4G01L	QSVLTQPPSASGTPGQTVPISCSGSSSNVGSHPVHWYQQLPGTAPKLLIYSDRQRPSEVPGRFSGSKSGTSASLRISGLQSDDEGDYYCAAWDDSLD (SEQ ID NO: 1111)	QSVLTQPPSASGTPGQTVPISCSGS (SEQ ID NO: 1112)	SSNVGSHP (SEQ ID NO: 1113)	VHWYQQLPGTAPKLLIY (SEQ ID NO: 1114)	SDR (SEQ ID NO: 1115)	QRPSEVPGRFSGSKSGTSASLRISGLQSDDEGDYYC (SEQ ID NO: 1116)	AAWDDSLDGVV (SEQ ID NO: 1117)	cagtctgtgctgacgcagccaccctcggcgtctgggacccccggccagacggtccccatctcttgttctggaagcagttccaacgtcggaagtcatcctgtacactggtaccagcaactcccaggaacggcccccaaactcctcatttatagtgatcgtcagcgcccctcagaggtccctggccgattctctggctccaagtctggcacctcagcctccctgagaatcagtgggctccagtctgacgatgagggtgattattattgtgcagcatgggacgacagcctggatggagtggtcttcggcggagggaccaaactgaccgtcctaggtcagcccaaggctgccccctcggtcactctgttcccgccctcgagtgaggagcttcaagccaacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccccgtcaag (SEQ ID NO: 1118)	QSVLTQPPSASGTPGQTVPISCSGSSSNVGSHPVHWYQQLPGTAPKLLIYSDRQRPSEVPGRFSGSKSGTSASLRISGLQSDDEGDYYCAAWDDSLDGVVFGGGTKLTVL (SEQ ID NO: 1119)	FGGGTKLTVL (SEQ ID NO: 1120)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
114	019-4G05H	EVQLVESGGDLVQPGGSLRLSCAGSGFTFSSSWMHWVRQAPGKGLVWVSRINSGGNFKKYADSVRGRFTISRDNTRNTLYLHMSSLRHEDTALYYCAR (SEQ ID NO: 1121)	EVQLVESGGDLVQPGGSLRLSCAGS (SEQ ID NO: 1122)	GFTFSSSW (SEQ ID NO: 1123)	MHWVRQAPGKGLVWVSR (SEQ ID NO: 1124)	INSGGNFK (SEQ ID NO: 1125)	KYADSVRGRFTISRDNTRNTLYLHMSSLRHEDTALYYC (SEQ ID NO: 1126)	ARDHDYGDYRGNAYDI (SEQ ID NO: 1127)	gaggtgcagctggtggagtcggggggagacttagttcagccgggggggtccctgagactctcctgtgcaggctctggattcaccttcagtagttcctggatgcactgggtccgccaagctccagggaaggggctggtgtgggtctcacgtattaatagtggtgggaatttcaaaaaatacgcggactccgtgaggggccgattcaccatctccagagacaacaccaggaacaccctatatctgcatatgagcagtctgagacacgaggacacggctctttattactgtgcaagagatcatgactacggtgactacagagggaacgcgtatgatatctggggccaagggacaatggtcaccgtctcttcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtg (SEQ ID NO: 1128)	EVQLVESGGDLVQPGGSLRLSCAGSGFTFSSSWMHWVRQAPGKGLVWVSRINSGGNFKKYADSVRGRFTISRDNTRNTLYLHMSSLRHEDTALYYCARDHDYGDYRGNAYDIWGQGTMVTVSS (SEQ ID NO: 1129)	WGQGTMVTVSS (SEQ ID NO: 1130)
115	019-4G05L	DIQMTQSPSSLSASVGDRVTITCQASQDISNYFNWYQQKPGKAPKLLIFDTSKLETGVPSRFSGRQSGTDYTFTISSLQPEDIATYFCQQ (SEQ ID NO: 1131)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 1132)	QDISNY (SEQ ID NO: 1133)	FNWYQQKPGKAPKLLIF (SEQ ID NO: 1134)	DTS (SEQ ID NO: 1135)	KLETGVPSRFSGRQSGTDYTFTISSLQPEDIATYFC (SEQ ID NO: 1136)	QQLDS (SEQ ID NO: 1137)	gacatccagatgacccagtctccatcctccctgtctgcatctgtgggagacagagtcaccatcacttgccaggcgagtcaggacattagcaactatttcaattggtatcagcagaaaccagggaaagcccctaagctcctaatcttcgatacatccaagttggaaacaggggtcccatcaaggttcagtggaagacaatctgggacagattatactttcaccatcagcagcctgcagcctgaagatattgcaacatatttctgtcagcagcttgatagtttcggcggagggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagc (SEQ ID NO: 1138)	DIQMTQSPSSLSASVGDRVTITCQASQDISNYFNWYQQKPGKAPKLLIFDTSKLETGVPSRFSGRQSGTDYTFTISSLQPEDIATYFCQQLDSFGGGTKVEIK (SEQ ID NO: 1139)	FGGGTKVEIK (SEQ ID NO: 1140)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
116	020-2C05H	QLQLQESGPGLVKPSETLSLTCTVSGGSISNNIYYWTWIRQPPGKGLEWIGSIYYSGNIYYNPSLKSRVTISVDTSKNQFSLKLRSVTAADTAVYYCAR (SEQ ID NO: 1141)	QLQLQESGPGLVKPSETLSLTCTVS (SEQ ID NO: 1142)	GGSISNNIYY (SEQ ID NO: 1143)	WTWIRQPPGKGLEWIGS (SEQ ID NO: 1144)	IYYSGNI (SEQ ID NO: 1145)	YYNPSLKSRVTISVDTSKNQFSLKLRSVTAADTAVYYC (SEQ ID NO: 1146)	ARHRVGTGPEVGDWFDP (SEQ ID NO: 1147)	cagctgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctggtggctccatcagcaataatatttactactggacctggatccgccagccccagggaaggggctggagtggattgggagtatctattatagtgggaacatctactacaacccgtccctcaagagtcgagtcaccatatccgtagacacgtccaagaaccaattctccctgaagctgaggtctgtgaccgccgcagacacggctgtgtattactgtgcgagacatagggtgggcactggccccgaagttggggactggttcgacccctggggccagggaaccctggtcaccgtctcctcagcgtcgaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaacctgtgacggtctcgtgg (SEQ ID NO: 1148)	QLQLQESGPGLVKPSETLSLTCTVSGGSISNNIYYWTWIRQPPGKGLEWIGSIYYSGNIYYNPSLKSRVTISVDTSKNQFSLKLRSVTAADTAVYYCARHRVGTGPEVGDWFDPWGQGTLVTVSS (SEQ ID NO: 1149)	WGQGTLVTVSS (SEQ ID NO: 1150)
117	020-2C05L	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYDASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNSWP (SEQ ID NO: 1151)	EIVMTQSPATLSVSPGERATLSCRAS (SEQ ID NO: 1152)	QSVSSN (SEQ ID NO: 1153)	LAWYQQKPGQAPRLLIY (SEQ ID NO: 1154)	DAS (SEQ ID NO: 1155)	TRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYC (SEQ ID NO: 1156)	QQYNSWPPMYT (SEQ ID NO: 1157)	gaaatagtgatgacgcagtctccagccaccctgtctgtgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgttagcagcaacttagcctggtaccagcagaaacctggccaggctcccaggctcctcatctatgatgcatccaccagggccactggtatcccagccaggttcagtggcagtgggtctgggacagagttcactctcaccatcagcagcctgcagtctgaagattttgcagtttattactgtcagcagtataataactggcctcccatgtacacttttggccaggggaccaaggtggagatcaaacgtacggtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactc (SEQ ID NO: 1158)	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYDASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNSWPPMYTFGQGTKVEIK (SEQ ID NO: 1159)	FGQGTKVEIK (SEQ ID NO: 1160)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
118	020-3B04H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYAMSWVRQAPGKGLEWVSGISGRGDSTYYADSVKGRFTISRDNSQNTLYLQMISLRAEDTAEYYCAK (SEQ ID NO: 1161)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 1162)	GFTFSDYA (SEQ ID NO: 1163)	MSWVRQAPGKGLEWVSG (SEQ ID NO: 1164)	ISGRGDST (SEQ ID NO: 1165)	YYADSVKGRFTISRDNSQNTLYLQMISLRAEDTAEYYC (SEQ ID NO: 1166)	AKDHRG (SEQ ID NO: 1167)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcagcctctggattcacctttagtgactatgccatgagctgggtccgccaggctccagggaaggggctggagtgggtctcaggtattagtggtcgtggtgatagcacatactatgcagactccgtgaagggccggttcaccatctccagagacaattcccagaacacgctgtatctgcaaatgatcagcctgagagccgaggacacggccgaatattactgtgcgaaagatcatagggggctggggccagggaaccctggtcaccgtctcctcagcctccaccaagggcccatcggtcttccccctggcaccctcctccaagagcacctctgggggcacagcggccctgg (SEQ ID NO: 1168)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYAMSWVRQAPGKGLEWVSGISGRGDSTYYADSVKGRFTISRDNSQNTLYLQMISLRAEDTAEYYCAKDHRGWGQGTLVTVSS (SEQ ID NO: 1169)	WGQGTLVTVSS (SEQ ID NO: 1170)
119	020-3B04L	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKSGKAPKLLIYDASNLDTGVPSRFSGSGSGTDFTFTISSLQPEDFATYYCQQFDKFP (SEQ ID NO: 1171)	DIQMTQSPSSLSASVGDRVTITCQAS (SEQ ID NO: 1172)	QDISNY (SEQ ID NO: 1173)	LNWYQQKSGKAPKLLIY (SEQ ID NO: 1174)	DAS (SEQ ID NO: 1175)	NLDTGVPSRFSGSGSGTDFTFTISSLQPEDFATYYC (SEQ ID NO: 1176)	QQFDKFPWT (SEQ ID NO: 1177)	gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccaggcgagtcaggacattagcaactatttaaattggtatcagcagaaatcagggaaagcccctaagctcctgatctacgatgcatccaatttggatacaggggtcccatcaaggttcagtggaagtggatctgggacagattttactttcaccatcagcagcctgcagcctgaagattttgcaacatattactgtcaacagtttgataaattcccttggacgttcggccaagggaccaaggtggaaatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataact (SEQ ID NO: 1178)	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKSGKAPKLLIYDASNLDTGVPSRFSGSGSGTDFTFTISSLQPEDFATYYCQQFDKFPWTFGQGTKVEIK (SEQ ID NO: 1179)	FGQGTKVEIK (SEQ ID NO: 1180)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
120	020-3808H	QLQLQESGPGLVKPSETLSLTCSVSGGSISSSTYYWGWIRQPPGKGLEWIGSLYYSGSTDFNPSLKSRVTISVDTSNNRVSLKLRSVTAADTAVYYCAR (SEQ ID NO: 1181)	QLQLQESGPGLVKPSETLSLTCSVS (SEQ ID NO: 1182)	GGSISSSTYY (SEQ ID NO: 1183)	WGWIRQPPGKGLEWIGS (SEQ ID NO: 1184)	LYYSGST (SEQ ID NO: 1185)	DFNPSLKSRVTISVDTSNNRVSLKLRSVTAADTAVYYC (SEQ ID NO: 1186)	ARHAKAPDSFGGAEYFDY (SEQ ID NO: 1187)	cagctgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgctctgtctctggtggctccatcagcagcagtacttactactggggctggatccgccagcccccagggaaggggctggagtggattgggagtctctactatagtgggagcaccgacttcaacccgtccctcaagagtcgagtcaccatatccgtagacacgtccaacaaccgggtctccctgaagctgaggtctgtgaccgccgcagatacggctgtgtattactgtgcgagacacgcgaaagcacccgattcgtttgggggagctgagtactttgactactggggccagggaaccctggtcatcgtctcctcagcctccaccaagggcccatcggtcttccccctggcac (SEQ ID NO: 1188)	QLQLQESGPGLVKPSETLSLTCSVSGGSISSSTYYWGWIRQPPGKGLEWIGSLYYSGSTDFNPSLKSRVTISVDTSNNRVSLKLRSVTAADTAVYYCARHAKAPDSFGGAEYFDYWGQGTLVIVSS (SEQ ID NO: 1189)	WGQGTLVIVSS (SEQ ID NO: 1190)
121	020-3808L	EIVMTQSPATLSVSPGEGATLSCRASQSVSSNLAWYQQRPGQAPRLLIYDASTRATGVPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNEWP (SEQ ID NO: 1191)	EIVMTQSPATLSVSPGEGATLSCRAS (SEQ ID NO: 1192)	QSVSSN (SEQ ID NO: 1193)	LAWYQQRPGQAPRLLIY (SEQ ID NO: 1194)	DAS (SEQ ID NO: 1195)	TRATGVPARFSGSGSGTEFTLTISSLQSEDFAVYYC (SEQ ID NO: 1196)	QQYNEWPPMYT (SEQ ID NO: 1197)	gaaatagtgatgacgcagtctccagccaccctgtctgtgtctccaggggaaggagccaccctctcctgcagggccagtcagagtgttagcagcaacttagcctggtatcagcagagacctggccaggctcccaggctcctcatctatgatgcatccaccagggccactggtgtcccagccaggttcagtggcagtgggtctgggacagagttcactctcaccatcagcagcctgcagtctgaagattttgcagtttattactgtcagcagtataatgagtggcctcctatgtacacttttggccaggggaccaagctggagatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctga (SEQ ID NO: 1198)	EIVMTQSPATLSVSPGEGATLSCRASQSVSSNLAWYQQRPGQAPRLLIYDASTRATGVPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNEWPPMYTFGQGTKLEIK (SEQ ID NO: 1199)	FGQGTKLEIK (SEQ ID NO: 1200)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
122	020-3F04H	QVQLVESGGGVVQPGRSLRLSCAASGFSFSNYGIHWVRQAQGKGLEWVAVISHTGSNKYYADSVKGRFTISRDNSKNMLYLQMNSLRVEDTAVYYCA (SEQ ID NO: 1201)	QVQLVESGGGVVQPGRSLRLSCAAS (SEQ ID NO: 1202)	GFSFSNYG (SEQ ID NO: 1203)	IHWVRQAQGKGLEWVAV (SEQ ID NO: 1204)	ISHTGSNK (SEQ ID NO: 1205)	YYADSVKGRFTISRDNSKNMLYLQMNSLRVEDTAVYYC (SEQ ID NO: 1206)	ATLGGDIVLEPGTRSDYYYGLDV (SEQ ID NO: 1207)	caggtgcagctggtggagtctgggggaggcgtggtccagcctgggaggtccctgagactctcctgtgcagcctctggattcagtttcagtaattatggcatacactgggtccgccaggctcaaggcaaggggctggagtgggtggcagttatatcacacactggaagtaataaatattatgcagactccgtgaagggccgattcaccatctccagagacaattccaagaacatgttgtatctgcaaatgaacagcctgagagttgaggacacggctgtgtattactgtgcgacactgggtggggacattgttctagaaccaggtactaggtcggactactactacggtttggacgtctggggccaagggaccacggtcaccgtctcctcagcatccccgaccagccccaaggtct (SEQ ID NO: 1208)	QVQLVESGGGVVQPGRSLRLSCAASGFSFSNYGIHWVRQAQGKGLEWVAVISHTGSNKYYADSVKGRFTISRDNSKNMLYLQMNSLRVEDTAVYYCATLGGDIVLEPGTRSDYYYGLDVWGQGTTVTVSS (SEQ ID NO: 1209)	WGQGTTVTVSS (SEQ ID NO: 1210)
123	020-3F04L	DIQMTQSPSTLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPNLLIYKASSLKSGVPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYYTNS (SEQ ID NO: 1211)	DIQMTQSPSTLSASVGDRVTITCRAS (SEQ ID NO: 1212)	QSISTW (SEQ ID NO: 1213)	LAWYQQKPGKAPNLLIY (SEQ ID NO: 1214)	KAS (SEQ ID NO: 1215)	SLKSGVPSRFSGSGSGTDFTLTISSLQPDDFATYYC (SEQ ID NO: 1216)	QQYYTNSRM (SEQ ID NO: 1217)	gacatccagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgccgggccagtcagagtattagtacctggttggcctggtatcagcagaaaccagggaaagcccctaacctcctgatctataaggcgtccagtttaaaaagtggggtcccatcacggttcagcggcagtggatctgggacagacttcactctcaccatcagcagcctgcagcctgatgattttgcaacttattactgccaacaatattatactaattctaggatgttcggccaagggaccaaggtggaaatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcag (SEQ ID NO: 1218)	DIQMTQSPSTLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPNLLIYKASSLKSGVPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYYTNSRMFGQGTKVEIK (SEQ ID NO: 1219)	FGQGTKVEIK (SEQ ID NO: 1220)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
124	020-3G06H	QVQLVESGGGLVKPGGSLRLSCAASGFNFSDYYMSWIRQAPGKRLEWVSYISSSGDNTLYADSMRGRFTISRDNAKKSLYLQLSSLRAEDTAVFYCAR (SEQ ID NO: 1221)	QVQLVESGGGLVKPGGSLRLSCAAS (SEQ ID NO: 1222)	GFNFSDYY (SEQ ID NO: 1223)	MSWIRQAPGKRLEWVSY (SEQ ID NO: 1224)	ISSSGDNT (SEQ ID NO: 1225)	LYADSMRGRFTISRDNAKKSLYLQLSSLRAEDTAVFYC (SEQ ID NO: 1226)	ARASAYYYDSSGRAAAFDI (SEQ ID NO: 1227)	caggtgcagctggtggagtctgggggaggcttggtcaagcctggagggtccctgagactctcgtgtgcagcctctggattcaacttcagtgactactacatgagctggatccgccaggctccagggaagcggctggagtgggtttcatacattagcagtagtggtgataacacactctacgcagactctatgaggggccgtttcaccatctccagggacaacgccaagaagtcactgtatttgcaattgagcagcctgagagccgaggacacggccgtgttttactgtgcgagagcctccgcgtattattatgatagtagtggccgggcggctgcttttgatatctggggccaagggacaagggtcaccgtctcttcagcctccaccaagggcccatcggtcttccccctggcac (SEQ ID NO: 1228)	QVQLVESGGGLVKPGGSLRLSCAASGFNFSDYYMSWIRQAPGKRLEWVSYISSSGDNTLYADSMRGRFTISRDNAKKSLYLQLSSLRAEDTAVFYCARASAYYYDSSGRAAAFDIWGQGTRVTVSS (SEQ ID NO: 1229)	WGQGTRVTVSS (SEQ ID NO: 1230)
125	020-3G08L	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLEWYVQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGRDFTLKISRVEAEDVGVYYCMQVLQTP (SEQ ID NO: 1231)	DIVMTQSPLSLPVTPGEPASISCRSS (SEQ ID NO: 1232)	QSLLHSNGYNY (SEQ ID NO: 1233)	LEWYVQKPGQSPQLLIY (SEQ ID NO: 1234)	LGS (SEQ ID NO: 1235)	NRASGVPDRFSGSGSGRDFTLKISRVEAEDVGVYYC (SEQ ID NO: 1236)	MQVLQTPLFT (SEQ ID NO: 1237)	gatattgtgatgactcagtctccactctccctgcccgtcacccctggagagccggcctccatctcctgcaggtctagtcagagcctcctgcatagtaatggatacaactatttggagtggtacgtgcagaagccaggacagtctccacagctcctgatctatttgggttctaatcgggcctccggggtccctgacaggttcagtggcagtggatcaggcagagattttacactgaaaatcagcagagtggaggctgaggatgtaggggtttattactgcatgcaagttctacaaactcctctattcactttcggccctgggaccaaagtggatatcaaacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaactcccag (SEQ ID NO: 1238)	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLEWYVQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGRDFTLKISRVEAEDVGVYYCMQVLQTPLFTFGPGTKVDIK (SEQ ID NO: 1239)	FGPGTKVDIK (SEQ ID NO: 1240)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
126	014-2A04H	QVQLQESGPGLVKPSQILSLSCNVSGGSISSGSYYWSWIRQPAGKGLEWIGRLYTSGTTNYNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCAR (SEQ ID NO: 1241)	QVQLQESGPGLVKPSQILSLSCNVS (SEQ ID NO: 1242)	GGSISSGSYY (SEQ ID NO: 1243)	WSWIRQPAGKGLEWIGR (SEQ ID NO: 1244)	LYTSGTT (SEQ ID NO: 1245)	NYNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYC (SEQ ID NO: 1246)	ARGIKGDYGGGANWFDP (SEQ ID NO: 1247)	acatccagatgacccagtctccatctgccatgtctgcatctgtaggagacagagtcaccatcacttgtcgggcgagtcagggcattagcaattattagcctggtttcagcagaaaccagggaaagtccctaagcgcctgatctattctgcatccactttgcaaagtggggtcccatcaaggttcagcggcagtggatctgggacagaattcactctcacaatcagcagcctgcagcctgaagattttgcaacttattactgtctacagcataatagttaccctctcactttcggcggagggaccaaggtggaaatcaaac (SEQ ID NO: 1248)	QVQLQESGPGLVKPSQILSLSCNVSGGSISSGSYYWSWIRQPAGKGLEWIGRLYTSGTTNYNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGIKGDYGGGANWFDPWGQGTLVTVSS (SEQ ID NO: 1249)	WGQGTLVTVSS (SEQ ID NO: 1250)
127	014-2A04L	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYRASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNNWP (SEQ ID NO: 1251)	EIVMTQSPATLSVSPGERATLSCRAS (SEQ ID NO: 1252)	QSVSSN (SEQ ID NO: 1253)	LAWYQQKPGQAPRLLIY (SEQ ID NO: 1254)	RAS (SEQ ID NO: 1255)	TRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYC (SEQ ID NO: 1256)	QQYNNWPPYT (SEQ ID NO: 1257)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctacttactccatcagcagtggttactactggggctggatccggcagcccccagggaaggggctggagtggattggaagtatctatcatagtgggaccacctactacaacccgtccctcaagagtcgaatcaccacatcagtagacacgtccaagaaccagttctccctgaaactgaccctctgtgaccgccgcagacacggccgtgtattattgtgcgaggtatatagtgtctacgatcaactactttgacgactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 1258)	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYRASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNNWPPYTFGQGTKVEIK (SEQ ID NO: 1259)	FGQGTKVEIK (SEQ ID NO: 1260)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
128	014-2B03H	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGNYYWSWIRQPAGKGLEWIGRIYTSGSTNYNPSLKSRITMSVDMSKNQFSLKLSSLTAADTAVYYCA (SEQ ID NO: 1261)	QVQLQESGPGLVKPSQTLSLTCTVS (SEQ ID NO: 1262)	GGSISSGNYY (SEQ ID NO: 1263)	WSWIRQPAGKGLEWIGR (SEQ ID NO: 1264)	IYTSGST (SEQ ID NO: 1265)	NYNPSLKSRITMSVDMSKNQFSLKLSSLTAADTAVYYC (SEQ ID NO: 1266)	ARARFFGISNWFDP (SEQ ID NO: 1267)	gaaattgtgttgacgcagtctccaggcaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgtgaacagcatctacttagcctggtaccagcagaaacctggccaggctcccagggtcctcatctatggtacatccagcagggccactggcatcccagacaggttcagtggcagtgggtctgggacagacttcactctcaccattagcagactggagcctgaagattttgcagtgtattactgtcagctgtatggtggctcaccttttattcgctttcggccctgggaccaaagtggatatcaaac (SEQ ID NO: 1268)	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGNYYWSWIRQPAGKGLEWIGRIYTSGSTNYNPSLKSRITMSVDMSKNQFSLKLSSLTAADTAVYYCARARFFGISNWFDPWGQGTLVTVSS (SEQ ID NO: 1269)	WGQGTLVTVSS (SEQ ID NO: 1270)
129	014-2B03L	DIQMTQSPSSLSASVGDRVTITCRASQTISSYLNWYQQKPGKAPKLLIYGASSLQSGVPSRVSGSGSGTDFTLTISSLQPEDFATYYCQQSYSAP (SEQ ID NO: 1271)	DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 1272)	QTISSY (SEQ ID NO: 1273)	LNWYQQKPGKAPKLLIY (SEQ ID NO: 1274)	GAS (SEQ ID NO: 1275)	SLQSGVPSRVSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 1276)	QQSYSAPLT (SEQ ID NO: 1277)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcagcctctggattcacctttagcagctatgccatgagttgggtccgccaggctccagggaaggggctggagtgggtctcaactattagtgggagtggtggtagcacatactacgcagactccgtgaagggccggttcaccatctccagagacaattctaagaacacgttatatctgcaaatgaacagcctgaaagccgaggacacggccgtatactactgtgcgaaagatccccgtagtagtgtcccctgggtggcctactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 1278)	DIQMTQSPSSLSASVGDRVTITCRASQTISSYLNWYQQKPGKAPKLLIYGASSLQSGVPSRVSGSGSGTDFTLTISSLQPEDFATYYCQQSYSAPLTFGQGTKVEIK (SEQ ID NO: 1279)	FGQGTKVEIK (SEQ ID NO: 1280)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
130	014-2B06H	VQLVQSGDEVKKPGSSVRVSCKTSGSTFSTYPISWVRQAPGQGLEWMGGIIPIVGTANYAQKFQDRVAITADQSTSTAYMDLTSLRSEDTAVYYCAR (SEQ ID NO: 1281)	VQLVQSGDEVKKPGSSVRVSCKTS (SEQ ID NO: 1282)	GSTFSTYP (SEQ ID NO: 1283)	ISWVRQAPGQGLEWMGG (SEQ ID NO: 1284)	IIPIVGTA (SEQ ID NO: 1285)	NYAQKFQDRVAITADQSTSTAYMDLTSLRSEDTAVYYC (SEQ ID NO: 1286)	ARVGGALIRSSGSDY (SEQ ID NO: 1287)	ttgtgatgactcagtccccactctccctgcccgtcaccccttggacagccggcctccatctcctgcaggtctagtcaaagcctcgtacacagtgatggaaacacctacttgaattggtttcagcagaggccaggccaatctccaaggcgcctaatttataaggtttctaaccgggactctggggtcccagacagattcagcggcagtgggtcaggcactgatttcacactgaaaatcagcagggtggaggctgaggatgttggggtttattactgcatgcagggtacacactggcctccgtacacttttggccaggggaccaaggtggagatcaaac (SEQ ID NO: 1288)	VQLVQSGDEVKKPGSSVRVSCKTSGSTFSTYPISWVRQAPGQGLEWMGGIIPIVGTANYAQKFQDRVAITADQSTSTAYMDLTSLRSEDTAVYYCARVGGALIRSSGSDYWGQGTLVTVSS (SEQ ID NO: 1289)	WGQGTLVTVSS (SEQ ID NO: 1290)
131	014-2B06L	IQMTQSPSAMSASVGDRVTITCRASQGISNYLAWFQQKPGKVPKRLIYSASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP (SEQ ID NO: 1291)	IQMTQSPSAMSASVGDRVTITCRAS (SEQ ID NO: 1292)	QGISNY (SEQ ID NO: 1293)	LAWFQQKPGKVPKRLIY (SEQ ID NO: 1294)	SAS (SEQ ID NO: 1295)	TLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYC (SEQ ID NO: 1296)	LQHNSYPLT (SEQ ID NO: 1297)	gaggtgcagctgttggagtctgggggaggcttggtacagccaggggggtccctgagactctcctgtgcagcctctggattcacatttagcaactatgccatgagctgggtccgccaggctccagggaaggggctggagtgggtctcaggtattagtgctggtggtagtaacaaatactacgcagactccgtgaagggccggttcaccgtctccagagacaattccaagaacacgctgtttctgcaaatgaacagcctgagagtcgaggacacggccgtatattattgtgcgaatcggatgggactacggccggactactttgactactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 1298)	IQMTQSPSAMSASVGDRVTITCRASQGISNYLAWFQQKPGKVPKRLIYSASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPLTFGGGTKVEIK (SEQ ID NO: 1299)	FGGGTKVEIK (SEQ ID NO: 1300)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
132	015-2F03H	QVQLQESGPGLVKPSETLSLTCTVSTYSISSGYYWGWIRQPPGKGLEWIGSIYHSGTTYYNPSLKSRITTSVDTSKNQFSLKLTSVTAADTAVYYCA (SEQ ID NO: 1301)	QVQLQESGPGLVKPSETLSLTCTVS (SEQ ID NO: 1302)	TYSISSGYY (SEQ ID NO: 1303)	WGWIRQPPGKGLEWIGS (SEQ ID NO: 1304)	IYHSGTT (SEQ ID NO: 1305)	YYNPSLKSRITTSVDTSKNQFSLKLTSVTAADTAVYYC (SEQ ID NO: 1306)	ARYIVSTINYFDD (SEQ ID NO: 1307)	gaaattgtgttgacgcagtctccaggcaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgttagcagcagctccttagcctggtaccagcagaaacctggccaggctcccaggctcctcatctatgatgcatccagcagggccactggcatcccagacaggttcagtggcagtgggtctgggacagacttcactctcaccatcagcagactggagcctgaggattttgcagtgtattactgtcagcagtatggtacctcagctaaaacttttggccaggggaccaaggtggagatcaaac (SEQ ID NO: 1308)	QVQLQESGPGLVKPSETLSLTCTVSTYSISSGYYWGWIRQPPGKGLEWIGSIYHSGTTYYNPSLKSRITTSVDTSKNQFSLKLTSVTAADTAVYYCARYIVSTINYFDDWGQGTLVTVSS (SEQ ID NO: 1309)	WGQGTLVTVSS (SEQ ID NO: 1310)
133	015-2F03L	EIVLTQSPGTLSLSPGERATLSCRASQSVNSIYLAWYQQKPGQAPRVLIYGTSSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQLYGGSP (SEQ ID NO: 1311)	EIVLTQSPGTLSLSPGERATLSCRAS (SEQ ID NO: 1312)	QSVNSIY (SEQ ID NO: 1313)	LAWYQQKPGQAPRVLIY (SEQ ID NO: 1314)	GTS (SEQ ID NO: 1315)	SRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 1316)	QLYGGSPLFA (SEQ ID NO: 1317)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcagcctctggattcacctttagcagctatgccatgaactgggtccgccaggctccagggaaggggctggagtgggtctcagctattagtggtagtggtggtagcacatactacgcagactccgtgaagggccggttcaccatttccagagacaattccaagaacacgctgtatctgcaaatgagcagcctgagagccgaggacacggccgtatattactgtgcgaaatccccggcgagcagctggtactttgaccactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 1318)	EIVLTQSPGTLSLSPGERATLSCRASQSVNSIYLAWYQQKPGQAPRVLIYGTSSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQLYGGSPLFAFGPGTKVDIK (SEQ ID NO: 1319)	FGPGTKVDIK (SEQ ID NO: 1320)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
134	020-2A04H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAQGKGLEWVSTISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCAK (SEQ ID NO: 1321)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 1322)	GFTFSSYA (SEQ ID NO: 1323)	MSWVRQAQGKGLEWVST (SEQ ID NO: 1324)	ISGSGGST (SEQ ID NO: 1325)	YYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYC (SEQ ID NO: 1326)	AKDPRSSVPWVAY (SEQ ID NO: 1327)	gaaatagtgatgacgcagtctccagccaccctgtctgtgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgttagcagcaacttagcctggtaccagcagaaacctggccaggctcccaggctcgtcatctatggtgcatccaccagggccactggtatcccagccaggttcagtggcagtgggtctgggacagagttcactctcaccatcagcagcctgcagtctgaagattttgcagtttattactgtcagcaagataataactggcccacgtggacgttcggccaagggaccaaggtggaaatcaaac (SEQ ID NO: 1328)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAQGKGLEWVSTISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCAKDPRSSVPWVAYWGQGTLVTVSS (SEQ ID NO: 1329)	WGQGTLVTVSS (SEQ ID NO: 1330)
135	020-2A04L	VMTQSPLSLPVTLGQPASISCRSSQSLVHSDGNTYLNWFQQRPGQSPRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWP (SEQ ID NO: 1331)	VMTQSPLSLPVTLGQPASISCRSS (SEQ ID NO: 1332)	QSLVHSDGNTY (SEQ ID NO: 1333)	LNWFQQRPGQSPRRLIY (SEQ ID NO: 1334)	KVS (SEQ ID NO: 1335)	NRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC (SEQ ID NO: 1336)	MQGTHWPPYT (SEQ ID NO: 1337)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcagcctctggattcacatctaatagctttgtcatgaattgggtccgccaggctccagggaagggcctggagtgggtctcggctattaagggtactgtaaatagtacattctacgcagattccgtgaagggccgcttcaccatctccagagacaattctaagaacacggtgtatctgcaaatgagcagcctgagagtcgaggacacggccatttattactgccgcggggtggttcggggagggaatcaacggttgggacgtctggggccaagggaccacggtcaccgtctcctca (SEQ ID NO: 1338)	VMTQSPLSLPVTLGQPASISCRSSQSLVHSDGNTYLNWFQQRPGQSPRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPYTFGQGTKVEIK (SEQ ID NO: 1339)	FGQGTKVEIK (SEQ ID NO: 1340)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
136	020-2B03H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNYAMSWVRQAPGKGLEWVSGISAGGSNKYYADSVKGRFTVSRDNSKNTLFLQMNSLRVEDTAVYYCA (SEQ ID NO: 1341)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 1342)	GFTFSNYA (SEQ ID NO: 1343)	MSWVRQAPGKGLEWVSG (SEQ ID NO: 1344)	ISAGGSNK (SEQ ID NO: 1345)	YYADSVKGRFTVSRDNSKNTLFLQMNSLRVEDTAVYYC (SEQ ID NO: 1346)	ANRMGLRPDYFDY (SEQ ID NO: 1347)	gatattgtgatgactcagtctccgctctccctgcccgtcacccctggagcgccggcctccatctcctgcagatccagtcggagcctcctgcatagagatggatacaactatgtagattggtacctgcagaagccagggcagtctccacagctcctgatctatttgggttctaatcgggcctccggggtccctgacaggttcagtggcagtggatcaggcacagatttcacactgaaaatgagcagagtggaggctgaggatgttggggtttattactgcatgcaagctctacaaactccgtacaattttggccaggggaccaaggtggagatcaaac (SEQ ID NO: 1348)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNYAMSWVRQAPGKGLEWVSGISAGGSNKYYADSVKGRFTVSRDNSKNTLFLQMNSLRVEDTAVYYCANRMGLRPDYFDYWGQGTLVTVSS (SEQ ID NO: 1349)	WGQGTLVTVSS (SEQ ID NO: 1350)
137	020-2B03L	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSSLAWYQQKPGQAPRLLIYDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGTSA (SEQ ID NO: 1351)	EIVLTQSPGTLSLSPGERATLSCRAS (SEQ ID NO: 1352)	QSVSSSS (SEQ ID NO: 1353)	LAWYQQKPGQAPRLLIY (SEQ ID NO: 1354)	DAS (SEQ ID NO: 1355)	SRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 1356)	QQYGTSAKT (SEQ ID NO: 1357)	acatccagatgacccagtctccatctgccatgtctgcatctgtaggagacagagtcaccatcacttgtcgggcgagtcagggcattagcaattatttagcctggtttcagcagaaaccagggaaagtccctaagcgcctgatctattctgcatccactttgcaaagtggggtcccatcaaggttcagcggcagtggatctgggacagaattcactctcacaatcagcagcctgcagcctgaagattttgcaacttattactgtctacagcataatagttaccctctcactttcggcggagggaccaaggtggaaatcaaac (SEQ ID NO: 1358)	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSSLAWYQQKPGQAPRLLIYDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGTSAKTFGQGTKVEIK (SEQ ID NO: 1359)	FGQGTKVEIK (SEQ ID NO: 1360)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
138	020-2805H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMNWVRQAPGKGLEWVSAISGSGGSTYHADSVKGRFTISRDNSKNTLYLQMSSLRAEDTAVYYCAK (SEQ ID NO: 1361)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 1362)	GFTFSSYA (SEQ ID NO: 1363)	MNWVRQAPGKGLEWVSA (SEQ ID NO: 1364)	ISGSGGST (SEQ ID NO: 1365)	YHADSVKGRFTISRDNSKNTLYLQMSSLRAEDTAVYYC (SEQ ID NO: 1366)	AKSPASSWYFDH (SEQ ID NO: 1367)	caggtgcagctgcaggagtcgggcccaggactggtgaagccttcggagaccctgtccctcacctgcactgtctctacttactccatcagcagtggttactactggggctggatccggcagcccccagggaaggggctggagtggattggaagtatctatcatagtgggaccacctactacaacccgtccctcaagagtcgaatcaccacatcagtagacacgtccaagaaccagttctccctgaaactgacctctgtgaccgccgcagacacggccgtgtattattgtgcgaggtatatagtgtctacgatcaactactttgacgactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 1368)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMNWVRQAPGKGLEWVSAISGSGGSTYHADSVKGRFTISRDNSKNTLYLQMSSLRAEDTAVYYCAKSPASSWYFDHWGQGTLVTVSS (SEQ ID NO: 1369)	WGQGTLVTVSS (SEQ ID NO: 1370)
139	020-2805L	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLVIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQDNNW (SEQ ID NO: 1371)	EIVMTQSPATLSVSPGERATLSCRAS (SEQ ID NO: 1372)	QSVSSN (SEQ ID NO: 1373)	LAWYQQKPGQAPRLVIY (SEQ ID NO: 1374)	GAS (SEQ ID NO: 1375)	TRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYC (SEQ ID NO: 1376)	QQDNNWPTWT (SEQ ID NO: 1377)	gaaattgtgttgacgcagtctccaggcaccctgtctttgtctccaggggaaagagccaccctctcctgcagggccagtcagagtgtgaacagcatctacttagcctggtaccagcagaaacctggccaggctcccaggctcctcatctatggtacatccagcagggccactggcatcccagacaggttcagtggcagtgggtctgggacagacttcactctcaccattagcagactggagcctgaagattttgcagtgtattactgtcagctgtatggtggctcacctttattcgctttcggccctgggaccaaagtggatatcaaac (SEQ ID NO: 1378)	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLVIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQDNNWPTWTFGQGTKVEIK (SEQ ID NO: 1379)	FGQGTKVEIK (SEQ ID NO: 1380)

FIG. 12 (continued)

	A	G	H	I	J	K	L	M	N	O	P
Row	Name	V-REGION (1)	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	Sequence	Translated Sequence (V-REGION)	FR4-IMGT
140	020-2D03H	EVQLLESGGGLVQPGGSLRLSCAASGFTSNSFVMNWVRQAPGKGLEWVSAIKGTVNSTFYADSVKGRFTISRDNSKNTVYLQMSSLRVEDTAIYY (SEQ ID NO: 1381)	EVQLLESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 1382)	GFTSNSFV (SEQ ID NO: 1383)	MNWVRQAPGKGLEWVSA (SEQ ID NO: 1384)	IKGTVNST (SEQ ID NO: 1385)	FYADSVKGRFTISRDNSKNTVYLQMSSLRVEDTAIYYC (SEQ ID NO: 1386)	RGWFGEGINGWDV (SEQ ID NO: 1387)	gaggtgcagctgttggagtctgggggaggcttggtacagcctggggggtccctgagactctcctgtgcagcctctggattcacctttagcagctatgccatgagttgggtccgccaggctcaagggaaggggctggagtgggtctcaactattagtgggagtggtggtagcacatactacgcagactccgtgaagggccggttcaccatctccagagacaattctaagaacacgttatatctgcaaatgaacagcctgaaagccgaggacacggccgtatactactgtgcgaaagatccccgtagtagtgtcccctgggtggcctactggggccagggaaccctggtcaccgtctcctcag (SEQ ID NO: 1388)	EVQLLESGGGLVQPGGSLRLSCAASGFTSNSFVMNWVRQAPGKGLEWVSAIKGTVNSTFYADSVKGRFTISRDNSKNTVYLQMSSLRVEDTAIYYCRGWFGEGINGWDVWGQGTTVTVSS (SEQ ID NO: 1389)	WGQGTTVTVSS (SEQ ID NO: 1390)
141	020-2D03L	DIVMTQSPLSLPVTPGAPASISCRSSRSLLHRDGYNYVDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKMSRVEAEDVGVYYCMQALQT (SEQ ID NO: 1391)	DIVMTQSPLSLPVTPGAPASISCRSS (SEQ ID NO: 1392)	RSLLHRDGYNY (SEQ ID NO: 1393)	VDWYLQKPGQSPQLLIY (SEQ ID NO: 1394)	LGS (SEQ ID NO: 1395)	NRASGVPDRFSGSGSGTDFTLKMSRVEAEDVGVYYC (SEQ ID NO: 1396)	MQALQTPYN (SEQ ID NO: 1397)	ttgtgatgactcagtccccactctccctgcccgtcaccccttggacagccggcctccatctcctgcaggtctagtcaaagcctcgtacacagtgatggaaacacctacttgaattggtttcagcagaggccaggccaatctccaaggcgcctaatttataaggtttctaaccgggactctggggtcccagacagattcagcggcagtgggtcaggcactgatttcacactgaaaatcagcagggtggaggctgaggatgttggggtttattactgcatgcagggtacacactggcctccgtacacttttggccaggggaccaaggtggagatcaaac (SEQ ID NO: 1398)	DIVMTQSPLSLPVTPGAPASISCRSSRSLLHRDGYNYVDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKMSRVEAEDVGVYYCMQALQTPYNFGQGTKVEIK (SEQ ID NO: 1399)	FGQGTKVEIK (SEQ ID NO: 1400)

FIG. 12 (continued)

	Number	Age (years)	Female (%)	Interval after given 2009/10 TIV (days)
Pandemic (H1N1) 2009 vaccine	24	39.5 (26 - 64)	79.2	-77 (-4 to -160)
2009/10 TIV	27	29 (21 - 47)	74.1	N/A

FIG. 13

NAME	V-GENE	V Mutations	V %ID	J-GENE	D-GENE	CDR lengths	AA JUNCTION
05-1C01H	IGHV1-69*01	24	92	IGHJ4*02	IGHD3-10*01	8.8.13	CAGGSDDHAWGSFYW
05-1C01K	IGKV2or 2D-40*01	6	98	IGKJ2*01		12.3.9	CMQRIAFFFTF
05-1D08H	IGHV4-31*06	35	89	IGHJ4*02	IGHD6-19*01	10.7.16	CARGLEGITVGWYYFDFW
05-1D08K	IGKV1-13*02	20	91	IGKJ4*01		6.3.9	CQQFNSFPLTF
05-2G02H	IGHV1-18*01	22	92	IGHJ4*02	IGHD3-9*01	8.8.15	CARDRRDLLTGSLGDYW
05-2G02K	IGKV2 or 2D-30*01	13	96	IGKJ2*01		11.3.9	CMQGTYWPFTF
09-2A04H	IGHV1-69*06	36	88	IGHJ1*01	IGHD5-18*01	8.8.13	CASPAYNSQFALLHW
09-2A04K	IGKV4-1*01	7	98	IGKJ2*01		12.3.10	CQQYYSNSMYTF
09-2A06H	IGHV1-69*09	20	93	IGHJ4*02	IGHD3-22*01	8.8.18	CASPDLTMVFVPHTGPLDFW
09-2A06K	IGKV1-5*03	17	94	IGKJ1*01		6.3.8	CQHYDTYSGTF
09-2G01H	IGHV4-59*03	18	95	IGHJ6*03	IGHD5-12*01	8.7.19	CARDCSGFSGMDSFYYFMDVW
09-2G01K	IGKV3-11*01	17	94	IGKJ4*01		6.3.11	CQYRSHWPPAVTF
09-2A01H	IGHV4-39*06	13	96	IGHJ4*02	IGHD2-8*01	10.7.19	CARGLTGMVYALLPSYFDFW
09-3A01K	IGKV1-5*03	9	98	IGKJ1*01		6.3.8	CQQHNSYSGAF
09-3A02H	IGHV3-33*01	20	93	IGHJ3*02	IGHD3-3*01	8.8.15	CAKDRILPYDTDAFDIW
09-3A02K	IGKV1-5*03	25	91	IGKJ3*01		6.3.10	CQSYHTSSRVTF
09-3D04H	IGHV3-23*01	21	93	IGHJ4*02	IGHD6-6*01	8.8.18	CAKDRVVGRPWEYSLDFW
09-3D04K	IGKV3-15*01	16	94	IGKJ4*01		6.3.10	CQQYNNWPPLTF
09-3E08H	IGHV3-30*01	12	96	IGHJ4*02	IGHD4-11*01	8.7.11	CASRHYNYDDDYG
09-3E08K	IGKV2-30*02	2	99	IGKJ5*01		11.3.8	CMQGTHWPTF
09-3F05H	IGHV3-7*01	22	92	IGHJ5*02	IGHD3-10*01	8.8.18	CARAGSYGDYRPINWWFDPW
09-3F05K	IGKV1-5*03	23	92	IGKJ2*01		6.3.9	CQHYSNYSYTF
09-3G01H	IGHV3-30*04	13	95	IGHJ4*02	IGHD3-16*01	8.8.15	CARDPSNPFHWSNFDSW
09-3G01K	IGKV3-11*01	6	97	IGKJ5*01		6.3.10	CQQRSNWPPITF
09-3G09H	IGHV3-33*01	18	94	IGHJ4*02	IGHD4-17*01	8.8.18	CAKDLAVTPPAQGYLDRW
09-3G09K	IGKV3-11*01	5	98	IGKJ5*01		6.3.10	CQQRSNWPPITF
14-2A04H	IGHV4-61*02	8	97	IGHJ5*02	IGHD4-22*01	10.7.17	CARGIKGDYGGGANWFDPW
14-2A04K	IGKV3-15*01	2	100	IGKJ2*01		6.3.10	CQQYNNWPPYTF
14-2B03H	IGHV4-61*02	11	96	IGHJ5*02	IGHD3-16*02	10.7.14	CARARFFGIGNWFDPW
14-2B03K	IGKV1 or 1D-39*01	5	98	IGKJ1*01		6.3.9	CQQSYSAPLTF
14-2B08H	IGHV1-69*01	17	94	IGHJ4*02	IGHD3-10*01	8.8.15	CARVGGALIRSGGSDYW
14-2B08K	IGKV1D-17*02	2	99	IGKJ4*01		6.3.9	CLQHNSYPLTF
15-1A01H	IGHV1-69*04	26	91	IGHJ6*03	IGHD6-19*01	8.8.17	CARDDYMTVDRDYYYMDVW
15-1A01K	IGKV3-15*01	11	96	IGKJ3*01		6.3.11	CQQYNNWPPLFSF
15-1A03H	IGHV3-7*01	27	91	IGHJ6*03	IGHD5-24*01	8.8.22	CARVSREEWATVDDPHDYYYMDVW
15-1A03K	IGKV1 or 1D-39*01	24	92	IGKJ4*01		6.3.9	CQQNYNPLFTF
15-1A08H	IGHV3-7*01	32	89	IGHJ6*03	IGHD5-24*01	8.8.22	CVRVSREEWATVDDPHDYYYMDVW
15-1A08K	IGKV1 or 1D-39*01	28	91	IGKJ4*01		6.3.9	CQQSYNSLFTF
15-2A01H	IGHV3-7*01	19	93	IGHJ6*03	IGHD5-24*01	8.8.22	CARVSREEWATVDDPHDYYYMDVW
15-2A01K	IGKV1 or 1D-39*01	24	91	IGKJ4*01		6.3.9	CQQSYNRLFTF
15-2A08H	IGHV1-2*02	21	93	IGHJ3*02	IGHD4-17*01	8.8.16	CARDFDYGDYRGSAFDIW
15-2A08K	IGKV1 or 1D-33*01	13	94	IGKJ2*01		6.3.5	CQQLNTF
15-2B04H	IGHV1-2*02	39	87	IGHJ3*02	IGHD4-17*01	8.8.17	CARDIDTGDYRGADVLGMW
15-2B04K	IGKV1 or 1D-33*01	24	90	IGKJ3*01		6.3.5	CQQLYTF
15-2C03H	IGHV3-7*01	23	92	IGHJ6*03	IGHD5-24*01	8.8.22	CARVSREEWATVDDPHDYYYMDVW
15-2C03K	IGKV1 or 1D-39*01	19	93	IGKJ4*01		6.3.9	CQQSYITLFTF
15-2C04H	IGHV3-23*01	21	93	IGHJ4*02	IGHD5-24*01	8.8.19	CAREEPTDYEMTITGGDFGYW
15-2C04K	IGKV1 or 1D-39*01	15	95	IGKJ2*01		6.3.9	CQRSYITPFTF
15-2C08H	IGHV1-2*02	34	88	IGHJ3*02	IGHD4-17*01	8.8.17	CARDIDSGDYRAADVFDIW
15-2C08K	IGKV1 or 1D-33*01	19	95	IGKJ3*01		6.3.4	CQQLTTF
15-2D02H	IGHV1-2*02	35	88	IGHJ3*02	IGHD4-17*01	8.8.17	CARDIDSGDYRAADVFDIW
15-2D02K	IGKV1 or 1D-33*01	9	96	IGKJ2*01		6.3.5	CQQLATF
15-2E01H	IGHV1-2*02	33	89	IGHJ3*02	IGHD4-17*01	8.8.17	CARDIDSGDYRAADVFDIW
15-2E01K	IGKV1 or 1D-33*01	19	95	IGKJ3*01		6.3.5	CQQLTTF
15-2E08H	IGHV3-7*01	27	93	IGHJ6*03	IGHD5-24*01	8.8.22	CARVSREEWATVDDPHDYYYMDVW
15-2E08K	IGKV1 or 1D-39*01	24	92	IGKJ4*01		6.3.9	CQQSYNSLFTF
15-2F01H	IGHV1-18*01	14	95	IGHJ6*03	IGHD3-16*02	8.8.24	CAREGYDHLWGTYRFEAIDYYYYDVW
15-2F01K	IGKV3-20*01	10	90	IGKJ1*01		7.3.8	CHQYGSSTGTF
15-2F02H	IGHV1-2*02	42	86	IGHJ3*02	IGHD4-17*01	8.8.17	CARDIDFGDYRAADVFHIW
15-2F02K	IGKV1 or 1D-33*01	22	91	IGKJ3*01		6.3.5	CQQLDTF
15-2F03H	IGHV4-b*02	6	97	IGHJ4*02	IGHD5-12*01	9.7.13	CARYNVSTINYFDDW
15-2F03K	IGKV3-20*01	6	97	IGKJ3*01		7.3.10	CQLYGGSPLFAF
15-2F04H	IGHV1-2*02	19	93	IGHJ3*02	IGHD4-17*01	8.8.16	CARDFDYGDYRGSAFDIW
15-2F04K	IGKV1 or 1D-33*01	23	90	IGKJ3*01		6.3.5	CQQLNTF
15-2F05H	IGHV3-23*01	25	91	IGHJ4*03	IGHD5-24*01	8.8.19	CARESFTDTEMTINGSDFAYW
15-2F05K	IGKV1 or 1D-39*01	18	94	IGKJ3*01		6.3.9	CQRSFITPFTF
15-2G04H	IGHV1-2*02	22	92	IGHJ3*02	IGHD4-17*01	8.8.16	CARDFDYGDYRGSAFDIW
15-2G04K	IGKV1 or 1D-33*01	23	90	IGKJ3*01		6.3.5	CQQLNTF
18-2D01H	IGHV5-a*01	18	95	IGHJ6*03	IGHD3-10*02	8.8.17	CTRDSFYDVDLSSFYMDVW
18-2D01K	IGKV3-20*01	10	96	IGKJ2*01		7.3.8	CQQYGSSRNTF
18-2D03H	IGHV1-18*01	17	94	IGHJ3*02	IGHD5-24*01	8.8.15	CARDRIDYVVYDAFDIW
18-2D03K	IGKV1-5*03	15	94	IGKJ1*01		6.3.8	CQLYDGFRTF
19-2A02H	IGHV1-18*01	21	93	IGHJ3*02	IGHD4-17*01	8.8.16	CARRGDYGDYRGDAFDIW
19-2A02K	IGKV1 or 1D-33*01	9	95	IGKJ3*01		6.3.5	CQQVFTF
19-2A05H	IGHV3-21*01	24	92	IGHJ3*02	IGHD5-24*01	8.8.27	AKDRVRDGDNDWDSVDATYWGYGVFDT
19-2A05K	IGKV4-1*01	7	98	IGKJ1*01		12.3.9	CQQHYRIPQTF
19-2A08H	IGHV3-74*01	28	91	IGHJ3*02	IGHD4-17*01	8.8.18	CVRDNDYGDYRGNAFDIW
19-2A08K	IGKV1 or 1D-33*01	22	91	IGKJ4*01		6.3.5	CEQLHTF
19-2F05H	IGHV3-21*01	14	95	IGHJ3*02	IGHD5-24*01	8.8.27	ARDRVRDGDNYWDSVDATYWGYGAFDI
19-2F05K	IGKV4-1*01	9	97	IGKJ1*01		12.3.9	CQQHFTTPQTF
19-4D01H	IGHV4-59*01	10	93	IGHJ6*03	IGHD3-3*01	8.7.19	CARAVSTLVSVDYYFYYMDVW
19-4D01L	IGLV3-21*01	24	92	IGLJ1*01		6.3.10	CQVWDRNNDFLF
19-4G05H	IGHV3-74*01	24	92	IGHJ3*02	IGHD4-17*01	8.8.18	CARDHDYGDYRGNAYDIW
19-4G05K	IGKV1 or 1D-33*01	14	95	IGKJ4*01		6.3.5	CQQLDSF

FIG. 14A

20-2A04H	IGHV3-23*01	9	97	IGHJ4*02	IGHD2-2*01	8.8.13	CAKDPRSSVPWVAYW
20-2A04K	IGKV2-30*02	2	99	IGKJ2*01		11.3.10	CMQGTHWPPYTF
20-2B03H	IGHV3-23*01	13	95	IGHJ4*02	IGHD4-17*01	8.8.13	CANRMGLRPDYFDYW
20-2B03K	IGKV3-20*01	5	98	IGKJ2*01		7.3.8	CQQYGTSAKTF
20-2B05H	IGHV3-23*01	4	98	IGHJ4*02	IGHD6-13*01	8.8.12	CAKSPASSWYFDHW
20-2B05K	IGKV3-15*01	3	99	IGKJ1*01		6.3.10	CQQDNNWPTWTF
20-2C05H	IGHV4-39*01	9	97	IGHJ5*02	IGHD4-23*01	10.7.17	CARHRVGTGPEVGDWFDPW
20-2C05K	IGKV3-15*01	3	99	IGKJ2*01		6.3.11	CQQYNSWPPMYTF
20-2D03H	IGHV3-23*01	26	91	IGHJ5*02	IGHD3-10*01	8.8.13	CRDWFGEGINSWDVW
20-2D03K	IGKV2 or 2D-28*01	11	96	IGKJ2*01		11.3.9	CMQALQTPYNF
20-3F04H	IGHV3-30*03	14	95	IGHJ6*02	IGHD2-2*01	8.8.23	CATLGGDIVLEPGTRSDYYYGLDVW
20-3F04K	IGKV1-5*03	13	90	IGKJ1*01		6.3.9	CQQYYTNSRMF
20-3G06H	IGHV3-11*01	15	94	IGHJ3*02	IGHD3-22*01	8.8.19	CARASAYYYDSSGRAAAFDIW
20-3G06K	IGKV2-28*01	6	98	IGKJ2*01		11.3.10	CMQVLQTPLFTF

FIG. 14A (continued)

Name	V-GENE	J-GENE	D-GENE	AA JUNCTION
05-1D03H	IGHV5-51*01	IGHJ6*02	IGHD4-23*01	CARHVASHWGDYYGMDLW
05-1D03L	IGKV3-15*01	IGKJ1*01		CQQYNDWLGGTF
05-1D06H	IGHV4-31*06	IGHJ4*02	IGHD6-19*01	CARGLEGITVGAYYFDFW
05-1D06L	IGKV1-13*02	IGKJ4*01		CQQFNSFPLTF
05-1F02H	IGHV4-31*06	IGHJ4*02	IGHD6-19*01	CARGLEGITVGVYYCDFW
05-1F02L	IGKV1-13*02	IGKJ4*01		CQQFNSYPLTF
18-1B01H	IGHV3-30*03 or IGHV3-30*18	IGHJ4*02	IGHD2-8*02	CARDQELVVLYYFDFW
18-1B01L	IGLV3-21*02	IGLJ2*01 or IGLJ3*01		CQVYDNSVDHAVF
18-1B03H	IGHV3-23*01	IGHJ5*02	IGHD4-17*01	CAKEPYRDYLGNWPDPW
18-1B03L	IGKV4-1*01	IGKJ3*01		CHQHYTIPPTF
18-1C01H	IGHV1-69*01	IGHJ5*02	IGHD5-24*01	CARRQVATYWFDPW
18-1C01L	IGLV3-21*02	IGLJ1*01		CQVWDSNSGHFVF
18-1D04H	IGHV3-23*01	IGHJ4*02	IGHD6-19*01	CATSPATSGWWWAYW
18-1D04L	IGKV3-20*01	IGKJ2*01		CHQYDIPPQTF
18-2B05H	IGHV3-23*01	IGHJ4*02	IGHD6-13*01	CARPTPYGTTWFGRVDSW
18-2B05L	IGKV1-39*01 or IGKV1D-39*01	IGKJ3*01		CQQTYRTPITF
18-2E03H	IGHV3-74*01 or IGHV3-74*03	IGHJ4*02	IGHD5-12*01	CARGDLVSTANFDYW
18-2E03L	IGKV3-20*01	IGKJ2*01		CQQYENSQHGSSPPYTF
19-1B04H	IGHV3-74*01	IGHJ3*02	IGHD4-17*01	CARDHDYGDYRGNAFDMW
19-1B04L	IGKV1-33*01 or IGKV1D-33*01	IGKJ4*01		CQQLHTF
19-4A01H	IGHV4-39*01	IGHJ3*01	IGHD3-10*01	CARLFGELVGYQAFDVW
19-4A01L	IGLV1-44*01	IGLJ1*01		CAAWDDSLNGYVF
19-4C01H	IGHV4-31*03	IGHJ6*02	IGHD2-21*02	CARELGDYPYYYAMDVW
19-4C01L	IGKV1-9*01	IGKJ1*01		CQQVITFPRTF
19-4C02H	IGHV4-39*02	IGHJ6*02	IGHD3-10*01	CARRWFGELDYYGSDVW
19-4C02L	IGLV4-69*01	IGLJ2*01 or IGLJ3*01		CQTWGTDXQVF
19-4C05H	IGHV4-59*01	IGHJ6*03	IGHD5-18*01	CARGVSALVSVDYYYYYMDVW
19-4C05L	IGLV3-21*01	IGLJ1*01		CQVWDRNIDPHF
19-4D02H	IGHV4-59*01	IGHJ6*03	IGHD5-18*01	CARGVSALVSVDYYYYYMDVW
19-4D02L	IGLV3-21*01	IGLJ1*01		CQVWDRNIDPHF
19-4E01H	IGHV4-59*01 or IGHV4-59*03	IGHJ6*02	IGHD4-17*01	VYYCVRADGDSEGFGYHYGMDVW
19-4E01L	IGKV1-17*01	IGKJ1*01		CLQHNDYPLTF
19-4E03H	IGHV1-69*01	IGHJ3*02	IGHD4-11*01	CARAARLYQQAYDIW
19-4E03L	IGKV1-13*02	IGKJ3*01		CQQFHSYPLFTF
19-4F03H	IGHV4-39*01	IGHJ3*01 or IGHJ3*02	IGHD3-10*02	CARLFGELVGYQAFDFW
19-4F03L	IGLV1-44*01	IGLJ1*01		CAAWDDSLDGYVF
19-4G01H	IGHV3-30*03 or IGHV3-30*18	IGHJ6*02	IGHD6-13*01	CAKIFSWQQLDYYYYAMDVW
19-4G01L	IGLV1-44*01	IGLJ2*01 or IGLJ3*01		CAAWDDSLDGVVF
20-3B04H	IGHV3-23*01	IGHJ4*02	IGHD7-27*01	CAKDHRGW
20-3B04L	IGKV1-33*01 or IGKV1D-33*01	IGKJ1*01		CQQFDKFPWTF
20-3B06H	IGHV4-39*01	IGHJ4*02	IGHD3-16*01	CARHAKAPDSFGGAEYFDYW
20-3B06L	IGKV3-15*01	IGKJ2*01		CQQYNEWPPMYTF

FIG. 14B

ANTIBODIES DIRECTED AGAINST INFLUENZA

CROSS REFERENCE TO RELATED APPLICATIONS

This Application is a continuation of U.S. application Ser. No. 14/350,632 filed Apr. 9, 2014, which is the National Stage of International Application Number PCT/US2012/060912 filed Oct. 18, 2012, which claims priority to U.S. Provisional Application No. 61/603,895 filed Feb. 27, 2012 and to U.S. Provisional Application No. 61/548,704 filed Oct. 18, 2011. The entirety of each of these applications is hereby incorporated by reference for all purposes.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

This invention was made with government support under AI057266, HHSN266200700006C and RR025008 awarded by The National Institutes of Health. The government has certain rights in the invention.

THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT

There is a joint research agreement between Emory University and The University of Chicago.

INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED AS A TEXT FILE VIA THE OFFICE ELECTRONIC FILING SYSTEM (EFS-WEB)

The Sequence Listing associated with this application is provided in text format in lieu of a paper copy, and is hereby incorporated by reference into the specification. The name of the text file containing the Sequence Listing is 11177USCON_ST25.txt. The text file is 604 KB, was created on Jan. 4, 2016, and is being submitted electronically via EFS-Web.

FIELD

This relates the field of influenza viruses, specifically to monoclonal antibodies, and antigen binding fragments thereof, that specifically bind an influenza virus protein.

BACKGROUND

Influenza is the seventh leading cause of death in the United States (Beigel J H (2008), Crit Care Med 36(9):2660-2666). The elderly, the very young, pregnant women and otherwise immune-compromised populations account for over 90% of influenza-related deaths. The pandemic H1N1 influenza virus strain is immunologically distinct from other influenza viruses, leaving large population groups susceptible to infection (Brockwell-Staats et al., Influenza Other Respi Viruses 3:207-21, 2009; Dawood et al., N Engl J Med 360:2605-2615, 2009; Garten et al., Science 325:197-201, 2009; Hancock K, et al. (2009) N Engl J Med 361(20):1945-1952). The Center for Disease Control (CDC) reports that the 2009 H1N1 pandemic strain caused an estimated 60 million cases and 256,000 hospitalizations. An unusually high frequency of severe disease occurred in younger and otherwise healthy patients (Hancock et al., 2009, supra). In addition, rare infections with avian H5N1 influenza strains in humans had close to a 50% mortality rate (Subbarao and Joseph, 2007, *Nat Rev Immunol* 7:267-278). Emergence of a zoonotic or antigenically distinct strain that combined even a fraction of the morbidity and mortality of the pandemic H1N1 and H5N1 viruses would have dire consequences.

Antibodies play a key role in protection against influenza infection in vivo (Gerhard et al., 1997*; Immunological reviews* 159:95-103; Luke et al., 2006*, Annals of internal medicine* 145:599-609; Puck et al., 1980*, Journal of infectious diseases* 142:844-849; Simmons et al., 2007*, PloS Medicine* 4:e178). The fact that there was little or no pre-existing antibody titers present prior to the emergence of this pandemic virus, and that the virus atypically caused such severe disease in young adults illustrates the importance of comprehensively understanding the B cell responses and antibody specificities induced by infection with this influenza virus. A need remains for reagents to treat and diagnose an influenza virus infection in a subject.

SUMMARY

Antibodies that specifically bind influenza virus hemagglutin A (HA), and antigen binding fragments thereof are disclosed herein. In some embodiments, these antibodies are broadly cross reactive. In additional embodiments, the antibodies inhibit hemmagglutination activity and neutralize more than one of H1N1, H5N1 and H3N2. In some embodiments, the antibody specifically binds H1N1 and H5N1. In other embodiments, the antibody specifically binds H1N1 and H3N2. In yet other embodiments, the antibody specifically binds H1N1, H5N1 and H3N2. In further embodiments, the antibody specifically binds HA of one or more of Pandemic (H1N1) 2009; A/Brevig mission/1/18(H1N1) 1918; and A/Brisbane/59/07(H1N1) 2007A/Indonesia/5/05 (H5N1) 2005; A/Brisbane10/07 (H3N2) 2007. The antibody can bind the HA globular head and or the HA stalk. In some embodiments, the antibody specifically binds a complex of HA1 and HA2.

In several embodiments, nucleic acids encoding these monoclonal antibodies, vectors including these nucleic acids, and host cells transformed with these vectors are also disclosed. Compositions are disclosed that include these antibodies, antigen binding fragments, nucleic acids, vectors and host cells.

Methods of using these antibodies, and antigen binding fragments, nucleic acids, vectors and host cells, such as for diagnosis and treatment of an influenza virus infection are also provided. In some embodiments, these antibodies and antigen binding fragments are used to diagnose an influenza virus infection is provided. In other embodiments, these antibodies, antigen binding fragments, nucleic acids, vectors, or host cells are used for the treatment and or prevention of an influenza virus.

The foregoing and other objects, features, and advantages of the invention will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. **1A-1D**. Rapid and potent plasmablast and serological responses after vaccination with the monovalent pandemic H1N1 2009 vaccine. Healthy adult volunteers were vaccinated with the pandemic H1N1 2009 monovalent vaccine. A control group was vaccinated with the 2008/09 TIV in 2008. FIG. **1A** shows fold change in serum antibody titers between day 0 and day 28 were determined by HA1.

FIG. 1B shows the number of vaccine-specific IgG-producing plasmablasts were determined by ELISPOT at 0, 7, 14 and 28 days post-vaccination. FIG. 1C shows the number of vaccine-specific plasmablasts correlates with improved serum antibody titers by HA1 (Spearman's rank correlation). FIG. 1D shows the numbers of vaccine-specific IgG-, IgA-, and IgM-producing plasmablasts at day 7 after vaccination as determined by ELISPOT. Dotted lines=limit of detection.

FIGS. 2A-2D. Stem-binding antibodies are induced following pandemic H1N1 2009 vaccination. Human mAbs were generated from plasmablasts isolated from individuals vaccinated with the pandemic H1N1 2009 vaccine. FIG. 2A shows binding to the pandemic H1N1 2009 virus by ELISA. FIG. 2B shows binding to pandemic H1N1 2009 HA by ELISA. FIG. 2C shows all HA-binding mAbs were tested for HA1 and neutralization activity. Three putative stem-binding mAbs are highlighted in blue. Dotted lines represent the highest concentration of mAb tested. Data are representative of 2-4 repeat experiments. FIG. 2D shows the 3 putative stem-binding mAbs were tested by competition ELISA with 2 known stem-binding mAbs (70-1F02 and 70-5B03)(8). Percentage inhibition is the ratio of binding with or without competitor. The reciprocal stem-binding mAb for each assay in the pair was used as a positive control and EM4C04 which binds the HA head was used as a negative control. Bars represent means+/−SEM for three repeats. The V_H gene usage of the individual stem-binding mAbs is indicated on the right.

FIGS. 3A-3C. The pandemic H1N1 2009 vaccine induces highly cross-reactive HA-specific antibodies. FIG. 3A shows twenty-eight pandemic H1N1 HA-binding mAbs were tested for binding to HAs from the indicated influenza strains by ELISA. FIG. 3B shows twenty-five HA head-binding mAbs were tested for neutralizing activity against the indicated panel of H1N1 virus strains. Two mAbs (20-3G06 and 15-1A03) expressed poorly and were not tested for cross-reactivity (ND). FIG. 3C shows three stem-binding mAbs were tested for neutralizing activity against various influenza virus strains. Influenza strains are arranged from left to right in order of sequence similarity to the pandemic H1N1 2009. Monoclonal antibodies are arranged according to degree of binding by ELISA to pandemic H1N1 2009 HA and grouped according to cross-reactivity by ELISA (blue: stem-binders, bind all H1N1, H5N1 and H3N2; black: bind all H1N1; red: bind A/California/04/09 and A/Brevig Mission/1/18; green: bind A/California/04/09 only). Dotted lines represent limits of detection. Data are representative of 2-4 repeats.

FIGS. 4A-4B. Monoclonal antibodies induced following the pandemic H1N1 2009 vaccine display high levels of somatic hypermutation consistent with a recall response. Variable genes from plasmablasts induced following the pandemic H1N1 2009 vaccine were amplified by single-cell RT-PCR and scored for numbers of somatic mutations. FIG. 4A shows the number of mutations per V_H gene following pandemic H1N1 2009 vaccination are compared with previously published data (12, 27-29). The red line shows the mean (p-values are from Student's t-tests). FIG. 4B shows the number of mutations per V_H gene in HA-specific mAbs only. Colors represent the degree of cross-reactivity as in FIG. 3.

FIGS. 5A-5B. Memory B cells reactive to the pandemic H1N1 2009 influenza are detectable even prior to the emergence of the pandemic strain. PBMCs obtained prior to vaccination were tested for the presence of memory B cells reactive against the pandemic H1N1 2009 HA by polyclonal activation followed by detection using ELISPOT. The percentage of IgG-secreting memory B cells compared with total IgG-secreting cells is shown in subjects from FIG. 5A the year that the pandemic H1N1 2009 emerged (2009/10) and FIG. 5B the previous year (2008/09).

FIG. 6. A model contrasting the antibody response induced after vaccination with seasonal versus pandemic influenza vaccines. The pre-existing influenza-specific B cell pool primarily consists of memory cells that recognize epitopes in the globular head of HA from recent seasonal strains that undergo antigenic drift and thus change relatively little year to year (shown in green). These are highly expanded due to recurrent stimulation over several winter seasons while memory B cells specific for epitopes in the stem of HA (shown in red) are crowded out. Following an infection or vaccination with drifted seasonal influenza strains, the large numbers of immunodominant head-reactive memory B cells undergo re-expansion while those against conserved epitopes cannot compete. In a pandemic strain, many epitopes in the HA head are replaced while conserved epitopes in the stem and head remain. Cross-reactive memory B cells specific for the conserved epitopes now have a greater chance of being recruited into the response.

FIG. 7. The 2008/09 trivalent inactivated influenza vaccine induces a rapid plasmablast response. Healthy adult volunteers were vaccinated with the 2008/09 TIV. PBMCs were taken at 0, 7, 14 and 28 days post-vaccination and the number of vaccine-specific IgG-producing plasmablasts were determined by ELISPOT. Dotted lines represent the limits of detection for each assay.

FIG. 8. Sequence homology of HAs from H1N1 strains. HA sequences were obtained from GENBANK®. Sequences were aligned using ClustalW2 and displayed as a phylogenetic tree. Numbers in brackets represent pairwise alignment scores. Correlation analysis was done using Spearman's rank correlation and comparison between groups using Student's t-test.

FIGS. 9A-9D. Plasmablasts induced by the monovalent (H1N1) 2009 vaccine cross-react with the 2009/10 seasonal TIV. Healthy adult volunteers were vaccinated with pandemic (H1N1) 2009 vaccine. FIG. 9A shows the numbers of IgG-producing plasmablasts in day 7 PBMCs that reacted against pandemic (H1N1) 2009 virus or the 2009/10 TIV (which contained the A/Brisbane/59/07 H1N1 strain) were determined by ELISPOT. FIG. 9B shows example of plasmablast isolation by flow cytometry. FIG. 9C shows representative ELISPOT images showing total IgG-producing plasmablasts and those reactive against indicated HA proteins. FIG. 9D shows ELISPOT scoring of sorted plasmablasts reactive against HA derived from the indicated viruses. ELISPOT for 1 donor is not shown due to insufficient plasmablast numbers post-sort.

FIGS. 10A-10C. Patterns of crossreactivity among HA specific vaccine-induced monoclonal antibodies. The 28 HA specific monoclonal antibodies were analyzed by ELISA for their binding to HA proteins derived from either the pandemic H1N1 2009 or the Brisbane H1N1 (A/Brisbane/59/07 (H1N1)) influenza strains. The antibodies showed binding patterns that conformed to three distinct categories. One category (9/28 antibodies) showed very similar binding to both HAs (FIG. 10A). Another category (14/28) showed better binding to the pandemic H1N1 HA, likely representing ongoing adaptation through affinity maturation (FIG. 10B), while the last category (5/28) bound better to the Brisbane HA (FIG. 10C), consistent with OAS (original antigenic sin).

FIG. **11**. Cross-reactivity of HA-specific monoclonal antibodies by HA1. Twenty-eight pandemic (H1N1) HA-binding mAbs were tested for neutralizing activity against a panel of H1N1 virus strains. Influenza strains are arranged in order of sequence similarity to the pandemic (H1N1) 2009 and mAbs are arranged according to cross-reactivity and degree of binding to pandemic (H1N1) 2009 HA. Dotted lines represent limits of detection. Data are representative of 2-4 repeat experiments.

FIG. **12** (Table 1). Amino acid sequence information for H1N1 binding antibodies. Table 1 provides detailed information, including sequence information, about each of the antibodies that were confirmed to bind influenza. Each antibody is identified in Col. A by antibody name and an indication of whether the heavy or light chain is being described. Heavy chains are indicated by H and light chains are indicated by L at the end of the identifier in Col. A. For example, line 2 of Table 1 discloses 005-2G02H, which is a heavy chain for one of the cloned antibodies, and line 3 of Table 1 discloses 005-2G02L, which is the light chain for the same antibody. Accordingly, each pair of rows (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, 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, and 140/141) represent paired heavy and light chains from a cloned human antibody. Col. G provides the V region amino acid sequence. Col. H provides the FR1 amino acid sequence. Col. I provides the CDR1 amino acid sequence. Col. J provides the FR2 amino acid sequence. Col. K provides the CDR2 amino acid sequence. Col. L provides the FR3 amino acid sequence. Col. M provides the CDR3 amino acid sequence. Col. N provides the nucleotide sequence. Col. O provides the translated V region amino acid sequence. Column P provides the FR4 amino acid sequence.

FIG. **13**. Clinical characteristics of study and control groups (Table 2). Number of subjects, age, gender and time interval between receiving pandemic (H1N1) 2009 vaccine and 2009/10 TIV are shown. Age and interval between vaccinations are expressed as median and range.

FIGS. **14**A and **14**B. Sequence, mutation and V-gene rearrangement data for pandemic (H1N1) 2009 virus-specific mAbs (Table 3). Variable genes were amplified from plasmablasts stimulated by pandemic (H1N1) 2009 vaccine by single-cell RT-PCR and then determined using in-house analysis software compared with the Immunogentics V gene dataset and the IMGT search engine. FIG. **14**A discloses SEQ ID NOS 1401-1478, residues 2-28 of SEQ ID NO: 1479 and SEQ ID NOS 1480-1498, respectively, in order of appearance, and FIG. **14**B discloses SEQ ID NOS 1499-1540, respectively, in order of appearance.

DETAILED DESCRIPTION

Influenza viruses are segmented negative-strand RNA viruses that belong to the Orthomyxoviridae family. There are three types of Influenza viruses, A, B and C. Influenza A viruses infect a wide variety of birds and mammals, including humans, horses, marine mammals, pigs, ferrets, and chickens. In animals, most influenza A viruses cause localized infections of the respiratory and intestinal tract. Animals infected with influenza A often act as a reservoir for the

influenza viruses and certain subtypes have been shown to cross the species barrier to humans.

The influenza A virus genome encodes nine structural proteins and one nonstructural (NS1) protein with regulatory functions. The influenza virus segmented genome contains eight negative-sense RNA (nsRNA) gene segments (PB2, PB1, PA, NP, M, NS, HA and NA) that encode at least ten polypeptides, including RNA-directed RNA polymerase proteins (PB2, PB1 and PA), nucleoprotein (NP), neuraminidase (NA), hemagglutinin (subunits HA1 and HA2), the matrix proteins (M1 and M2) and the non-structural proteins (NS1 and NS2) (Krug et al., In "The Influenza Viruses," R. M. Krug, ed., Plenum Press, N. Y., 1989, pp. 89 152).

HA is a viral surface glycoprotein generally comprising approximately 560 amino acids and representing 25% of the total virus protein. It is responsible for adhesion of the viral particle to, and its penetration into, a host cell in the early stages of infection. Cleavage of the virus HA0 precursor into the HA1 and HA2 sub-fragments is a necessary step in order for the virus to infect a cell. Thus, cleavage is required in order to convert new virus particles in a host cell into virions capable of infecting new cells. Cleavage is known to occur during transport of the integral HA0 membrane protein from the endoplasmic reticulum of the infected cell to the plasma membrane. In the course of transport, hemagglutinin undergoes a series of co- and post-translational modifications including proteolytic cleavage of the precursor HA into the amino-terminal fragment HA1 and the carboxy terminal HA2.

Antibodies, including human and/or humanized forms, as well as fragment, derivatives/conjugates and compositions thereof that bind to an HA domain of influenza A are provided herein. Methods of using these antibodies are also provided.

In several embodiments, these antibodies are broadly cross reactive. In additional embodiments, the antibodies inhibit hemmagglutination activity and neutralize more than one of H1N1, H5N1 and H3N2. In some embodiments, the antibody specifically binds H1N1 and H3N2. In further embodiments, the antibody specifically binds HA of one or more of Pandemic (H1N1) 2009; A/Brevig mission/1/18 (H1N1) 1918; and A/Brisbane/59/07(H1N1) 2007A/Indonesia/5/05 (H5N1) 2005; A/Brisbane10/07 (H3N2) 2007. The antibody can bind the HA globular head and or the HA stalk. In some embodiments the antibodies are broadly cross-reactive and provide heterosubtypic protection.

Terms

Unless otherwise noted, technical terms are used according to conventional usage. Definitions of common terms in molecular biology can be found in Benjamin Lewin, Genes V, published by Oxford University Press, 1994 (ISBN 0-19-854287-9); Kendrew et al. (eds.), The Encyclopedia of Molecular Biology, published by Blackwell Science Ltd., 1994 (ISBN 0-632-02182-9); and Robert A. Meyers (ed.), Molecular Biology and Biotechnology: a Comprehensive Desk Reference, published by VCH Publishers, Inc., 1995 (ISBN 1-56081-569-8). Terms describing protein structure and structural elements of proteins can be found in Creighton, Proteins, Structures and Molecular Properties, W.H. Freeman & Co., New York, 1993 (ISBN 0-717-7030) which is incorporated by reference herein in its entirety.

Unless otherwise explained, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. The singular terms "a," "an," and "the" include plural referents unless context clearly indicates otherwise. Similarly, the word "or" is intended to include A, B or both unless the context clearly indicates otherwise.

It is further to be understood that all base sizes or amino acid sizes, and all molecular weight or molecular mass values, given for nucleic acids or polypeptides are approximate, and are provided for descriptive purposes, unless otherwise indicated. Although many methods and materials similar or equivalent to those described herein can be used, particular suitable methods and materials are described below. In case of conflict, the present specification, including explanations of terms, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

To facilitate review of the various embodiments of this disclosure, the following explanations of terms are provided:

Administration: The introduction of a composition into a subject by a chosen route. Administration can be local or systemic. For example, if the chosen route is intravenous, the composition is administered by introducing the composition into a vein of the subject. In some examples a disclosed antibody that specifically binds HA, or a nucleic acid encoding the antibody, is administered to a subject.

Amino acid substitution: The replacement of one amino acid in peptide with a different amino acid.

Amplification: A technique that increases the number of copies of a nucleic acid molecule (such as an RNA or DNA). An example of amplification is the polymerase chain reaction, in which a biological sample is contacted with a pair of oligonucleotide primers, under conditions that allow for the hybridization of the primers to a nucleic acid template in the sample. The primers are extended under suitable conditions, dissociated from the template, and then re-annealed, extended, and dissociated to amplify the number of copies of the nucleic acid. The product of amplification can be characterized by electrophoresis, restriction endonuclease cleavage patterns, oligonucleotide hybridization or ligation, and/or nucleic acid sequencing using standard techniques. Other examples of amplification include strand displacement amplification, as disclosed in U.S. Pat. No. 5,744,311; transcription-free isothermal amplification, as disclosed in U.S. Pat. No. 6,033,881; repair chain reaction amplification, as disclosed in PCT Publication No. WO 90/01069; ligase chain reaction amplification, as disclosed in EP-A-320 308; gap filling ligase chain reaction amplification, as disclosed in U.S. Pat. No. 5,427,930; and NASBA™ RNA transcription-free amplification, as disclosed in U.S. Pat. No. 6,025,134.

Animal: Living multi-cellular vertebrate organisms, a category that includes, for example, mammals and birds. The term mammal includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary subjects.

Antibody: A polypeptide substantially encoded by an immunoglobulin gene or immunoglobulin genes, or antigen binding fragments thereof, which specifically binds and recognizes an analyte (antigen) such as HA or an antigenic fragment of HA, such as a conserved domain from the stalk or head of the HA protein. Immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon and mu constant region genes, as well as the myriad immunoglobulin variable region genes. encompass monoclonal antibodies (including full-length monoclonal antibodies), polyclonal antibodies, multispecific antibodies formed from at least two different epitope binding fragments (e.g., bispecific antibodies), human antibodies, humanized antibodies, camelised antibodies, chimeric antibodies, single-chain Fvs (scFv), single-chain antibodies, single domain antibodies, domain antibodies, Fab fragments, F(ab')2 fragments, antibody fragments that exhibit the desired biological activity (e.g. the antigen binding portion), disulfide-linked Fvs (dsFv), and anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), intrabodies, and epitope-binding fragments of any of the above. In particular, antibodies include immunoglobulin molecules and immunologically active fragments of immunoglobulin molecules, i.e., molecules that contain at least one antigen-binding site. Immunoglobulin molecules can be of any isotype, for example, IgG, IgE, IgM, IgD, IgA and IgY), subisotype (e.g., IgG_1, IgG_2, IgG_3, IgG4, IgA1 and IgA2) or allotype (e.g., Gm, e.g., G1m(f, z, a or x), G2m(n), G3m(g, b, or c), Am, Em, and Km(1, 2 or 3). Antibodies can be derived from any mammal, including, but not limited to, humans, monkeys, pigs, horses, rabbits, dogs, cats, mice, etc., or other animals such as birds (e.g. chickens).

Native antibodies are usually heterotetrameric glycoproteins of about 150,000 daltons, composed of two identical light (L) chains and two identical heavy (H) chains. Each light chain is linked to a heavy chain by one covalent disulfide bond, while the number of disulfide linkages varies between the heavy chains of different immunoglobulin isotypes. Each heavy and light chain also has regularly spaced intrachain disulfide bridges. Each heavy chain has at one end a variable domain (V_H) followed by a number of constant domains (C_H). Each light chain has a variable domain at one end (V_L) and a constant domain (C_L) at its other end; the constant domain of the light chain is aligned with the first constant domain of the heavy chain, and the light chain variable domain is aligned with the variable domain of the heavy chain. References to "V_H" or "VH" refer to the variable region of an immunoglobulin heavy chain, including that of an antibody fragment, such as Fv, scFv, dsFv or Fab. References to "V_L" or "VL" refer to the variable region of an immunoglobulin light chain, including that of an Fv, scFv, dsFv or Fab. Light chains are classified as either lambda chains or kappa chains based on the amino acid sequence of the light chain constant region. The variable domain of a kappa light chain may also be denoted herein as VK.

Light and heavy chain variable domains contain a "framework" region interrupted by three hypervariable regions, also called "complementarity-determining regions" or "CDRs." The CDRs are primarily responsible for binding to an epitope of an antigen. The precise amino acid sequence boundaries of a given CDR can be readily determined using any of a number of well-known schemes, including those described by Kabat et al. ("Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991; "Kabat" numbering scheme), Al-Lazikani et al., (JMB 273, 927-948, 1997; "Chothia" numbering scheme), and Lefranc, et al. ("IMGT unique numbering for immunoglobulin and T cell receptor variable domains and Ig superfamily V-like domains," Dev. Comp. Immunol., 27:55-77, 2003; "IMGT" numbering scheme). The CDRs of each chain are typically referred to as CDR1, CDR2, and CDR3, numbered sequentially starting from the N-terminus, and are also typically identified by the chain in which the particular CDR is located. Thus, a V_H CDR3 is located in the variable domain of the heavy chain of the antibody in which it is found, whereas a V_L CDR1 is the CDR1 from the variable domain of the light chain of the antibody in which it is found. Light chain CDRs are sometimes referred to as CDR L1, CDR L2, and CDR L3. Heavy chain CDRs are sometimes referred to as CDR H1, CDR H2, and CDR H3. The location of the the framework region and

CDRs readily can be identified (see, Kabat et al., *Sequences of Proteins of Immunological Interest*, U.S. Department of Health and Human Services, 1991, which is hereby incorporated by reference in its entirety). Thus one of ordinary skill in the art will recognize the numbering of the residues in the disclosed antibodies when made with reference to the Kabat convention; the Kabat database is now maintained online. The sequences of the framework regions of different light or heavy chains are relatively conserved within a species. The framework region of an antibody, that is the combined framework regions of the constituent light and heavy chains, serves to position and align the CDRs in three-dimensional space.

A "monoclonal antibody" is an antibody produced by a single clone of B-lymphocytes or by a cell into which the light and heavy chain genes of a single antibody have been transfected. Monoclonal antibodies are produced by methods known to those of skill in the art, for instance by making hybrid antibody-forming cells from a fusion of myeloma cells with immune spleen cells. These fused cells and their progeny are termed "hybridomas." Monoclonal antibodies include humanized and fully human monoclonal antibodies. In some examples monoclonal antibodies are isolated from a subject. The amino acid sequences of such isolated monoclonal antibodies can be determined.

A "humanized" immunoglobulin is an immunoglobulin including a human framework region and one or more CDRs from a non-human (such as a mouse, rat, or synthetic) immunoglobulin. The non-human immunoglobulin providing the CDRs is termed a "donor," and the human immunoglobulin providing the framework is termed an "acceptor." In one embodiment, all the CDRs are from the donor immunoglobulin in a humanized immunoglobulin. Constant regions need not be present, but if they are, they must be substantially identical to human immunoglobulin constant regions, such as at least about 85-90%, such as about 95% or more identical. Hence, all parts of a humanized immunoglobulin, except possibly the CDRs, are substantially identical to corresponding parts of natural human immunoglobulin sequences. A "humanized antibody" is an antibody comprising a humanized light chain and a humanized heavy chain immunoglobulin. A humanized antibody binds to the same antigen as the donor antibody that provides the CDRs. The acceptor framework of a humanized immunoglobulin or antibody may have a limited number of substitutions by amino acids taken from the donor framework. Humanized or other monoclonal antibodies can have additional conservative amino acid substitutions, such as in the framework region, which have substantially no effect on antigen binding or other immunoglobulin functions. Humanized immunoglobulins can be constructed by means of genetic engineering (for example, see U.S. Pat. No. 5,585,089).

Antigen: A compound, composition, or substance that can stimulate the production of antibodies or a T cell response in an animal, including compositions that are injected or absorbed into an animal. An antigen reacts with the products of specific humoral and/or cellular immunity, including those induced by heterologous antigens, such as the disclosed antigens. "Epitope" or "antigenic determinant" refers to the region of an antigen to which B and/or T cells respond. In one embodiment, T cells respond to the epitope, when the epitope is presented in conjunction with an MHC molecule. Epitopes can be 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 denaturing solvents. An epitope typically includes at least 3, and more usually, at least 5, about 9, or about 8-10 amino acids in a unique spatial conformation. Methods of determining spatial conformation of epitopes include, for example, x-ray crystallography and nuclear magnetic resonance.

Examples of antigens include, but are not limited to, peptides, lipids, polysaccharides, and nucleic acids containing antigenic determinants, such as those recognized by an immune cell. In some examples, antigens include peptides derived from a pathogen of interest. Exemplary pathogens include bacteria, fungi, viruses and parasites. In specific examples, an antigen is derived from influenza, such as HA or antigenic fragment thereof, such as the HA stalk or globular domain.

A "target epitope" is a specific epitope on an antigen that specifically binds an antibody of interest, such as a monoclonal antibody. In some examples, a target epitope includes the amino acid residues that contact the antibody of interest, such that the target epitope can be selected by the amino acid residues determined to be in contact with the antibody of interest.

Binding affinity: Affinity of an antibody or antigen binding fragment thereof for an antigen. An antibody specifically binds its target epitope. In one embodiment, affinity is calculated by a modification of the Scatchard method described by Frankel et al., *Mol. Immunol.,* 16:101-106, 1979. In another embodiment, binding affinity is measured by an antigen/antibody dissociation rate. In yet another embodiment, a high binding affinity is measured by a competition radioimmunoassay. In several examples, a high binding affinity is at least about 1×10^{-8} M. In other embodiments, a high binding affinity is at least about 1.5×10^{-8}, at least about 2.0×10^{-8}, at least about 2.5×10^{-8}, at least about 3.0×10^{-8}, at least about 3.5×10^{-8}, at least about 4.0×10^{-8}, at least about 4.5×10^{-8}, or at least about 5.0×10^{-8} M.

Chimeric antibody: An antibody which includes sequences derived from two different antibodies, which typically are of different species. In some examples, a chimeric antibody includes one or more CDRs and/or framework regions from one human antibody and CDRs and/or framework regions from another human antibody. In other examples, a chimeric antibody includes one or more CDRs and/or framework regions from one human antibody and CDRs and/or framework regions from a chimpanzee antibody.

Contacting: Placement in direct physical association; includes both in solid and liquid form, which can take place either in vivo or in vitro. Contacting includes contact between one molecule and another molecule, for example the amino acid on the surface of one polypeptide, such as an antigen, that contacts another polypeptide, such as an antibody. Contacting can also include contacting a cell for example by placing an antibody in direct physical association with a cell.

Epitope: A protein determinant that is specifically bound by an antibody. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and non-conformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

Framework Region: Amino acid sequences interposed between CDRs. Includes variable light and variable heavy framework regions. The framework regions serve to hold the CDRs in an appropriate orientation for antigen binding.

Fc polypeptide: The polypeptide comprising the constant region of an antibody excluding the first constant region immunoglobulin domain. Fc region generally refers to the last two constant region immunoglobulin domains of IgA, IgD, and IgG, and the last three constant region immunoglobulin domains of IgE and IgM. An Fc region may also include part or all of the flexible hinge N-terminal to these domains. For IgA and IgM, an Fc region may or may not comprise the tailpiece, and may or may not be bound by the J chain. For IgG, the Fc region comprises immunoglobulin domains Cgamma2 and Cgamma3 (Cγ2 and Cγ3) and the lower part of the hinge between Cgamma1 (Cγ1) and Cγ2. Although the boundaries of the Fc region may vary, the human IgG heavy chain Fc region is usually defined to comprise residues C226 or P230 to its carboxyl-terminus, wherein the numbering is according to the EU index as in Kabat. For IgA, the Fc region comprises immunoglobulin domains Calpha2 and Calpha3 (Cα2 and Cα3) and the lower part of the hinge between Calpha1 (Cα1) and Cα2. Encompassed within the definition of the Fc region are functionally equivalent analogs and variants of the Fc region. A functionally equivalent analog of the Fc region may be a variant Fc region, comprising one or more amino acid modifications relative to the wild-type or naturally existing Fc region. Variant Fc regions will possess at least 50% homology with a naturally existing Fc region, such as about 80%, and about 90%, or at least about 95% homology. Functionally equivalent analogs of the Fc region may comprise one or more amino acid residues added to or deleted from the N- or C-termini of the protein, such as no more than 30 or no more than 10 additions and/or deletions. Functionally equivalent analogs of the Fc region include Fc regions operably linked to a fusion partner. Functionally equivalent analogs of the Fc region must comprise the majority of all of the Ig domains that compose Fc region as defined above; for example IgG and IgA Fc regions as defined herein must comprise the majority of the sequence encoding CH_2 and the majority of the sequence encoding CH_3. Thus, the CH_2 domain on its own, or the CH_3 domain on its own, are not considered Fc region. The Fc region may refer to this region in isolation, or this region in the context of an Fc fusion polypeptide (such as an immunoadhesin)

Hemagglutinin (HA): An influenza virus surface glycoprotein that is a homotrimeric integral membrane glycoprotein. HA mediates binding of the virus particle to a host cells and subsequent entry of the virus into the host cell. The nucleotide and amino acid sequences of numerous influenza HA proteins are known in the art and are publically available, such as through the NCBI Influenza Virus Resource database (Bao et al., *J Virol* 82:596-601, 2008). HA (along with NA) is one of the two major influenza virus antigenic determinants. The crystal structure of hemagglutinin is deposited as PDB code 5 hmg. The three identical monomers that constitute HA are constructed into a central a helix coil; three spherical heads contain the sialic acid binding sites. In nature, HA monomers are synthesized as precursors that are then glycosylated and cleaved into two smaller polypeptides: the HA1 and HA2 subunits. Each HA monomer consists of a long, helical chain anchored in the membrane by HA2 and topped by a large HA1 globular head which contains the sialic acid receptor binding sites. The HA2 protein chain facilitates membrane fusion; the C-terminal end of the protein is embedded in the viral membrane. The stalk of HA is comprised of portions of HA1 and HA2.

Host cells: Cells in which a vector can be propagated and its DNA expressed, for example a disclosed antibody can be expressed in a host cell. The cell may be prokaryotic or eukaryotic. The term also includes any progeny of the subject host cell. It is understood that all progeny may not be identical to the parental cell since there may be mutations that occur during replication. However, such progeny are included when the term "host cell" is used.

Immunoadhesin: A molecular fusion of a protein with the Fc region of an immunoglobulin, wherein the immunoglobulin retains specific properties, such as Fc receptor binding and increased half-life. An Fc fusion combines the Fc region of an immunoglobulin with a fusion partner, which in general can be any protein, polypeptide, peptide, or small molecule. In one example, and immunoadhesin includes the hinge, CH_2, and CH_3 domains of the immunoglobulin gamma 1 heavy chain constant region. In another example, the immunoadhesin includes the CH_2, and CH_3 domains of an IgG.

Immunologically reactive conditions: Includes reference to conditions which allow an antibody raised against a particular epitope to specifically bind to that epitope to a detectably greater degree than, and/or to the substantial exclusion of, binding to substantially all other epitopes. Immunologically reactive conditions are dependent upon the format of the antibody binding reaction and typically are those utilized in immunoassay protocols or those conditions encountered in vivo. See Harlow & Lane, supra, for a description of immunoassay formats and conditions. The immunologically reactive conditions employed in the methods are "physiological conditions" which include reference to conditions (e.g., temperature, osmolarity, pH) that are typical inside a living mammal or a mammalian cell. While it is recognized that some organs are subject to extreme conditions, the intra-organismal and intracellular environment normally lies around pH 7 (e.g., from pH 6.0 to pH 8.0, more typically pH 6.5 to 7.5), contains water as the predominant solvent, and exists at a temperature above 0° C. and below 50° C. Osmolarity is within the range that is supportive of cell viability and proliferation.

IgA: A polypeptide belonging to the class of antibodies that are substantially encoded by a recognized immunoglobulin alpha gene. In humans, this class or isotype comprises IgA_1 and IgA_2. IgA antibodies can exist as monomers, polymers (referred to as pIgA) of predominantly dimeric form, and secretory IgA. The constant chain of wild-type IgA contains an 18-amino-acid extension at its C-terminus called the tail piece (tp). Polymeric IgA is secreted by plasma cells with a 15-kDa peptide called the J chain linking two monomers of IgA through the conserved cysteine residue in the tail piece.

IgG: A polypeptide belonging to the class or isotype of antibodies that are substantially encoded by a recognized immunoglobulin gamma gene. In humans, this class comprises IgG_1, IgG_2, IgG_3, and IgG_4. In mice, this class comprises IgG_1, IgG_2a, IgG_2b, IgG_3.

Influenza virus: A segmented negative-strand RNA virus that belongs to the Orthomyxoviridae family. There are three types of influenza viruses, A, B and C. Influenza A viruses infect a wide variety of birds and mammals, including humans, horses, marine mammals, pigs, ferrets, and chickens. In animals, most influenza A viruses cause mild localized infections of the respiratory and intestinal tract. However, highly pathogenic influenza A strains, such as H5N1, cause systemic infections in poultry in which mortality may reach 100%. In 2009, H1N1 influenza was the most common cause of human influenza. A new strain of swine-origin H1N1 emerged in 2009 and was declared pandemic by the World Health Organization. This strain was referred to as "swine flu." H1N1 influenza A viruses were also responsible for the Spanish flu pandemic in 1918, the Fort Dix outbreak in 1976, and the Russian flu epidemic in 1977-1978. Influenza A viruses are categorized into subtypes based on the type of two proteins, hemagglutinin (H) and neuraminidase (N) that are on the surface of the viral envelope. Different influenza viruses encode for different hemagglutinin and neuraminidase proteins. Influenza A viruses include the following subtypes: H1N1 (Spanish flu or Swine flu), H2N2 (Asian flu), H3N2 (Hong Kong flu), H5N1 (bird flu), H7N7, H1N2, H9N2, H7N2, H7N3 and H10N7. An antibody that is "broadly neutralizing" or "broadly crossreactive," specifically binds to a polypeptide on more than one subtype and/or strain and inhibits viral entry and/or replication. For example, a broadly neutralizing antibody can specifically bind HA from at least two of H1N1 (Spanish flu or Swine flu), H2N2 (Asian flu), H3N2 (Hong Kong flu), H5N1 (bird flu), H7N7, H1N2, H9N2, H7N2, H7N3 and H10N7.

Inhibiting or treating a disease/infection: Inhibiting the full development of a disease or condition, for example, in a subject who is at risk for a disease such as an influenza infection. "Treatment" refers to a therapeutic intervention that ameliorates a sign or symptom of an infection or pathological condition (such as the flu) after it has begun to develop. The term "ameliorating," with reference to a disease/infection or pathological condition, refers to any observable beneficial effect of the treatment. The beneficial effect can be evidenced, for example, by a delayed onset of clinical symptoms of the disease in a susceptible subject, a reduction in severity of some or all clinical symptoms of the disease, a slower progression of the disease, a reduction in the viral load, an improvement in the overall health or well-being of the subject, or by other parameters well known in the art that are specific to the particular disease. A "prophylactic" treatment is a treatment administered to a subject who does not exhibit signs of a disease/infection or exhibits only early signs for the purpose of decreasing the risk of developing pathology.

Isolated: An "isolated" biological component (such as a cell, for example a B cell, a nucleic acid, peptide, protein or antibody) has been substantially separated, produced apart from, or purified away from other biological components in the cell of the organism in which the component naturally occurs, such as, other chromosomal and extrachromosomal DNA and RNA, and proteins. Nucleic acids, peptides and proteins which have been "isolated" thus include nucleic acids and proteins purified by standard purification methods. The term also embraces nucleic acids, peptides, and proteins prepared by recombinant expression in a host cell as well as chemically synthesized nucleic acids. In some examples an antibody, such as an antibody specific for HA can be isolated, for example isolated from a subject infected with an influenza virus.

K_d: The dissociation constant for a given interaction, such as a polypeptide ligand interaction or an antibody antigen interaction. For example, for the bimolecular interaction of an antibody (such as 05-2G02, 09-2A06, and 09-3A01) and an antigen (such as HA) it is the concentration of the individual components of the bimolecular interaction divided by the concentration of the complex.

Label: A detectable compound or composition that is conjugated directly or indirectly to another molecule, such as an antibody or a protein, to facilitate detection of that molecule. Specific, non-limiting examples of labels include fluorescent tags, enzymatic linkages, and radioactive isotopes. In some examples, a disclosed antibody as labeled.

Neuraminidase (NA): An influenza virus membrane glycoprotein. NA is involved in the destruction of the cellular receptor for the viral HA by cleaving terminal sialic acid residues from carbohydrate moieties on the surfaces of infected cells. NA also cleaves sialic acid residues from viral proteins, preventing aggregation of viruses. NA (along with HA) is one of the two major influenza virus antigenic determinants.

Neutralizing antibody: An antibody which reduces the infectious titer of an infectious agent by binding to a specific antigen on the infectious agent. In some examples the infectious agent is a virus. In some examples, an antibody that is specific for HA reduces the infectious titer of influenza virus.

Nucleic acid: A polymer composed of nucleotide units (ribonucleotides, deoxyribonucleotides, related naturally occurring structural variants, and synthetic non-naturally occurring analogs thereof) linked via phosphodiester bonds, related naturally occurring structural variants, and synthetic non-naturally occurring analogs thereof. Thus, the term includes nucleotide polymers in which the nucleotides and the linkages between them include non-naturally occurring synthetic analogs, such as, for example and without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides, peptide-nucleic acids (PNAs), and the like. Such polynucleotides can be synthesized, for example, using an automated DNA synthesizer. The term "oligonucleotide" typically refers to short polynucleotides, generally no greater than about 50 nucleotides. It will be understood that when a nucleotide sequence is represented by a DNA sequence (i.e., A, T, G, C), this also includes an RNA sequence (i.e., A, U, G, C) in which "U" replaces "T."

Conventional notation is used herein to describe nucleotide sequences: the left-hand end of a single-stranded nucleotide sequence is the 5'-end; the left-hand direction of a double-stranded nucleotide sequence is referred to as the 5'-direction. The direction of 5' to 3' addition of nucleotides to nascent RNA transcripts is referred to as the transcription direction. The DNA strand having the same sequence as an mRNA is referred to as the "coding strand;" sequences on the DNA strand having the same sequence as an mRNA transcribed from that DNA and which are located 5' to the 5'-end of the RNA transcript are referred to as "upstream sequences;" sequences on the DNA strand having the same sequence as the RNA and which are 3' to the 3' end of the coding RNA transcript are referred to as "downstream sequences."

"cDNA" refers to a DNA that is complementary or identical to an mRNA, in either single stranded or double stranded form.

"Encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (i.e., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene encodes a protein if transcription and translation of mRNA produced by that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and non-coding strand, used as the template for transcription, of a gene or cDNA can be referred to as encoding the protein or other product of that gene or cDNA. Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. Nucleotide sequences that encode proteins and RNA may include introns.

"Recombinant nucleic acid" refers to a nucleic acid having nucleotide sequences that are not naturally joined together. This includes nucleic acid vectors comprising an amplified or assembled nucleic acid which can be used to transform a suitable host cell. A host cell that comprises the recombinant nucleic acid is referred to as a "recombinant host cell." The gene is then expressed in the recombinant host cell to produce, e.g., a "recombinant polypeptide." A recombinant nucleic acid may serve a non-coding function (e.g., promoter, origin of replication, ribosome-binding site, etc.) as well.

A first sequence is an "antisense" with respect to a second sequence if a polynucleotide whose sequence is the first sequence specifically hybridizes with a polynucleotide whose sequence is the second sequence.

Terms used to describe sequence relationships between two or more nucleotide sequences or amino acid sequences include "reference sequence," "selected from," "comparison window," "identical," "percentage of sequence identity," "substantially identical," "complementary," and "substantially complementary."

For sequence comparison of nucleic acid sequences, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Default program parameters are used. Methods of alignment of sequences for comparison are well known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482, 1981, by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443, 1970, by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444, 1988, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by manual alignment and visual inspection (see, e.g., *Current Protocols in Molecular Biology* (Ausubel et al., eds 1995 supplement)).

One example of a useful algorithm is PILEUP. PILEUP uses a simplification of the progressive alignment method of Feng & Doolittle, *J. Mol. Evol.* 35:351-360, 1987. The method used is similar to the method described by Higgins & Sharp, *CABIOS* 5:151-153, 1989. Using PILEUP, a reference sequence is compared to other test sequences to determine the percent sequence identity relationship using the following parameters: default gap weight (3.00), default gap length weight (0.10), and weighted end gaps. PILEUP can be obtained from the GCG sequence analysis software package, e.g., version 7.0 (Devereaux et al., *Nuc. Acids Res.* 12:387-395, 1984.

Another example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and the BLAST 2.0 algorithm, which are described in Altschul et al., *J. Mol. Biol.* 215:403-410, 1990 and Altschul et al., *Nucleic Acids Res.* 25:3389-3402, 1977. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (ncbi.nlm.nih.gov). The BLASTN program (for nucleotide sequences) uses as defaults a word length (W) of 11, alignments (B) of 50, expectation (E) of 10, M=5, N=−4, and a comparison of both strands. An oligonucleotide is a linear polynucleotide sequence of up to about 100 nucleotide bases in length.

A polynucleotide or nucleic acid sequence refers to a polymeric form of nucleotide at least 10 bases in length. A recombinant polynucleotide includes a polynucleotide that is not immediately contiguous with both of the coding sequences with which it is immediately contiguous (one on the 5' end and one on the 3' end) in the naturally occurring genome of the organism from which it is derived. The term therefore includes, for example, a recombinant DNA which is incorporated into a vector; into an autonomously replicating plasmid or virus; or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (e.g., a cDNA) independent of other sequences. The nucleotides can be ribonucleotides, deoxyribonucleotides, or modified forms of either nucleotide. The term includes single- and double-stranded forms of DNA. An HA polynucleotide is a nucleic acid encoding a HA polypeptide; and an HA antibody polynucleotide is a nucleic acid encoding an antibody that specifically binds HA.

Pharmaceutically acceptable carriers: The pharmaceutically acceptable carriers of use are conventional. *Remington's Pharmaceutical Sciences*, by E. W. Martin, Mack Publishing Co., Easton, Pa., 19th Edition, 1995, describes compositions and formulations suitable for pharmaceutical delivery of the disclosed antibodies.

In general, the nature of the carrier will depend on the particular mode of administration being employed. For instance, parenteral formulations usually comprise injectable fluids that include pharmaceutically and physiologically acceptable fluids such as water, physiological saline, balanced salt solutions, aqueous dextrose, glycerol or the like as a vehicle. For solid compositions (e.g., powder, pill, tablet, or capsule forms), conventional non-toxic solid carriers can include, for example, pharmaceutical grades of mannitol, lactose, starch, or magnesium stearate. In addition to biologically neutral carriers, pharmaceutical compositions to be administered can contain minor amounts of non-toxic auxiliary substances, such as wetting or emulsifying agents, preservatives, and pH buffering agents and the like, for example sodium acetate or sorbitan monolaurate.

Pharmaceutical agent: A chemical compound or composition capable of inducing a desired therapeutic or prophylactic effect when properly administered to a subject or a cell. In some examples a pharmaceutical agent includes one or more of the disclosed antibodies.

Polypeptide: Any chain of amino acids, regardless of length or post-translational modification (e.g., glycosylation or phosphorylation). In one embodiment, the polypeptide is an HA polypeptide. In one embodiment, the polypeptide is a disclosed antibody or a fragment thereof. A "residue" refers to an amino acid or amino acid mimetic incorporated in a polypeptide by an amide bond or amide bond mimetic. A polypeptide has an amino terminal (N-terminal) end and a carboxy terminal end.

Purified: The term purified does not require absolute purity; rather, it is intended as a relative term. Thus, for example, a purified peptide preparation is one in which the peptide or protein (such as an antibody) is more enriched than the peptide or protein is in its natural environment within a cell. For example, other molecules, e.g. polypeptide, nucleic acid molecules that have been identified and separated and/or recovered from a component of its natural environment. In some examples, purified antibodies have been separated from one or more components of their natural environment. In one embodiment, a preparation is purified such that the protein or peptide represents at least 50% of the total peptide or protein content of the preparation.

The antibodies that specifically bind HA as disclosed herien can be purified by any of the means known in the art. See for example *Guide to Protein Purification*, ed. Deutscher, *Meth. Enzymol.* 185, Academic Press, San Diego, 1990; and Scopes, *Protein Purification: Principles and Practice*, Springer Verlag, New York, 1982. Substantial purification denotes purification from other proteins, antibodies, or cellular components. A substantially purified protein is at least 60%, 70%, 80%, 90%, 95% or 98% pure. Thus, in one specific, non-limiting example, a substantially purified protein is 90% free of other proteins or cellular components.

Outbreak: As used herein, an influenza virus "outbreak" refers to a collection of virus isolates from within a single country in a given year.

Recombinant: A recombinant nucleic acid is one that has a sequence that is not naturally occurring or has a sequence that is made by an artificial combination of two otherwise separated segments of sequence. This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques.

Sequence identity: The similarity between amino acid sequences is expressed in terms of the similarity between the sequences, otherwise referred to as sequence identity. Sequence identity is frequently measured in terms of percentage identity (or similarity or homology); the higher the percentage, the more similar the two sequences are. Homologs or variants of a polypeptide will possess a relatively high degree of sequence identity when aligned using standard methods.

Methods of alignment of sequences for comparison are well known in the art. Various programs and alignment algorithms are described in: Smith and Waterman, *Adv. Appl. Math.* 2:482, 1981; Needleman and Wunsch, *J. Mol. Biol.* 48:443, 1970; Pearson and Lipman, *Proc. Natl. Acad. Sci. U.S.A.* 85:2444, 1988; Higgins and Sharp, *Gene* 73:237, 1988; Higgins and Sharp, *CABIOS* 5:151, 1989; Corpet et al., *Nucleic Acids Research* 16:10881, 1988; and Pearson and Lipman, *Proc. Natl. Acad. Sci. U.S.A.* 85:2444, 1988. Altschul et al., *Nature Genet.* 6:119, 1994, presents a detailed consideration of sequence alignment methods and homology calculations.

The NCBI Basic Local Alignment Search Tool (BLAST) (Altschul et al., *J. Mol. Biol.* 215:403, 1990) is available from several sources, including the National Center for Biotechnology Information (NCBI, Bethesda, Md.) and on the internet, for use in connection with the sequence analysis programs blastp, blastn, blastx, tblastn and tblastx. A description of how to determine sequence identity using this program is available on the NCBI website on the internet. The BLASTP program (for amino acid sequences) uses as defaults a word length (W) of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915, 1989).

Homologs and variants of a V_L or a V_H of an antibody that specifically binds a polypeptide are typically characterized by possession of at least about 75%, for example at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity counted over the full length alignment with the amino acid sequence of interest. Proteins with even greater similarity to the reference sequences will show increasing percentage identities when assessed by this method, such as at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% sequence identity. When less than the entire sequence is being compared for sequence identity, homologs and variants will typically possess at least 80% sequence identity over short windows of 10-20 amino acids, and may possess sequence identities of at least 85% or at least 90% or 95% depending on their similarity to the reference sequence. Methods for determining sequence identity over such short windows are available at the NCBI website on the internet. One of skill in the art will appreciate that these sequence identity ranges are provided for guidance only; it is entirely possible that strongly significant homologs could be obtained that fall outside of the ranges provided.

Specifically bind: When referring to an antibody, refers to a binding reaction which determines the presence of a target protein, peptide, or polysaccharide in the presence of a heterogeneous population of proteins and other biologics. Thus, under designated conditions, an antibody binds preferentially to a particular target protein, peptide or polysaccharide (such as an antigen of a pathogen, for example HA) and do not bind in a significant amount to other proteins or polysaccharides present in the sample or subject. Specific binding can be determined by methods known in the art. With reference to an antibody antigen complex, specific binding of the antigen and antibody has a K_d of less than about 10^{-6} Molar, 10^{-7} Molar, 10^{-8} Molar, 10^{-9}, or even less than about 10^{-10} Molar. Generally, an antibody specifically binds the target antigen with a K_d of is less than 10^{-8} Molar.

Therapeutic agent: Used in a generic sense, it includes treating agents, prophylactic agents, and replacement agents. A therapeutic agent is used to ameliorate a specific set of conditions in a subject with a disease or a disorder.

Therapeutically effective amount: A quantity of a specific substance, such as a disclosed antibody, sufficient to achieve a desired effect in a subject being treated. For instance, this can be the amount necessary to inhibit influenza virus replication or treat the flu. In several embodiments, a therapeutically effective amount is the amount necessary to reduce a sign or symptom of the flu, and/or to decrease viral titer in a subject. When administered to a subject, a dosage will generally be used that will achieve target tissue concentrations that has been shown to achieve a desired in vitro effect.

Vector: A nucleic acid molecule as introduced into a host cell, thereby producing a transformed host cell. A vector may include nucleic acid sequences that permit it to replicate in a host cell, such as an origin of replication. A vector may also include one or more selectable marker genes and other genetic elements known in the art.

Virus: Microscopic infectious organism that reproduces inside living cells. A virus consists essentially of a core of a single nucleic acid surrounded by a protein coat, and has the ability to replicate only inside a living cell. "Viral replication" is the production of additional virus by the occurrence of at least one viral life cycle. A virus may subvert the host cells' normal functions, causing the cell to behave in a manner determined by the virus. For example, a viral infection may result in a cell producing a cytokine, or responding to a cytokine, when the uninfected cell does not normally do so.

Antibodies that Specifically Bind Influenza HA

Antibodies and antigen binding fragments of these antibodies are disclosed herein that specifically bind HA of influenza virus. In some embodiments, the antibody or antigen binding fragment specifically binds to HA of H1N1 influenza. In some embodiments, it specifically binds the HA of H5N1 influenza. In some embodiments, the antibody or antigen binding fragment specifically binds the HA of both H1N1 and H5N1. In some embodiments, the antibody or antigen binding fragment also specifically binds to the HA of H3N2. In further embodiments, the antibody specifically binds H1N1, H5N1 and/or H3N2. Thus, in some embodiments, the antibody, antibody fragment binds to the HA domain of two or more different subclasses of influenza A, such as H1N1, H5N1 and/or H3N2. These antibodies are broadly cross reactive. In some embodiments, the antibodies bind the stem of HA.

The antibody, antibody fragment can cross-react with two different influenza strains/subtypes (e.g., two or more different strains of H1N1 such as the 2009 pandemic strain or the 1918 pandemic strain). In some cases, the antibody, antibody fragment or peptide may cross-react with three or more, five or more or ten or more different influenza strains and/or subtypes. Thus, the antibody, antibody fragment binds to the HA domain (and in some cases can neutralize) two or more of the following H1N1 strains: Pandemic (H1N1) 2009; A/Brevig mission/1/18(H1N1) 1918; and A/Brisbane/59/07(H1N1) 2007. Some antibodies, antibody fragments immunospecifically bind to a particular type of influenza, e.g., H1N1 or H5N1. In some cases the antibody, antibody fragment immunospecifically binds to an influenza virus, e.g., influenza A, HA domain. In some cases the antibody, antibody fragment or peptide binds or binds and neutralizes a H1N1 strain and/or subtype and an H1N5 strain and/or subtype. In some non-limiting examples, the purified antibody or antibody fragment binds to at least three H1 influenza strains selected from the strains in panel A of FIG. **3**.

In specific non-limiting embodiments, the isolated antibody binds the HA stalk. The HA stalk includes portions of the HA1 and HA2 subunits of HA. Thus, the antibody can bind epitopes on HAL epitopes on HA2, or an epitope found on a complex of HA1 and HA2.

In other non-limiting embodiments, the isolated antibody binds the HA globular head. In further non-limiting embodiments, the strain and/or subtype antibody neutralizes one or more strains and/or subtypes of H1N1 influenza, one or more strains and/or subtypes of H5N1 influenza or one or more strains and/or subtypes of both H1N1 and H5N1 influenza. In yet other non-limiting embodiments, the antibody has hemagglutination inhibition activity. In additional embodiments, the antibody binds one (e.g., 2, 3, 4 or 5) or more of: Pandemic (H1N1) 2009; A/Brevig mission/1/18 (H1N1) 1918; and A/Brisbane/59/07(H1N1) 2007A/Indonesia/5/05 (H5N1) 2005; A/Brisbane10/07 (H3N2) 2007.

In other embodiments, the antibody is an IgG antibody; such an IgG1 antibody; is an IgG1, kappa antibody; is an IgG1, lambda antibody, or a IgM, IgA, IgD or IgE antibody. The antibody can be a humanized antibody or a fully human antibody. Antigen binding fragments of these antibodies are also provided herein. In some embodiments, that antigen binding is selected from a Fab, a F(ab')2 fragment, a Fd fragment, an Fv fragment, a scFv, and a domain antibody (dAb) fragment.

Generally, an anti-influenza antibody immunospecifically bind an epitope specific to an HA domain of an influenza A virus and does not specifically bind to other polypeptides. Isolated monoclonal antibodies that specifically bind HA are disclosed herein. Also disclosed herein are compositions including these monoclonal antibodies and a pharmaceutically acceptable carrier. Nucleic acids encoding these antibodies, expression vectors comprising these nucleic acids, and isolated host cells that express the nucleic acids are also provided.

Compositions comprising the monoclonal antibodies specific for HA can be used for research, diagnostic and therapeutic purposes. In one embodiment, the monoclonal antibodies disclosed herein can be used to diagnose or treat a subject having an influenza infection. In another embodiment, the antibodies can be used to determine viral titer in a subject. The antibodies disclosed herein also can be used to study the biology of the human immunodeficiency virus.

Naturally-occurring antibodies are immunoglobulin molecules comprised of four polypeptide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, called complementarity determining regions (CDR), interspersed with regions that are more conserved, called framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. CDRs and FRs may be defined according to Kabat or IMGT. Thus, antibodies are provided herein that include the CDRs of the variable domains presented in FIG. **12**. Antibodies are also provided herein that include the CDRs presented in FIG. **12**.

Each CDR can include amino acid residues from a complementarity determining region as defined by Kabat (i.e. about residues 24-34 (CDR-L1), 50-56 (CDR-L2) and 89-97 (CDR-L3) in the light chain variable domain (SEQ ID NOS 11, 31, 51, 71, 91, 111, 131, 151, 171, 191, 211, 231, 251, 271, 291, 311, 331, 351, 371, 391, 411, 431, 451, 471, 491, 511, 531, 551, 571, 591, 611, 631, 651, 671, 691, 711, 731, 751, 771, 791, 811, 831, 851, 871, 891, 911, 931, 951, 971, 991, 1011, 1031, 1051, 1071, 1091, 1111, 1131, 1151, 1171, 1191, 1211, 1231, 1251, 1271, 1291, 1311, 1331, 1351, 1371, and 1391) and 31-35 (CDR-H1), 50-65 (CDR-H2) and 95-102 (CDR-H3) in the heavy chain variable domain (SEQ ID NOS 1, 21, 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301, 321, 341, 361, 381, 401, 421, 441, 461, 481, 501, 521, 541, 561, 581, 601, 621, 641, 661, 681, 701, 721, 741, 761, 781, 801, 821, 841, 861, 881, 901, 921, 941, 961, 981, 1001, 1021, 1041, 1061, 1081, 1101, 1121, 1141, 1161, 1181, 1201, and 1221, 1241, 1261, 1281, 1301, 1321, 1341, 1361, and 1381) (Kabat et al., (1991) *Sequences of Proteins of Immunological Interest,* 5th Edition, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Bethesda, Md. (NIH Publication No. 91-3242, which is specifically incorporated herein by reference in its entirety). In some embodiments, the antibody includes those residues from a hypervariable loop (i.e. about residues 26-32 (CDR-L1), 50-52 (CDR-L2) and 91-96 (CDR-L3) in the light chain variable domain (SEQ ID NO:1) and 26-32 (CDR-H1), 53-55 (CDR-H2) and 96-101 (CDR-H3) in the heavy chain variable domain (SEQ ID NO:2), see Chothia and Lesk J. Mol. Biol. 196:901-917 (1987)). In some instances, a complementarity determining region can include amino acids from both a CDR region defined according to Kabat and a hypervariable loop.

Framework regions are those variable domain residues other than the CDR residues. Each variable domain typically has four FRs identified as FR1, FR2, FR3 and FR4. If the CDRs are defined according to Kabat, the light chain FR residues are positioned at about residues 1-23 (LCFR1), 35-49 (LCFR2), 57-88 (LCFR3), and 98-107 (LCFR4) of SEQ ID NO:1) and the heavy chain FR residues are positioned about at residues 1-30 (HCFR1), 36-49 (HCFR2), 66-94 (HCFR3), and 103-113 (HCFR4) of SEQ ID NO:2. If the CDRs comprise amino acid residues from hypervariable loops, the light chain FR residues are positioned about at residues 1-25 (LCFR1), 33-49 (LCFR2), 53-90 (LCFR3), and 97-107 (LCFR4) in the light chain (SEQ ID NO:1) and the heavy chain FR residues are positioned about at residues 1-25 (HCFR1), 33-52 (HCFR2), 56-95 (HCFR3), and 102-113 (HCFR4) in the heavy chain (SEQ ID NO:2). In some instances, when the CDR comprises amino acids from both a CDR as defined by Kabat and those of a hypervariable loop, the FR residues will be adjusted accordingly.

The monoclonal antibodies can also include heavy and light chain variable domains including a CDR1, CDR2 and CDR3 with reference to the IMGT numbering scheme (unless the context indicates otherwise). The person of ordinary skill in the art will understand that various CDR numbering schemes (such as the Kabat, Chothia or IMGT numbering schemes) can be used to determine CDR positions. This numbering also can be used in reference to the heavy and light chains sequences disclosed herein. FIG. **12** provides the CDRs and framework regions according to the IMGT numbering scheme.

In certain embodiments, the anti-influenza antibodies are isolated and/or purified and/or pyrogen free antibodies. The present anti-influenza antibodies include at least one antigen binding domain that comprises at least one complementarity determining region (CDR1, CDR2 and CDR3). In one embodiment, the anti-influenza antibodies or antigen binding fragments thereof include a V_H that includes at least one V_H CDR (e.g., CDR-H1, CDR-H2 or CDR-H3). In another embodiment, the anti-influenza antibodies include a V_L that comprises at least one V_L CDR (e.g., CDR-L1, CDR-L2 or CDR-L3). In further embodiments the anti-influenza antibodies or antigen binding fragments thereof include three V_H CDRs (e.g., CDR-H1, CDR-H2 or CDR-H3) and or three V_L CDRs (e.g., CDR-L1, CDR-L2 or CDR-L3)

Disclosed herein are antibodies, antibody (antigen-binding) fragments wherein the antibody or the antibody fragment or the peptide binds to an HA domain of influenza (e.g., H1N1, H5N1, H3N2 or two or more of H1N1, H5N1 and H3N2) virus and comprises: (a) a V_H CDR1 comprising or consisting of an amino acid sequence identical to or having 1, 2, or 3 amino acid residue substitutions or deletions relative to a V_H CDR1 in column I of Table 1 (FIG. **12**); (b) a V_H CDR2 comprising or consisting of an amino acid sequence identical to or having 1, 2, or 3 amino acid residue substitutions or deletions relative to a V_H CDR2 in column K of Table 1 (FIG. **12**); (c) a V_H CDR3 comprising or consisting of an amino acid sequence identical to or having 1, 2, or 3 amino acid residue substitutions or deletions relative to a V_H CDR3 in column M of Table 1 (FIG. **12**); (d) a V_L CDR1 comprising or consisting of an amino acid sequence identical to or having 1, 2, or 3 amino acid residue substitutions or deletions relative to a V_L CDR1 in column I of Table 1 (FIG. **12**); (e) a V_L CDR2 comprising or consisting of an amino acid sequence identical to or having 1, 2, or 3 amino acid residue substitutions or deletions relative to a V_L CDR2 in column K of Table 1 (FIG. **12**); and (f) a V_L CDR3 comprising or consisting of an amino acid sequence identical to or having 1, 2, or 3 amino acid residue substitutions or deletions relative to a V_L CDR3 in column M of Table 1 (FIG. **12**). In certain embodiments the V_H and V_L CDRs are all from the same antibody in Table 1 (FIG. **12**). In certain embodiments, the anti-influenza antibodies or antigen binding fragments comprise a V_H CDR1 having an amino acid sequence identical to or comprising 1, 2, or 3 amino acid residue substitutions relative to a V_H CDR1 in column I of Table 1 (FIG. **12**), a V_H CDR2 having an amino acid sequence identical to or comprising 1, 2, or 3 amino acid residue substitutions relative to a V_H CDR2 in column K of Table 1 (FIG. **12**) and a V_H CDR3 having an amino acid sequence identical to or comprising 1, 2, or 3 amino acid residue substitutions relative to a V_H CDR3 in column M of Table 1 (FIG. **12**). In another embodiment, the anti-influenza antibodies comprise a V_L CDR1 having an amino acid sequence identical to or comprising 1, 2, or 3 amino acid residue substitutions relative to a V_L CDR1 in column I of Table 1 (FIG. **12**), a V_L CDR2 having an amino acid sequence identical to or comprising 1, 2, or 3 amino acid residue substitutions relative to a V_L CDR2 in column K of Table 1 (FIG. **12**), and a V_L CDR3 having an amino acid sequence identical to or comprising 1, 2, or 3 amino acid residue substitutions relative to a V_L CDR3 in column M of Table 1 (FIG. **12**). In certain embodiments, the anti-influenza antibodies or antigen binding fragments thereof comprise a V_H CDR1 having an amino acid sequence identical to a V_H CDR1 in column I of Table 1 (FIG. **12**), a V_H CDR2 having an amino acid sequence identical to a V_H CDR2 in column K of Table 1 (FIG. **12**) and a V_H CDR3 having an amino acid sequence identical to a V_H CDR3 in column M of Table 1 (FIG. **12**). In another embodiment, the anti-influenza antibodies comprise a V_L CDR1 having an amino acid sequence identical to a V_L CDR1 in column I of Table 1 (FIG. **12**), a V_L CDR2 having an amino acid sequence identical to a V_L CDR2 in column K of Table 1 (FIG. **12**); and a V_L CDR3 having an amino acid sequence identical to a VL CDR3 in column M of Table 1 (FIG. **12**). In certain embodiments the V_H and V_L CDRs are all from the same antibody in Table 1 (FIG. **12**).

In some embodiments, the antibody or antibody (antigen binding) fragment comprises a CDR1, CDR2 and CDR3 (V_H or V_L) having 1, 2, or 3 amino acid residue substitutions or deletions relative in Table 1 (FIG. **12**) to a CDR1, CDR2 or CDR3 Table 1, wherein the substitutions are conservative. In some embodiments, a CDR contains 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19 contiguous amino acids of a CDR depicted in Table 1. In certain embodiments, the anti-influenza antibodies comprise a heavy chain V-region having an amino acid sequence identical to or having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions relative to a heavy chain V-region in column G or O of Table 1 (FIG. **12**) and/or a light chain V-region having an amino acid sequence identical to or having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions relative to a light chain V-region in column G or O of Table 1 (FIG. **12**). In other embodiments, the antibody or antibody (antigen binding) fragment includes a deletion, such as a deletion of contiguous amino acids, such as at the amino or carboxy terminus.

In some embodiments, the isolated antibody or the antibody (antigen binding) fragment: (i) comprises a V_H domain comprising three CDRs and a V_L domain comprising three CDRs; and (ii) binds an HA domain of influenza virus (such as H1N1, H5N1 or both; or such as H1N1, H5N1, H3N2 or two or more of H1N1, H5N1 and H3N2) wherein the three CDRs of the V_H domain comprise: (a) a V_H CDR1 comprising the amino acid sequence of a V_H CDR1 in column I of Table 1 (FIG. **12**); (b) a V_H CDR2 comprising the amino acid sequence of a V_H CDR2 in column K of Table 1 (FIG. **12**); and (c) a V_H CDR3 comprising the amino acid sequence of a V_H CDR3 in column M of Table 1 (FIG. **12**). In additional embodiments, the isolated antibody or antibody (antigen binding) fragment: (i) comprises a V_H chain domain comprising three CDRs and a V_L chain domain comprising three CDRs; and (ii) binds an HA domain of influenza virus (e.g., H1N1, H5N1 or both) wherein the three CDRs of the V_L chain domain comprise: (a) a V_L CDR1 comprising the amino acid sequence of V_L CDR1 in column I of Table 1 (FIG. **12**); (b) a V_L CDR2 comprising the amino acid sequence of a V_L CDR2 in column K of Table 1 (FIG. **12**); and (c) a V_L CDR3 comprising the amino acid sequence of a V_L CDR3 in column M of Table 1 (FIG. **12**). In certain embodiments the V_H and V_L CDRs are all from the same antibody in Table 1 (FIG. **12**).

An antibody or antibody (antigen binding) fragment can optionally comprise: (a) a V_H FR1 having the amino acid sequence of a V_H FR1 shown in Table 1 (FIG. **12**) (b) a V_H FR2 having the amino acid sequence of a V_H FR2 shown in Table 1 (FIG. **12**); (c) a V_H FR3 having the amino acid sequence of a V_H FR3 shown in Table 1 (FIG. **12**); (d) a V_H FR4 having the amino acid sequence of a V_H FR4 shown in Table 1 (FIG. **12**); (e) a V_L FR1 having the amino acid sequence of V_L FR1 shown in Table 1 (FIG. **12**)1; (f) a V_L FR2 having the amino acid sequence of a V_L FR2 shown in Table 1 (FIG. **12**); (g) a V_L FR3 having the amino acid sequence of a V_L FR3 shown in Table 1 (FIG. **12**); and (h) a V_L FR4 having the amino acid sequence of a V_L FR4 in shown in Table 1 (FIG. **12**).

In additional embodiments an antibody or antibody (antigen binding) fragment is disclosed, wherein the antibody or the fragment binds HA of an influenza A virus (e.g., H1N1, H5N1 or two of more of H1N1, H5N1 and H3N2) and comprises a heavy chain variable domain having an amino acid sequence identical to or comprising up to 10 (e.g., up to 9, 8, 7, 6, 5, 4, 3, 2 or 1) amino acid residue substitutions relative to the amino acid sequence of the heavy chain variable domain (G or O) of a selected antibody in Table 1 (FIG. **12**) and comprises a light chain variable domain having an amino acid sequence identical to or comprising up to 10 (e.g., up to 9, 8, 7, 6, 5, 4, 3, 2 or 1) amino acid residue substitutions relative to the amino acid sequence of the light chain variable domain (column G or O) of the selected antibody in Table 1 (FIG. **12**). In certain embodiments the heavy chain variable domain and the light chain variable domain are from the same antibody in Table 1 (FIG. **12**). In additional embodiments, disclosed is a purified antibody or antibody (antigen binding) fragment, wherein the antibody or the fragment binds HA of influenza virus (e.g., H1N1, H5N1 or two of more of H1N1, H5N1 and H3N2) and comprises a heavy chain variable domain having at least 90% or 95% identity to the amino acid sequence of the heavy chain variable domain (column G or O) of a selected antibody in Table 1 (FIG. **12**) and comprises a light chain variable domain having at least 90% or 95% identity to the amino acid sequence of the light chain variable domain (column G or O) of the selected antibody in Table 1 (FIG. **12**). In certain embodiments the heavy chain variable domain and the light chain variable domain are from the same antibody in Table 1 (FIG. **12**). In some examples, the antibody or antibody (antigen binding) fragment binds HA of influenza virus (e.g., H1N1, H5N1 two of more of H1N1, H5N1 and H3N2) and includes a heavy chain variable domain having the amino acid sequence of the heavy chain variable domain sequence (column G or O) of a selected antibody in Table 1 (FIG. **12**) and the light chain variable domain having the amino acid sequence of the light chain variable domain sequence (column G or O, respectively) of the selected antibody in Table 1 (FIG. **12**).

In yet other embodiments, disclosed is a purified antibody or antibody (antigen binding) fragment, wherein the antibody or the fragment binds the same epitope on HA of influenza virus (e.g., H1N1, H5N1 or two of more of H1N1, H5N1 and H3N2) as that bound by an antibody comprising: (a) a heavy chain variable domain having the amino acid sequence of the heavy chain variable domain sequence (column G) of a selected antibody in Table 1 (FIG. **12**); and (b) a light chain variable domain having the amino acid sequence of the light chain variable domain sequence (column G) of the selected antibody in Table 1 (FIG. **12**).

In yet other embodiments, disclosed is a purified antibody or antibody (antigen binding) fragment, wherein the antibody or the fragment binds to an HA domain of influenza virus (e.g., H1N1, H5N1 or both), comprising: (a) a polypeptide comprising an amino acid sequence identical to or having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions, or having up to 5 amino acid substitutions, as compared to a V-D-J sequence (FIG. **14**); and (a) a polypeptide comprising an amino acid sequence identical to, identical to or having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions, or having up to 5 amino acid substitutions compared to a V-J sequence (FIG. **14**). In certain embodiments, the anti-influenza antibodies comprise a heavy chain VDJ-region having an amino acid sequence identical to a heavy chain VDJ-region in column F of Table 1 (FIG. **12**) and a light chain VI-region identical to a light chain VI-region in column G of Table 1 (FIG. **12**). In certain embodiments, the anti-influenza antibodies comprise a heavy chain V-region having an amino acid sequence identical to a heavy chain V-region in column G of Table 1 (FIG. **12**) and a light chain V-region identical to a light chain V-region in column G of Table 1 (FIG. **12**).

In one embodiment, the anti-influenza antibodies bind HA of an H1N1 influenza virus, or an antigenic fragment thereof, wherein the antibody has at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% identity to the amino acid sequence of an antibody disclosed herein. In a further embodiment, the anti-influenza antibodies bind to HA of an H1N1 influenza virus, or an antigenic fragment thereof, wherein the antibody has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of an antibody described herein. In other embodiments, an anti-influenza antibody binds HA of an H1N1 influenza virus and an H5N1 influenza virus, or an antigenic fragment thereof, wherein the antibody has at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% identity to the amino acid sequence of an antibody disclosed herein. In further embodiments, the anti-influenza antibodies bind to HA of an H1N1 influenza virus polypeptide and an H5N1 influenza virus polypeptide, or an antigenic fragment thereof, wherein the antibody has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of an antibody disclosed herein. In yet other embodiments the an anti-influenza antibody binds HA of an H1N1 influenza virus, an H5N1 influenza virus, and an H3N2 influenza virus, or an antigenic fragment thereof, wherein the antibody has at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% identity to the amino acid sequence of an antibody disclosed herein. In further embodiments, the anti-influenza antibodies bind to HA of an H1N1 influenza virus polypeptide, an H5N1 influenza virus polypeptide and an H3N2 influenza virus polypeptide, or an antigenic fragment thereof, wherein the antibody has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or having at least 100% identity to the amino acid sequence of an antibody disclosed herein.

Conservative variants of the antibodies can be produced. Such conservative variants employed in antibody fragments, such as dsFv fragments or in scFv fragments, will retain critical amino acid residues necessary for correct folding and stabilizing between the V_H and the V_L regions, and will retain the charge characteristics of the residues in order to preserve the low pI and low toxicity of the molecules. Amino acid substitutions (such as at most one, at most two, at most three, at most four, or at most five amino acid substitutions) can be made in the V_H and the V_L regions to increase yield. In particular examples, the V_H sequence and/or V_L sequence is shown in FIG. **12**. Conservative amino acid substitution tables providing functionally similar amino acids are well known to one of ordinary skill in the art. The following six groups are examples of amino acids that are considered to be conservative substitutions for one another:

1) Alanine (A), Serine (S), Threonine (T);
2) Aspartic acid (D), Glutamic acid (E);
3) Asparagine (N), Glutamine (Q);
4) Arginine (R), Lysine (K);
5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); and
6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W).

In further embodiments, the antibody, antibody fragment or peptide comprises a heavy chain and/or light chain CDRs of an antibody selected from: 05-2G02, 09-2A06 and 09-3A01.

In some embodiments the antibody, antibody (antigen binding) fragment or peptide comprises:

a) a CDR1 comprising at least 7 contiguous amino acids of GYTFSNYG (SEQ ID NO: 3); a CDR2 comprising at least 7 contiguous amino acids of ISAYNGHT (SEQ ID NO: 5); and a CDR3 comprising at least 14 or 15 contiguous amino acids of ARDRRDLLTGSLGDY (SEQ ID NO: 7;

b) a CDR1 comprising GYTFSNYG (SEQ ID NO: 3); a CDR2 comprising ISAYNGHT (SEQ ID NO: 5); and a CDR3 comprising ARDRRDLLTGSLGDY (SEQ ID NO: 7);

c) a heavy chain variable domain comprising: a CDR1 comprising or consisting of GYTFSNYG (SEQ ID NO: 3); a CDR2 comprising or consisting of ISAYNGHT (SEQ ID NO: 5); and a CDR3 comprising or consisting of ARDRRDLLTGSLGDY (SEQ ID NO: 7);

d) a heavy chain variable domain comprising: QVQLVQSGPEVKKPGASIKVSCRAS GYTFSNYGITWVRQAPGQGLEWMGWISAYNGHT NSAQKFQGRVTMTTDTSTSTAYMEVRSLRSDDTAVYYCAR (SEQ ID NO: 1) or comprising the 05-2G02 heavy chain variable domain sequence provided in column O of FIG. **12**;

e) a CDR1 comprising at least 5 contiguous amino acids of RGLLYIDGNTY (SEQ ID NO: 13); a CDR2 comprising at least 2 contiguous amino acids of NVS (SEQ ID NO: 15); and a CDR3 comprising at least 8 contiguous amino acids of MQGTYWPFT (SEQ ID NO: 17);

f) a CDR1 comprising or consisting of RGLLYIDGNTY (SEQ ID NO: 13); a CDR2 comprising or consisting of NVS (SEQ ID NO: 15); and a CDR3 comprising MQGTYWPFT (SEQ ID NO: 17);

g) a light chain variable domain comprising: a CDR1 comprising or consisting of RGLLYIDGNTY (SEQ ID NO: 13); a CDR2 comprising or consisting of NVS (SEQ ID NO: 15); and a CDR3 comprising or consisting of MQGTYWPFT (SEQ ID NO: 17);

h) a light chain variable domain comprising: DVVMTQSPLSLPVTLGQPASISCRSS RGLLYIDGNTYLNWFQQRPGQSPRRLIHNVSNRD SGVPDRFSGSGSRTDFTLKISRVEAEDVGVYYC MQGTYW (SEQ ID NO: 11) or comprising the 05-2G02 light chain variable domain sequence provided in O of Column FIG. **12**.

In some embodiments the antibody (09-2A06), antibody fragment or peptide comprises:

a) a CDR1 comprising at least 8 contiguous amino acids of GGSFTSFV (SEQ ID NO: 23); a CDR2 comprising at least 7 contiguous amino acids of VIPIFATP (SEQ ID NO: 25); and a CDR3 comprising at least 14 or 15 contiguous amino acids of ASPDLTMVFVPHTGPLDF (SEQ ID NO: 27);

b) a CDR1 comprising GGSFTSFV (SEQ ID NO: 23); a CDR2 comprising VIPIFATP (SEQ ID NO: 25); and a CDR3 comprising ASPDLTMVFVPHTGPLDF (SEQ ID NO: 27);

c) a heavy chain variable domain comprising: a CDR1 comprising or consisting of GGSFTSFV (SEQ ID NO: 23); a CDR2 comprising or consisting of VIPIFATP (SEQ ID NO: 25); and a CDR3 comprising or consisting of ASPDLTMVFVPHTGPLDF (SEQ ID NO: 27);

d) a heavy chain variable domain comprising: QVQLVQSGAEVKRPGSSVTVSCKASG GSFTSFVISWVRQAPGQGLEWMGGVIPIFATPK YAQKFQGRLTITADKSTNTAYMELTSLRSEDTAMYYCA (SEQ ID NO: 21) or the 09-2A06 heavy chain variable domain amino acid sequence provided in column O of FIG. **12**;

e) a CDR1 comprising at least 5 contiguous amino acids of QSIDNW (SEQ ID NO: 33); a CDR2 comprising at least 2 contiguous amino acids of KAS (SEQ ID NO: 35); and a CDR3 comprising at least 8 contiguous amino acids of QHYDTYSGT (SEQ ID NO: 37);

f) a CDR1 comprising QSIDNW (SEQ ID NO: 33); a CDR2 comprising KAS (SEQ ID NO: 35); and a CDR3 comprising QHYDTYSGT (SEQ ID NO: 37);

g) a light chain variable domain comprising: a CDR1 comprising or consisting of QSIDNW (SEQ ID NO: 33); a CDR2 comprising or consisting of KAS (SEQ ID NO: 35); and a CDR3 comprising or consisting of QHYDTYSGT (SEQ ID NO: 37);

h) a light chain variable domain comprising: DIQMTQSPSTLSASVGDRVTITCRAS QSIDNWLAWYQQKPGKAPNLLIYKASSLRSGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQHYDTY (SEQ ID NO: 31) or the 09-2A06 light chain variable domain amino acid sequence provided in column O of FIG. **12**.

In further embodiments, the antibody (09-3A01), antibody fragment or peptide comprises:

a) a CDR1 comprising at least 8 contiguous amino acids of GGSITSNTYY (SEQ ID NO: 43); a CDR2 comprising at least 7 contiguous amino acids of ISFSGRT (SEQ ID NO: 45); and a CDR3 comprising at least 14 or 15 contiguous amino acids of ARQLTGMVYAILLPSYFDF (SEQ ID NO: 47);

b) a CDR1 comprising GGSITSNTYY (SEQ ID NO: 43); a CDR2 comprising ISFSGRT (SEQ ID NO: 45); and a CDR3 comprising ARQLTGMVYAILLPSYFDF (SEQ ID NO: 47);

c) a heavy chain variable domain comprising: a CDR1 comprising or consisting of GGSITSNTYY (SEQ ID NO: 43); a CDR2 comprising or consisting of ISFSGRT (SEQ ID NO: 45); and a CDR3 comprising or consisting of ARQLTGMVYAILLPSYFDF (SEQ ID NO: 47);

d) a heavy chain variable domain comprising: RLQLQESGPGLVKPSETLSLTCTVS

GGSITSNTYYWGWIRQPPGKGLESIGSISFSGRTYYSPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAFYYCAR (SEQ ID NO: 41) or the 0 9-3A01 heavy chain variable domain amino acid sequence provided in column O of FIG. **12**;

e) a CDR1 comprising at least 5 contiguous amino acids of QSIGSW (SEQ ID NO: 53); a CDR2 comprising at least 2 contiguous amino acids of KAS (SEQ ID NO: 55); and a CDR3 comprising at least 8 contiguous amino acids of QQHNSYSGA (SEQ ID NO: 57);

f) a CDR1 comprising QSIGSW (SEQ ID NO: 53); a CDR2 comprising KAS (SEQ ID NO: 55); and a CDR3 comprising QQHNSYSGA (SEQ ID NO: 57);

g) a light chain variable domain comprising: a CDR1 comprising or consisting of QSIGSW (SEQ ID NO: 53); a CDR2 comprising or consisting of KAS (SEQ ID NO: 55); and a CDR3 comprising or consisting of QQHNSYSGA (SEQ ID NO: 57);

h) a light chain variable domain comprising: DIQMTQSPSTLSASVGDRVTITCRASQSIGSWLAWYQQKPGKAPKLLIYKASTLESGVPSRFSGSGSGTEFTLTISSLQPDDLATYYCQQHNSY (SEQ ID NO: 51) or the 0 9-3A01 light chain variable domain amino acid sequence provided in column O in FIG. **12**.

In some embodiments, antibodies are disclosed herein, wherein the antibody includes:

a) a heavy chain variable domain comprising: a CDR1 comprising or consisting of GYTFSNYG (SEQ ID NO: 3); a CDR2 comprising or consisting of ISAYNGHT (SEQ ID NO: 5); and a CDR3 comprising or consisting of ARDRRDLLTGSLGDY (SEQ ID NO: 7) and a light chain variable domain comprising: a CDR1 comprising or consisting of RGLLYIDGNTY (SEQ ID NO: 13); a CDR2 comprising or consisting of NVS (SEQ ID NO: 15); and a CDR3 comprising or consisting of MQGTYWPFT (SEQ ID NO: 17);

b) a heavy chain variable domain comprising: a CDR1 comprising or consisting of GGSFTSFV (SEQ ID NO: 23); a CDR2 comprising or consisting of VIPIFATP (SEQ ID NO: 25); and a CDR3 comprising or consisting of ASPDLTMVFVPHTGPLDF (SEQ ID NO: 27) and a light chain variable domain comprising: a CDR1 comprising or consisting of QSIDNW (SEQ ID NO: 33); a CDR2 comprising or consisting of KAS (SEQ ID NO: 35); and a CDR3 comprising or consisting of QHYDTYSGT (SEQ ID NO: 37); or

c) a heavy chain variable domain comprising: a CDR1 comprising or consisting of GGSITSNTYY (SEQ ID NO: 43); a CDR2 comprising or consisting of ISFSGRT (SEQ ID NO: 45); and a CDR3 comprising or consisting of ARQLTGMVYAILLPSYFDF (SEQ ID NO: 47) and a light chain variable domain comprising: a CDR1 comprising or consisting of QSIGSW (SEQ ID NO: 53); a CDR2 comprising or consisting of KAS (SEQ ID NO: 55); and a CDR3 comprising or consisting of QQHNSYSGA (SEQ ID NO: 57).

In some embodiments, an antibody or antigen binding fragment thereof is provided that includes a heavy chain variable domain and a light chain variable domain, wherein the heavy chain variable domain includes one of: a) the amino acid sequence set forth as SEQ ID NO: 3, the amino acid sequence set for the as SEQ ID NO: 5 and the amino acid sequence set forth as SEQ ID NO: 7 [005-2G02]; b) the amino acid sequence set forth as SEQ ID NO: 23, the amino acid sequence set for the as SEQ ID NO: 25 and the amino acid sequence set forth as SEQ ID NO: 27 [09-2A06]; or c) the amino acid sequence set forth as SEQ ID NO: 43, the amino acid sequence set forth as SEQ ID NO: 45 and the amino acid sequence set forth as SEQ ID NO: 47 [09-3A01]. In further embodiments, the antibody or antigen binding fragment thereof includes a) a heavy chain variable domain including the amino acid sequence set forth as SEQ ID NO: 3, the amino acid sequence set forth as SEQ ID NO: 5 and the amino acid sequence set forth as SEQ ID NO: 7, and a light chain variable domain including the amino acid sequence set forth as SEQ ID NO: 13, the amino acid sequence set for the as SEQ ID NO: 15 and the amino acid sequence set forth as SEQ ID NO: 17 [005-2G02]; b) a heavy chain variable domain including the amino acid sequence set forth as SEQ ID NO: 23, the amino acid sequence set for the as SEQ ID NO: 25 and the amino acid sequence set forth as SEQ ID NO: 27, and a light chain variable domain including the amino acid sequence set forth as SEQ ID NO: 33, the amino acid sequence set for the as SEQ ID NO: 35 and the amino acid sequence set forth as SEQ ID NO: 37 [09-2A06]; or c) a heavy chain variable domain including the amino acid sequence set forth as SEQ ID NO: 43, the amino acid sequence set for the as SEQ ID NO: 45 and the amino acid sequence set forth as SEQ ID NO: 47 [09-3A01]; and a light chain variable domain including the amino acid sequence set forth as SEQ ID NO: 53, the amino acid sequence set for the as SEQ ID NO: 55 and the amino acid sequence set forth as SEQ ID NO: 57. These monoclonal antibodies and antigen binding fragments specifically bind influenza HA.

In further embodiments, the heavy chain variable domain of the antibody or antigen binding fragment includes one of a) the amino acid sequence set forth as SEQ ID NO: 1; b) the amino acid sequence set forth as SEQ ID NO: 21; or c) the amino acid sequence set forth as SEQ ID NO: 41. In other embodiments, the heavy chain variable domain includes or consists of one of: a) the amino acid sequence set forth as SEQ ID NO: 9; b) the amino acid sequence set forth as SEQ ID NO: 29; or c) the amino acid sequence set forth as SEQ ID NO: 49. In further embodiments, the heavy chain variable domain has an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence set for the as the amino acid sequence set forth as SEQ ID NO: 9, SEQ ID NO: 29 and/or SEQ ID NO: 49. In yet other embodiments, the heavy chain variable domain includes 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions in the amino acid sequence set forth as SEQ ID NO: 9, SEQ ID NO: 29 and/or SEQ ID NO: 49. These monoclonal antibodies and antigen binding fragments specifically bind influenza HA.

In additional embodiments, the light chain variable domain includes one of a) the amino acid sequence set forth as SEQ ID NO: 11; b) the amino acid sequence set forth as SEQ ID NO: 31; or c) the amino acid sequence set forth as SEQ ID NO: 51. In other embodiments, the light chain variable domain includes or consists of a) the amino acid sequence set forth as SEQ ID NO: 19; b) the amino acid sequence set forth as SEQ ID NO: 39; or c) the amino acid sequence set forth as SEQ ID NO: 59. In further embodiments, the light chain variable domain has an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence set for the as the amino acid sequence set forth as SEQ ID NO: 19, SEQ ID NO: 39 and/or SEQ ID NO: 59. In yet other embodiments, the light chain variable domain includes 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions in the amino acid sequence set forth as SEQ ID NO: 19, SEQ

ID NO: 39 and/or SEQ ID NO: 59. These monoclonal antibodies and antigen binding fragments specifically bind influenza HA.

In some embodiments, a) the heavy chain variable domain includes the amino acid sequence set forth as SEQ ID NO: 1 and the light chain variable domain includes the amino acid sequence set forth as SEQ ID NO: 11; b) the heavy chain variable domain includes the amino acid sequence set forth as SEQ ID NO: 21 and the light chain variable domain includes the amino acid sequence set forth as SEQ ID NO: 31; or c) the heavy chain variable domain includes the amino acid sequence set forth as SEQ ID NO: 41 and the light chain variable domain includes the amino acid sequence set forth as SEQ ID NO: 51, wherein the monoclonal antibody or antigen binding fragment specifically binds influenza HA. In yet other embodiments, a) the heavy chain variable domain includes or consists of the amino acid sequence set forth as SEQ ID NO: 9 and the light chain variable domain includes or consists of SEQ ID NO: 19; b) the heavy chain variable domain includes or consists of the amino acid sequence set forth as SEQ ID NO: 29 and the light chain variable domain includes or consists of the amino acid sequence set forth as SEQ ID NO: 39; or c) the heavy chain variable domain includes or consists of the amino acid sequence set forth as SEQ ID NO: 49 and the light chain variable domain includes or consists of the amino acid sequence set forth as SEQ ID NO: 59, wherein the monoclonal antibody or antigen binding fragment specifically binds influenza HA.

In some embodiments, an antibody is provided that binds the same epitope of HA as does the monoclonal antibodies 05-2G02, 09-2A06 and 09-3A01. These antibodies can be identified using assays such as, but not limited to, competitive binding assays.

Also disclosed herein is a sterile composition including the purified antibody or antibody fragment and a sterile composition comprising the purified antibody or antibody fragment and a pharmaceutically acceptable carrier. Pharmaceutical compositions are disclosed below.

The antibodies can be modified in the Fc region to provide desired effector functions or serum half-life. With the appropriate Fc regions, the naked antibody bound on the cell surface can induce cytotoxicity, e.g., via antibody-dependent cellular cytotoxicity (ADCC) or by recruiting complement in complement dependent cytotoxicity (CDC), or by recruiting nonspecific cytotoxic cells that express one or more effector ligands that recognize bound antibody on a influenza cell and subsequently cause phagocytosis of the influenza cell in antibody dependent cell-mediated phagocytosis (ADCP), or some other mechanism.

Where it is desirable to eliminate or reduce effector function, so as to minimize side effects or therapeutic complications, certain other Fc regions may be used. The Fc region of the antibodies of the invention can be modified to increase the binding affinity for FcRn and thus increase serum half-life. Alternatively, the Fc region can be conjugated to PEG or albumin to increase the serum half-life, or some other conjugation that results in the desired effect.

It is known that variants of the Fc region (e.g., amino acid substitutions and/or additions and/or deletions) enhance or diminish effector function of the antibody (See e.g., U.S. Pat. Nos. 5,624,821; 5,885,573; 6,538,124; 7,317,091; 5,648,260; 6,538,124; PCT Publication Nos. WO 03/074679; WO 04/029207; WO 04/099249; WO 99/58572; and US Published Patent Application Nos. 2006/0134105; 2004/0132101; 2006/0008883) and may alter the pharmacokinetic properties (e.g. half-life) of the antibody (see, U.S. Pat. Nos. 6,277,375 and 7,083,784). Thus, in certain embodiments, the anti-influenza antibodies include an altered Fc region (also referred to herein as "variant Fc region") in which one or more alterations have been made in the Fc region in order to change functional and/or pharmacokinetic properties of the antibodies. The serum half-life of proteins comprising Fc regions may be increased by increasing the binding affinity of the Fc region for FcRn. The term "antibody half-life" as used herein means a pharmacokinetic property of an antibody that is a measure of the mean survival time of antibody molecules following their administration. Antibody half-life can be expressed as the time required to eliminate 50 percent of a known quantity of immunoglobulin from the patient's body (or other mammal) or a specific compartment thereof, for example, as measured in serum, i.e., circulating half-life, or in other tissues. Half-life may vary from one immunoglobulin or class of immunoglobulin to another. In general, an increase in antibody half-life results in an increase in mean residence time (MRT) in circulation for the antibody administered. In a specific embodiment, the present invention provides an Fc variant antibody, wherein the Fc region comprises at least one non-naturally occurring amino acid at one or more positions selected from the group consisting of 252, 254, and 256. In one embodiment, the non-naturally occurring amino acids are selected from the group consisting of 252Y, 254T and 256E.

Diabodies are also provided herein. Diabodies are small antibody fragments with two antigen-binding sites, which fragments comprise a heavy chain variable domain (V_H) connected to a light chain variable domain (V_L) in the same polypeptide chain (V_H and V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding site (see e.g., Holliger et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6444; Poljak et al. (1994) *Structure* 2:1121).

Linear antibodies are also provided herein. Linear antibodies include a pair of tandem Fd segments (V_H-CH_1-V_H-CH_1) which, together with complementary light chain polypeptides, form a pair of antigen binding regions. Linear antibodies can be bispecific or monospecific.

The antibodies disclosed herein specifically include chimeric antibodies (immunoglobulins) in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity.

An antigen binding portion of an antibody specifically binds to an antigen (e.g., H1N1, H5N1 and/or H3N2). It has been shown that the antigen-binding function of an antibody can be performed by fragments of a full-length antibody, including:

(i) a Fab fragment, a monovalent fragment consisting of the V_L, V_H, C_L and CH1 domains;

(ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region;

(iii) a Fd fragment consisting of the V_H and CH_1 domains;

(iv) a Fv fragment consisting of the V_L and V_H domains of a single arm of an antibody,

(v) a dAb fragment (Ward et al, (1989) Nature 341:544 546), which consists of a V_H domain; and

(vi) an isolated complementarity determining region (CDR).

Antibody portions, such as Fab and F(ab')2 fragments, can be prepared from whole antibodies using conventional techniques, such as papain or pepsin digestion, respectively, of whole antibodies. Furthermore, although the two domains of the Fv fragment, V_L and V_H, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the V_L and V_H regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Bird et al. (1988) Science 242:423 426; and Huston et al. (1988) Proc. Natl. Acad. Sci. USA 85:5879 5883). Single chain Fv and other forms of single chain antibodies, such as diabodies are also encompassed by the present disclosure.

Any of the antibody or antigen-binding fragments disclosed herein can be part of a larger immunoadhesion molecule, formed by covalent or noncovalent association of the antibody or antibody portion with one or more other proteins or peptides. Examples of such immunoadhesion molecules include use of the streptavidin core region to make a tetrameric scFv molecule (Kipriyanov et al. (1995) *Human Antibodies and Hybridomas* 6:93) and use of a cysteine residue, a marker peptide and a C-terminal polyhistidine tag to make bivalent and biotinylated scFv molecules (Kipriyanov et al. (1994) *Mol. Immunol.* 31:1047).

Human antibodies are also disclosed herein that include antibodies having variable and constant regions derived from (or having the same amino acid sequence as those derived from) human germline immunoglobulin sequences. Human antibodies can include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo), for example in the CDRs and in particular CDR3.

The antibodies or antibody fragments disclosed herein can be derivatized or linked to another molecule (such as another peptide or protein). In general, the antibody or portion thereof is derivatized such that the binding to HA is not affected adversely by the derivatization or labeling. For example, the antibody can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (for example, a bispecific antibody or a diabody), a detection agent, a pharmaceutical agent, and/or a protein or peptide that can mediate associate of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

One type of derivatized antibody is produced by crosslinking two or more antibodies (of the same type or of different types, such as to create bispecific antibodies). Suitable crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (such as m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (such as disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company (Rockford, Ill.).

An antibody that specifically binds HA can be labeled with a detectable moiety. Useful detection agents include fluorescent compounds, including fluorescein, fluorescein isothiocyanate, rhodamine, 5-dimethylamine-1-napthalenesulfonyl chloride, phycoerythrin, lanthanide phosphors and the like. Bioluminescent markers are also of use, such as luciferase, green fluorescent protein, or yellow fluorescent protein. An antibody can also be labeled with enzymes that are useful for detection, such as horseradish peroxidase, β-galactosidase, luciferase, alkaline phosphatase, glucose oxidase and the like. When an antibody is labeled with a detectable enzyme, it can be detected by adding additional reagents that the enzyme uses to produce a reaction product that can be discerned. For example, when the agent horseradish peroxidase is present the addition of hydrogen peroxide and diaminobenzidine leads to a colored reaction product, which is visually detectable. An antibody may also be labeled with biotin, and detected through indirect measurement of avidin or streptavidin binding. It should be noted that the avidin itself can be labeled with an enzyme or a fluorescent label.

An antibody may be labeled with a magnetic agent, such as gadolinium. Antibodies can also be labeled with lanthanides (such as europium and dysprosium), and manganese. Paramagnetic particles such as superparamagnetic iron oxide are also of use as labels. An antibody may also be labeled with a predetermined polypeptide epitopes recognized by a secondary reporter (such as leucine zipper pair sequences, binding sites for secondary antibodies, metal binding domains, epitope tags). An antibody can also be labeled with a radiolabeled amino acid. The radiolabel may be used for both diagnostic and therapeutic purposes. Examples of labels include, but are not limited to, the following radioisotopes or radionucleotides: ^{3}H, ^{14}C, ^{15}N, ^{35}S, ^{90}Y, Y ^{99}Tc, ^{111}In, ^{125}I, ^{131}I. In some embodiments, labels are attached by spacer arms of various lengths to reduce potential steric hindrance.

An antibody can also be derivatized with a chemical group such as polyethylene glycol (PEG), a methyl or ethyl group, or a carbohydrate group. These groups may be useful to improve the biological characteristics of the antibody, such as to increase serum half-life or to increase tissue binding.

Means of detecting such labels are well known to those of skill in the art. Thus, for example, radiolabels may be detected using photographic film or scintillation counters, fluorescent markers may be detected using a photodetector to detect emitted illumination. Enzymatic labels are typically detected by providing the enzyme with a substrate and detecting the reaction product produced by the action of the enzyme on the substrate, and colorimetric labels are detected by simply visualizing the colored label.

Polynucleotides and Expression

Nucleotide sequences encoding the amino acid sequences disclosed herein, including V_H, V_L, CDR and FR sequences can be prepared; exemplary nucleic acid sequences encoding a V_H and a V_L are shown in FIG. **12**. Expression vectors are also provided for efficient expression in cells (e.g. mammalian cells).

Recombinant expression of an antibody, antigen binding fragment thereof or portion thereof (such as a CDR or FR) generally requires construction of an expression vector containing a polynucleotide that encodes the antibody or antibody fragment. Replicable vectors are provided including a nucleotide sequence encoding an antibody molecule, a heavy or light chain of an antibody, a heavy or light chain variable domain of an antibody or a portion thereof, or a heavy or light chain CDR, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of an antibody molecule (see, e.g., U.S. Pat. Nos. 5,981,216; 5,591,639; 5,658,759 and 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy, the entire light chain, or both the entire heavy and light chains.

Nucleic acid molecules (also referred to as polynucleotides) encoding the polypeptides provided herein (including, but not limited to antibodies) can readily be produced by one of skill in the art. For example, these nucleic acids can be produced using the amino acid sequences provided herein (such as the CDR sequences, heavy chain and light chain sequences), sequences available in the art (such as framework sequences), and the genetic code. Thus, degenerate variants are provided herein.

V_H nucleic acid sequences are set forth as SEQ ID NOS 8, 28, 48, 68, 88, 108, 128, 148, 168, 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, 688, 708, 728, 748, 768, 788, 808, 828, 848, 868, 888, 908, 928, 948, 968, 988, 1008, 1028, 1048, 1068, 1088, 1108, 1128, 1148, 1168, 1188, 1208, 1228, 1248, 1268, 1288, 1308, 1328, 1348, 1368, and 1388 and include degenerate variants; V_L nucleic acid sequences are set forth as SEQ ID NO S 18, 38, 58, 78, 98, 118, 138, 158, 178, 198, 218, 238, 258, 278, 298, 318, 338, 358, 378, 398, 418, 438, 458, 478, 498, 518, 538, 558, 578, 598, 618, 638, 658, 678, 698, 718, 738, 758, 778, 798, 818, 838, 858, 878, 898, 918, 938, 958, 978, 998, 1018, 1038, 1058, 1078, 1098, 1118, 1138, 1158, 1178, 1198, 1218, 1238, 1258, 1278, 1298, 1318, 1338, 1358, 1378, and 1398, and include degenerate variants thereof. One of skill in the art can readily use the genetic code to construct a variety of functionally equivalent nucleic acids, such as nucleic acids which differ in sequence but which encode the same antibody sequence, or encode a conjugate or fusion protein including the V_L and/or V_H nucleic acid sequence.

Nucleic acid sequences encoding the antibodies that specifically bind HA, such as the stalk of HA can be prepared by any suitable method including, for example, cloning of appropriate sequences or by direct chemical synthesis by methods such as the phosphotriester method of Narang et al., *Meth. Enzymol.* 68:90-99, 1979; the phosphodiester method of Brown et al., *Meth. Enzymol.* 68:109-151, 1979; the diethylphosphoramidite method of Beaucage et al., *Tetra. Lett.* 22:1859-1862, 1981; the solid phase phosphoramidite triester method described by Beaucage & Caruthers, *Tetra. Letts.* 22(20):1859-1862, 1981, for example, using an automated synthesizer as described in, for example, Needham-VanDevanter et al., *Nucl. Acids Res.* 12:6159-6168, 1984; and, the solid support method of U.S. Pat. No. 4,458,066. Chemical synthesis produces a single stranded oligonucleotide. This can be converted into double stranded DNA by hybridization with a complementary sequence or by polymerization with a DNA polymerase using the single strand as a template. One of skill would recognize that while chemical synthesis of DNA is generally limited to sequences of about 100 bases, longer sequences may be obtained by the ligation of shorter sequences.

Exemplary nucleic acids can be prepared by cloning techniques. Examples of appropriate cloning and sequencing techniques, and instructions sufficient to direct persons of skill through many cloning exercises are found in Sambrook et al., supra, Berger and Kimmel (eds.), supra, and Ausubel, supra. Product information from manufacturers of biological reagents and experimental equipment also provide useful information. Such manufacturers include the SIGMA Chemical Company (Saint Louis, Mo.), R&D Systems (Minneapolis, Minn.), Pharmacia Amersham (Piscataway, N.J.), CLONTECH Laboratories, Inc. (Palo Alto, Calif.), Chem Genes Corp., Aldrich Chemical Company (Milwaukee, Wis.), Glen Research, Inc., GIBCO BRL Life Technologies, Inc. (Gaithersburg, Md.), Fluka Chemica-Biochemika Analytika (Fluka Chemie AG, Buchs, Switzerland), Invitrogen (Carlsbad, Calif.), and Applied Biosystems (Foster City, Calif.), as well as many other commercial sources known to one of skill.

Nucleic acids can also be prepared by amplification methods. Amplification methods include polymerase chain reaction (PCR), the ligase chain reaction (LCR), the transcription-based amplification system (TAS), the self-sustained sequence replication system (3 SR). A wide variety of cloning methods, host cells, and in vitro amplification methodologies are well known to persons of skill.

Any of the nucleic acids encoding any of the antibodies, CDRs, FRs, V_H and/or V_L, disclosed herein (or fragment thereof) can be expressed in a recombinantly engineered cell such as bacteria, plant, yeast, insect and mammalian cells. These antibodies can be expressed as individual V_H and/or V_L chain, or can be expressed as a fusion protein. An immunoadhesin can also be expressed. Thus, in some examples, nucleic acids encoding a V_H and V_L, and immunoadhesin are provided. The nucleic acid sequences can optionally encode a leader sequence.

To create a single chain antibody, (scFv) the V_H- and V_L-encoding DNA fragments are operatively linked to another fragment encoding a flexible linker, e.g., encoding the amino acid sequence $(Gly_4\text{-}Ser)_3$ (SEQ ID NO: 1541), such that the V_H and V_L sequences can be expressed as a contiguous single-chain protein, with the V_L and V_H domains joined by the flexible linker (see, e.g., Bird et al., Science 242:423-426, 1988; Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883, 1988; McCafferty et al., Nature 348:552-554, 1990). Optionally, a cleavage site can be included in a linker, such as a furin cleavage site.

The nucleic acid encoding the V_H and/or the V_L optionally can encode an Fc domain (immunoadhesin). The Fc domain can be an IgA, IgM or IgG Fc domain. The Fc domain can be an optimized Fc domain, as described in U.S. Published Patent Application No. 20100/093979, incorporated herein by reference. In one example, the immunoadhesin is an IgG_1 Fc.

The single chain antibody may be monovalent, if only a single V_H and V_L are used, bivalent, if two V_H and V_L are used, or polyvalent, if more than two V_H and V_L are used. Bispecific or polyvalent antibodies may be generated that bind specifically to HA and another antigen, such as, but not limited to another influenza protein, or that bind two different HA epitopes. The encoded V_H and V_L optionally can include a furin cleavage site between the V_H and V_L domains.

It is expected that those of skill in the art are knowledgeable in the numerous expression systems available for expression of proteins including *E. coli*, other bacterial hosts, yeast, and various higher eukaryotic cells such as the COS, CHO, HeLa and myeloma cell lines. Once the expression vector is transferred to a host cell by conventional techniques, the transfected cells are then cultured by conventional techniques, such as to produce an antibody. Thus, host cells are provided containing a polynucleotide encoding an antibody or fragments thereof, or a heavy or light chain thereof, or portion thereof, or a single-chain antibody of the invention, operably linked to a heterologous promoter. In certain embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

Mammalian cell lines available as hosts for expression of recombinant antibodies are well known in the art and include many immortalized cell lines available from the American Type Culture Collection (ATCC), including but not limited to Chinese hamster ovary (CHO) cells, HeLa cells, baby hamster kidney (BHK) cells, monkey kidney cells (C_L)S), human hepatocellular carcinoma cells (e.g., Hep G2), human epithelial kidney 293 cells, and a number of other cell lines. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the antibody or portion thereof expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, W138, BT483, Hs578T, HTB2, BT2O and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any functional immunoglobulin chains), SP20, CRL7O3O and HsS78Bst cells. In one embodiment, human cell lines developed by immortalizing human lymphocytes can be used to recombinantly produce monoclonal antibodies. In one embodiment, the human cell line PER.C6. (Crucell, Netherlands) can be used. Additional cell lines which may be used as hosts for expression of recombinant antibodies include, but are not limited to, insect cells (e.g. Sf21/Sf9, *Trichoplusia ni* Bti-Tn5b1-4) or yeast cells (e.g. *S. cerevisiae, Pichia*, U.S. Pat. No. 7,326,681; etc), plants cells (for example, see US Published Patent Application No. 20080066200); and chicken cells (for example, see PCT Publication No. WO2008142124).

The host cell can be a gram positive bacteria including, but not limited to, *Bacillus, Streptococcus, Streptomyces, Staphylococcus, Enterococcus, Lactobacillus, Lactococcus, Clostridium, Geobacillus*, and *Oceanobacillus*. Methods for expressing protein in gram positive bacteria, such as *Lactobaccillus* are well known in the art, see for example, U.S. Published Patent Application No. 20100/080774. Expression vectors for *lactobacillus* are described, for example in U.S. Pat. No. 6,100,388, and U.S. Pat. No. 5,728,571. Leader sequences can be included for expression in *Lactobacillus*. Gram negative bacteria include, but not limited to, *E. coli, Pseudomonas, Salmonella, Campylobacter, Helicobacter, Flavobacterium, Fusobacterium, Ilyobacter, Neisseria*, and *Ureaplasma*.

One or more DNA sequences encoding the antibody or fragment thereof can be expressed in vitro by DNA transfer into a suitable host cell. The cell may be prokaryotic or eukaryotic. The term also includes any progeny of the subject host cell. It is understood that all progeny may not be identical to the parental cell since there may be mutations that occur during replication. Methods of stable transfer, meaning that the foreign DNA is continuously maintained in the host, are known in the art.

The expression of nucleic acids encoding the isolated proteins described herein can be achieved by operably linking the DNA or cDNA to a promoter (which is either constitutive or inducible), followed by incorporation into an expression cassette. The promoter can be any promoter of interest, including a cytomegalovirus promoter and a human T cell lymphotrophic virus promoter (HTLV)-1. Optionally, an enhancer, such as a cytomegalovirus enhancer, is included in the construct. The cassettes can be suitable for replication and integration in either prokaryotes or eukaryotes. Typical expression cassettes contain specific sequences useful for regulation of the expression of the DNA encoding the protein. For example, the expression cassettes can include appropriate promoters, enhancers, transcription and translation terminators, initiation sequences, a start codon (i.e., ATG) in front of a protein-encoding gene, splicing signal for introns, sequences for the maintenance of the correct reading frame of that gene to permit proper translation of mRNA, and stop codons. The vector can encode a selectable marker, such as a marker encoding drug resistance (for example, ampicillin or tetracycline resistance).

To obtain high level expression of a cloned gene, it is desirable to construct expression cassettes which contain, at the minimum, a strong promoter to direct transcription, a ribosome binding site for translational initiation (internal ribosomal binding sequences), and a transcription/translation terminator. For *E. coli*, this includes a promoter such as the T7, trp, lac, or lambda promoters, a ribosome binding site, and preferably a transcription termination signal. For eukaryotic cells, the control sequences can include a promoter and/or an enhancer derived from, for example, an immunoglobulin gene, HTLV, SV40 or cytomegalovirus, and a polyadenylation sequence, and can further include splice donor and/or acceptor sequences (for example, CMV and/or HTLV splice acceptor and donor sequences). The cassettes can be transferred into the chosen host cell by well-known methods such as transformation or electroporation for *E. coli* and calcium phosphate treatment, electroporation or lipofection for mammalian cells. Cells transformed by the cassettes can be selected by resistance to antibiotics conferred by genes contained in the cassettes, such as the amp, gpt, neo and hyg genes.

When the host is a eukaryote, such methods of transfection of DNA as calcium phosphate coprecipitates, conventional mechanical procedures such as microinjection, electroporation, insertion of a plasmid encased in liposomes, or virus vectors may be used. Eukaryotic cells can also be cotransformed with polynucleotide sequences encoding the antibody, labeled antibody, or functional fragment thereof, and a second foreign DNA molecule encoding a selectable phenotype, such as the herpes simplex thymidine kinase gene. Another method is to use a eukaryotic viral vector, such as simian virus 40 (SV40) or bovine papilloma virus, to transiently infect or transform eukaryotic cells and express the protein (see for example, *Eukaryotic Viral Vectors*, Cold Spring Harbor Laboratory, Gluzman ed., 1982). One of skill in the art can readily use an expression systems such as plasmids and vectors of use in producing proteins in cells including higher eukaryotic cells such as, but not limited to, COS, CHO, HeLa and myeloma cell lines.

Modifications can be made to a nucleic acid encoding a polypeptide described herein without diminishing its biological activity. Some modifications can be made to facilitate the cloning, expression, or incorporation of the targeting molecule into a fusion protein. Such modifications are well known to those of skill in the art and include, for example, termination codons, a methionine added at the amino terminus to provide an initiation, site, additional amino acids placed on either terminus to create conveniently located restriction sites, or additional amino acids (such as poly His) to aid in purification steps.

Once expressed, the recombinant immunoconjugates, antibodies, and/or effector molecules (such as a label) can be purified according to standard procedures of the art, including ammonium sulfate precipitation, affinity columns, column chromatography, and the like (see, generally, R. Scopes, PROTEIN PURIFICATION, Springer-Verlag, N. Y., 1982). The antibodies, immunoconjugates and effector molecules need not be 100% pure. Once purified, partially or to homogeneity as desired, if to be used therapeutically, the polypeptides should be substantially free of endotoxin.

Methods for expression of antibodies and/or refolding to an appropriate active form, including single chain antibodies, from bacteria such as *E. coli* have been described and are well-known and are applicable to the antibodies disclosed herein. See, Buchner et al., *Anal. Biochem.* 205:263-270, 1992; Pluckthun, *Biotechnology* 9:545, 1991; Huse et al., *Science* 246:1275, 1989 and Ward et al., *Nature* 341:544, 1989.

Often, functional heterologous proteins from *E. coli* or other bacteria are isolated from inclusion bodies and require solubilization using strong denaturants, and subsequent refolding. During the solubilization step, as is well known in the art, a reducing agent must be present to separate disulfide bonds. An exemplary buffer with a reducing agent is: 0.1 M Tris pH 8, 6 M guanidine, 2 mM EDTA, 0.3 M DTE (dithioerythritol). Reoxidation of the disulfide bonds can occur in the presence of low molecular weight thiol reagents in reduced and oxidized form, as described in Saxena et al., *Biochemistry* 9: 5015-5021, 1970, and especially as described by Buchner et al., supra.

Renaturation is typically accomplished by dilution (for example, 100-fold) of the denatured and reduced protein into refolding buffer. An exemplary buffer is 0.1 M Tris, pH 8.0, 0.5 M L-arginine, 8 mM oxidized glutathione (GSSG), and 2 mM EDTA.

As a modification to the two chain antibody purification protocol, the heavy and light chain regions are separately solubilized and reduced and then combined in the refolding solution. An exemplary yield is obtained when these two proteins are mixed in a molar ratio such that a 5-fold molar excess of one protein over the other is not exceeded. Excess oxidized glutathione or other oxidizing low molecular weight compounds can be added to the refolding solution after the redox-shuffling is completed.

In addition to recombinant methods, immunoconjugates, effector moieties, antibodies, antigen binding fragments, and CDRs and FRs of the present disclosure can also be constructed in whole or in part using standard peptide synthesis well known in the art. Solid phase synthesis of the polypeptides of less than about 50 amino acids in length can be accomplished by attaching the C-terminal amino acid of the sequence to an insoluble support followed by sequential addition of the remaining amino acids in the sequence. Techniques for solid phase synthesis are described by Barany & Merrifield, *The Peptides: Analysis, Synthesis, Biology. Vol. 2: Special Methods in Peptide Synthesis, Part A*. pp. 3-284; Merrifield et al., *J. Am. Chem. Soc.* 85:2149-2156, 1963, and Stewart et al., *Solid Phase Peptide Synthesis,* 2nd ed., Pierce Chem. Co., Rockford, Ill., 1984. Proteins of greater length may be synthesized by condensation of the amino and carboxyl termini of shorter fragments. Methods of forming peptide bonds by activation of a carboxyl terminal end (such as by the use of the coupling reagent N, N'-dicylohexylcarbodimide) are well known in the art. Once an antibody molecule has been produced, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigens Protein A or Protein G, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. Further, the antibodies or fragments thereof may be fused to heterologous polypeptide sequences (referred to herein as "tags") described above or otherwise known in the art to facilitate purification.

Compositions and Therapeutic Methods

Methods are disclosed herein for the prevention or treatment of an influenza virus infection. Prevention can include inhibition of infection with influenza. Treatment includes diminishing signs and symptoms of an influenza virus infection and/or reducing viral titer. The methods include contacting a cell with an effective amount of the monoclonal antibodies disclosed herein that specifically binds HA, or an antigen binding fragment thereof. The method can also include administering to a subject a therapeutically effective amount of a monoclonal antibody, or a nucleic acid encoding the antibody. The subject can be a human or a veterinary subject.

Methods are disclosed herein for reducing the risk of infection with H1N1 and/or H5N1 and/or H3N2 influenza virus in a human subject, the method including administering the antibody or antibody (antigen-binding) fragment. Methods are also disclosed for treating a human subject infected with H1N1 and/or H5N1 influenza virus, the method including administering the antibody or antibody (antigen-binding) fragment. Methods are also disclosed for preventing H1N1 and/or H5N1 and/or H3N2 influenza disease in a human subject, the method including administering the antibody or antibody (antigen-binding) fragment. Methods are also disclosed for ameliorating one or more symptoms associated with an H1N1 and/or H5N1 or H3N2 influenza infection in a human subject, the method including administering the antibody or antibody (antigen-binding) fragment. The method can include selecting a subject with an influenza virus infection.

In certain embodiments, the anti-influenza antibodies and compositions including one or more of the antibodies can be administered for prevention and/or treatment of influenza disease caused by an H1N1 influenza infection. Methods are provide for preventing, treating, ameliorating a symptom of, or reducing the risk of an influenza-mediated infection, disease or disorder, wherein the methods comprise administering anti-influenza antibodies of the invention.

Influenza virus infection does not need to be completely eliminated for the composition to be effective. For example, a composition can decrease influenza infection in a population by a desired amount, for example by at least 10%, at least 20%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, or even at least 100%, as compared to the rate of infection in the absence of the composition.

Compositions are provided that include one or more of the antibodies that specifically bind HA, or antigen binding fragments, and nucleic acids encoding these antibodies (and antigen binding fragments) that are disclosed herein in a carrier. The compositions can be prepared in unit dosage forms for administration to a subject. The amount and timing of administration are at the discretion of the treating physician to achieve the desired purposes. The antibody can be formulated for systemic or local administration. In one example, the antibody that specifically binds HA is formulated for parenteral administration, such as intravenous administration.

The compositions for administration can include a solution of the antibody that specifically binds HA, or an antigen binding fragment thereof, dissolved in a pharmaceutically acceptable carrier, such as an aqueous carrier. A variety of aqueous carriers can be used, for example, buffered saline and the like. These solutions are sterile and generally free of undesirable matter. These compositions may be sterilized by conventional, well known sterilization techniques. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, for example, sodium acetate, sodium chloride, potassium chloride, calcium chloride, sodium lactate and the like. The concentration of antibody in these formulations can vary widely, and will be selected primarily based on fluid volumes, viscosities, body weight and the like in accordance with the particular mode of administration selected and the subject's needs.

A typical pharmaceutical composition for intravenous administration includes about 0.1 to 10 mg of antibody per subject per day. Dosages from 0.1 up to about 100 mg per subject per day may be used, particularly if the agent is administered to a secluded site and not into the circulatory or lymph system, such as into a body cavity or into a lumen of an organ. Actual methods for preparing administrable compositions will be known or apparent to those skilled in the art and are described in more detail in such publications as *Remington's Pharmaceutical Science,* 19th ed., Mack Publishing Company, Easton, Pa. (1995).

Antibodies may be provided in lyophilized form and rehydrated with sterile water before administration, although they are also provided in sterile solutions of known concentration. The antibody solution is then added to an infusion bag containing 0.9% sodium chloride, USP, and typically administered at a dosage of from 0.5 to 15 mg/kg of body weight. Considerable experience is available in the art in the administration of antibody drugs, which have been marketed in the U.S. since the approval of RITUXAN® in 1997. Antibodies can be administered by slow infusion, rather than in an intravenous push or bolus. In one example, a higher loading dose is administered, with subsequent, maintenance doses being administered at a lower level. For example, an initial loading dose of 4 mg/kg may be infused over a period of some 90 minutes, followed by weekly maintenance doses for 4-8 weeks of 2 mg/kg infused over a 30 minute period if the previous dose was well tolerated.

A therapeutically effective amount of a nucleic acid encoding the antibody or an antigen binding fragment thereof can be administered to a subject. One approach to administration of nucleic acids is direct immunization with plasmid DNA, such as with a mammalian expression plasmid. The nucleotide sequence encoding the antibody or fragment thereof can be placed under the control of a promoter to increase expression of the molecule. Immunization by nucleic acid constructs is well known in the art and taught, for example, in U.S. Pat. No. 5,643,578, and U.S. Pat. No. 5,593,972 and U.S. Pat. No. 5,817,637. U.S. Pat. No. 5,880,103 describes several methods of delivery of nucleic acids to an organism. The methods include liposomal delivery of the nucleic acids.

In another approach to using nucleic acids, an antibody or antigen binding fragment thereof can also be expressed by attenuated viral hosts or vectors or bacterial vectors, which can be administered to a subject. Recombinant vaccinia virus, adeno-associated virus (AAV), herpes virus, retrovirus, cytomegalovirus, poxvirus or other viral vectors can be used to express the antibody. For example, vaccinia vectors are described in U.S. Pat. No. 4,722,848. BCG (*Bacillus* Calmette Guerin) provides another vector for expression of the disclosed antibodies (see Stover, *Nature* 351:456-460, 1991).

In one embodiment, a nucleic acid encoding the antibody or an antigen binding fragment thereof is introduced directly into cells. For example, the nucleic acid can be loaded onto gold microspheres by standard methods and introduced into the skin by a device such as Bio-Rad's Heliosä Gene Gun. The nucleic acids can be "naked," consisting of plasmids under control of a strong promoter.

Typically, the DNA is injected into muscle, although it can also be injected directly into other sites. Dosages for injection are usually around 0.5 mg/kg to about 50 mg/kg, and typically are about 0.005 mg/kg to about 5 mg/kg (see, e.g., U.S. Pat. No. 5,589,466).

A therapeutically effective amount of an HA-specific antibody or antigen binding fragment (or the nucleic acid encoding the antibody or antigen binding fragment) will depend upon the severity of the disease and/or infection and the general state of the patient's health. A therapeutically effective amount of the antibody is that which provides either subjective relief of a symptom(s) or an objectively identifiable improvement as noted by the clinician or other qualified observer. These compositions can be administered in conjunction with another therapeutic agent, either simultaneously or sequentially.

In one embodiment, administration of the antibody (or nucleic acid encoding the antibody) results in a reduction in the establishment of influenza virus infection and/or reducing subsequent disease progression in a subject. A reduction in the establishment of influenza virus infection and/or a reduction in subsequent disease progression encompass any statistically significant reduction in viral activity. In some embodiments, methods are disclosed for treating a subject with an influenza virus infection. These methods include administering to the subject a therapeutically effective amount of an antibody, or a nucleic acid encoding the antibody, thereby preventing or treating the influenza virus infection.

In additional embodiments, the subject is also administered an effective amount of an additional agent, such as anti-viral agent. The methods can include administration of one on more additional agents known in the art. For any application, the antibody, antigen binding fragment, or nucleic acid encoding the antibody or antigen binding fragment can be combined with antiretroviral therapy. Antiretroviral drugs include, but are not limited to, a neuraminidase inhibitor or an M2 protein inhibitor. Exemplary antiretroviral agents include oseltamivir, zanamivir, flutimide, rimantadine, adamantane derivatives, umifenovir, laninamivir, favipiravir, peramivir, and nitazoxanide.

Single or multiple administrations of the compositions including the antibody, antigen binding fragment, or nucleic acid encoding the antibody or antigen binding fragment, that are disclosed herein, are administered depending on the dosage and frequency as required and tolerated by the patient. In any event, the composition should provide a sufficient quantity of at least one of the antibodies disclosed herein to effectively treat the subject. The dosage can be administered once but may be applied periodically until either a therapeutic result is achieved or until side effects warrant discontinuation of therapy. In one example, a dose of the antibody is infused for thirty minutes every other day. In this example, about one to about ten doses can be administered, such as three or six doses can be administered every other day. In a further example, a continuous infusion is administered for about five to about ten days. The subject can be treated at regular intervals, such as monthly, until a desired therapeutic result is achieved. Generally, the dose is sufficient to treat or ameliorate symptoms or signs of disease without producing unacceptable toxicity to the subject.

Controlled-release parenteral formulations can be made as implants, oily injections, or as particulate systems. For a broad overview of protein delivery systems see, Banga, A. J., *Therapeutic Peptides and Proteins: Formulation, Processing, and Delivery Systems*, Technomic Publishing Company, Inc., Lancaster, Pa., (1995). Particulate systems include microspheres, microparticles, microcapsules, nanocapsules, nanospheres, and nanoparticles. Microcapsules contain the therapeutic protein, such as a cytotoxin or a drug, as a central core. In microspheres the therapeutic is dispersed throughout the particle. Particles, microspheres, and microcapsules smaller than about 1 μm are generally referred to as nanoparticles, nanospheres, and nanocapsules, respectively. Capillaries have a diameter of approximately 5 μm so that only nanoparticles are administered intravenously. Microparticles are typically around 100 μm in diameter and are administered subcutaneously or intramuscularly. See, for example, Kreuter, J., *Colloidal Drug Delivery Systems*, J. Kreuter, ed., Marcel Dekker, Inc., New York, N.Y., pp. 219-342 (1994); and Tice & Tabibi, *Treatise on Controlled Drug Delivery*, A. Kydonieus, ed., Marcel Dekker, Inc. New York, N.Y., pp. 315-339, (1992).

Polymers can be used for ion-controlled release of the antibody compositions disclosed herein. Various degradable and nondegradable polymeric matrices for use in controlled drug delivery are known in the art (Langer, *Accounts Chem. Res.* 26:537-542, 1993). For example, the block copolymer, polaxamer 407, exists as a viscous yet mobile liquid at low temperatures but forms a semisolid gel at body temperature. It has been shown to be an effective vehicle for formulation and sustained delivery of recombinant interleukin-2 and urease (Johnston et al., *Pharm. Res.* 9:425-434, 1992; and Pec et al., *J. Parent. Sci. Tech.* 44(2):58-65, 1990). Alternatively, hydroxyapatite has been used as a microcarrier for controlled release of proteins (Ijntema et al., *Int. J. Pharm.* 112:215-224, 1994). In yet another aspect, liposomes are used for controlled release as well as drug targeting of the lipid-capsulated drug (Betageri et al., *Liposome Drug Delivery Systems*, Technomic Publishing Co., Inc., Lancaster, Pa. (1993)). Numerous additional systems for controlled delivery of therapeutic proteins are known (see U.S. Pat. No. 5,055,303; U.S. Pat. No. 5,188,837; U.S. Pat. No. 4,235,871; U.S. Pat. No. 4,501,728; U.S. Pat. No. 4,837,028; U.S. Pat. No. 4,957,735; U.S. Pat. No. 5,019,369; U.S. Pat. No. 5,055,303; U.S. Pat. No. 5,514,670; U.S. Pat. No. 5,413,797; U.S. Pat. No. 5,268,164; U.S. Pat. No. 5,004,697; U.S. Pat. No. 4,902,505; U.S. Pat. No. 5,506,206; U.S. Pat. No. 5,271,961; U.S. Pat. No. 5,254,342 and U.S. Pat. No. 5,534,496).

Diagnostic Methods and Kits

A method is provided herein for the detection of the expression of HA in vitro or in vivo. In one example, expression of HA is detected in a biological sample, and can be used to detect an influenza virus infection. The sample can be any sample, including, but not limited to, tissue from biopsies, autopsies and pathology specimens. Biological samples also include sections of tissues, for example, frozen sections taken for histological purposes. Biological samples further include body fluids, such as blood, serum, plasma, sputum, spinal fluid, nasopharyngeal secretions or urine.

In one embodiment, methods are provided for determining the presence of influenza in a sample suspected of containing influenza, wherein the method includes exposing the sample to an anti-influenza antibody, and determining binding of the antibody to the influenza virus in the sample wherein binding of the antibody to the influenza virus in the sample is indicative of the presence of the influenza virus in the sample. In one embodiment, the sample is a biological sample. In another embodiment, the sample is a nasopharyngeal wash. The method can detect H1N1, H5N1, H3N2, or combinations thereof.

In several embodiments, a method is provided for detecting an influenza infection in a subject. The disclosure provides a method for detecting HA in a biological sample, wherein the method includes contacting a biological sample with the antibody under conditions conducive to the formation of an immune complex, and detecting the immune complex, to detect the HA in the biological sample. In another example, detection of HA in the sample confirms a diagnosis of an influenza infection in a subject. The method can detect H1N1, H5N1, H3N2, or combinations thereof.

In certain embodiments, the anti-influenza antibodies and compositions thereof can be used in vivo and/or in vitro for diagnosing influenza associated diseases. This can be achieved, for example, by contacting a sample to be tested, optionally along with a control sample, with the antibody under conditions that allow for formation of a complex between the antibody and influenza. Complex formation is then detected (e.g., using an ELISA). When using a control sample along with the test sample, complex is detected in both samples and any statistically significant difference in the formation of complexes between the samples is indicative of the presence of influenza in the test sample. The influenza virus can be H1N1, H5N1, H3N2, or combinations thereof.

In some embodiments, the disclosed antibodies are used to test vaccines. For example to test if a vaccine composition can induce or bind neutralizing antibodies to HA. Thus provided herein is a method for detecting testing a vaccine, wherein the method includes contacting a sample containing the vaccine, such as an HA protein, with the antibody under conditions conducive to the formation of an immune complex, and detecting the immune complex, to confirm the vaccine will be effective. In one example, the detection of the immune complex in the sample indicates that vaccine component, such as such as a HA antigen, assumes a conformation capable of inducing neutralizing antibodies, such as broadly neutralizing antibodies.

In one embodiment, the antibody is directly labeled with a detectable label. In another embodiment, the antibody that binds HA (the first antibody) is unlabeled and a second antibody or other molecule that can bind the antibody that binds HA is utilized. As is well known to one of skill in the art, a second antibody is chosen that is able to specifically bind the specific species and class of the first antibody. For example, if the first antibody is a human IgG, then the secondary antibody may be an anti-human-lgG. Other molecules that can bind to antibodies include, without limitation, Protein A and Protein G, both of which are available commercially.

Suitable labels for the antibody or secondary antibody are described above, and include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, magnetic agents and radioactive materials. Non-limiting examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase. Non-limiting examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin. Non-limiting examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin. A non-limiting exemplary luminescent material is luminol; a non-limiting exemplary a magnetic agent is gadolinium, and non-limiting exemplary radioactive labels include ^{125}I, ^{131}I, ^{35}S or ^{3}H.

The immunoassays and method disclosed herein can be used for a number of purposes. Kits for detecting an HA polypeptide will typically comprise an antibody that binds HA, such as any of the antibodies disclosed herein. In some embodiments, an antibody fragment, such as an Fv fragment or a Fab is included in the kit. In a further embodiment, the antibody is labeled (for example, with a fluorescent, radioactive, or an enzymatic label).

In one embodiment, a kit includes instructional materials disclosing means of use. The instructional materials may be written, in an electronic form (such as a computer diskette or compact disk) or may be visual (such as video files). The kits may also include additional components to facilitate the particular application for which the kit is designed. Thus, for example, the kit may additionally contain means of detecting a label (such as enzyme substrates for enzymatic labels, filter sets to detect fluorescent labels, appropriate secondary labels such as a secondary antibody, or the like). The kits may additionally include buffers and other reagents routinely used for the practice of a particular method. Such kits and appropriate contents are well known to those of skill in the art.

In one embodiment, the diagnostic kit comprises an immunoassay. Although the details of the immunoassays may vary with the particular format employed, the method of detecting HA in a biological sample generally includes the steps of contacting the biological sample with an antibody which specifically reacts, under immunologically reactive conditions, to HA. The antibody is allowed to specifically bind under immunologically reactive conditions to form an immune complex, and the presence of the immune complex (bound antibody) is detected directly or indirectly.

The following examples are provided to illustrate certain particular features and/or embodiments. These examples should not be construed to limit the disclosure to the particular features or embodiments described.

EXAMPLES

Described below is an analysis of plasmablast and monoclonal antibody responses induced by pandemic H1N1 infection in humans (see FIG. **13**). Unlike antibodies elicited by annual influenza vaccinations, most neutralizing antibodies induced by pandemic H1N1 infection were broadly cross-reactive against epitopes in the hemagglutinin (HA) stalk and head domain of multiple influenza strains/subtypes. The antibodies were from cells that had undergone extensive affinity maturation. Thus, it is possible that the plasmablasts producing these broadly neutralizing antibodies were predominantly derived from activated memory B cells specific for epitopes conserved in several influenza strains. Consequentially, most neutralizing antibodies were broadly reactive against divergent H1N1 and H5N1 influenza strains. Certain of the antibodies generated potently protected and rescued mice from lethal challenge with pandemic H1N1 or antigenically distinct influenza strains.

Described below are studies in which the B cell responses in 24 healthy adult volunteers immunized with the monovalent subunit pandemic H1N1 2009 vaccine were studied. In all cases a rapid, predominantly IgG-producing plasmablast response was found. These plasmablasts were isolated and monoclonal antibodies were generated by single-cell PCR. Over half (45/78) were virus-specific and 62% (28/45) bound to the pandemic 2009 HA. Strikingly, the majority of these antibodies (25/28) neutralized more than one influenza strain and exhibited high levels of somatic hypermutation, suggesting they were derived from recall of B cell memory. Indeed, memory B cells that recognized the pandemic H1N1 HA were detectable prior to vaccination not only in this cohort but also in stored samples obtained prior to the emergence of the pandemic strain. Three antibodies demonstrated extremely broad cross-reactivity and were found to bind the HA stem. Furthermore, one of them was found to recognize not only H1 and H5 but also H3 influenza viruses. This exceptional cross-reactivity indicates that antibodies capable of neutralizing most influenza subtypes might indeed be elicited by vaccination. These antibodies can be used to design influenza vaccines that can elicit these broadly cross-reactive antibodies at sufficiently high levels to provide heterosubtypic protection.

Example 1

Monovalent Pandemic H1N1 2009 Vaccine Induces Rapid Expansion of Antigen-Specific Plasmablasts

Humoral immune responses in 24 healthy adult volunteers immunized with the monovalent pandemic H1N1 2009 vaccine was examined (FIG. **1**). Subjects entered the study approximately 6 months after the first reports of pandemic H1N1 2009 cases. The vaccine administered contained the HA subunit from the pandemic influenza A/California/04/09 and was given separately after the 2009 seasonal influenza vaccine which contained a different H1N1 strain (A/Brisbane/59/07) as well as H3N2 and influenza B strains. Seventeen individuals (71%) receiving pandemic H1N1 2009 vaccine demonstrated an increase in hemagglutination inhibition (HA1) titer at 28 days post-vaccination (accepted as at least a 4-fold increase in HA1 titer) (FIG. **1***a*). Eighteen individuals (75%) exhibited HA1 titers conventionally considered protective (1:40) at day 28. Seroconversion rates were comparable to those seen with seasonal influenza vaccination (Hancock et al., 2009, N *Engl J Med* 361(20): 1945-1952).

An earlier study using seasonal TIV demonstrated that seroconversion is associated with a large, transient expansion of antibody-secreting cells (plasmablasts) in the blood (Wrammert et al., 2008*, Nature* 453(7195):667-671). The current study quantified the plasmablast response to pandemic H1N1 2009 vaccine in PBMCs at day 0, 7, 14 and 30 post-vaccination by ELISPOT using this approach. The vaccine-specific plasmablast response was found to peak at day 7 before returning to background levels by day 14 (FIG. **1***b*). These kinetics were the same as those seen in controls who were given the 2008/09 TIV, which contained components from influenza A/Brisbane/59/07 H1N1, A/Brisbane 10/07 (H3N2) and B/Florida/4/06 (FIG. **7**). Following immunization with the pandemic H1N1 2009 vaccine, there was a positive correlation between the increases in HA1 titer and peak plasmablast numbers (r^2=0.53, p<0.0001)(FIG. **1***c*). The rapidity of the plasmablast response strongly suggested a recall rather than primary response. Indeed, IgG-producing cells greatly outnumbered IgM-producing cells (p=0.0483, mean+/−SEM: 520+/−254 SFU/10^6 vs. 5.36+/−1.48 SFU/10^6). This was also seen in the response to 2008/09 TIV (p=0.0066, 535.8+/−154 SFU/10^6 vs. 63.3+/−50.0 SFU/10^6), a known recall response (FIG. **1***d*). Together, these data show that the B cell responses induced by seasonal TIV and the pandemic H1N1 2009 vaccine were similar in terms of speed and isotype, suggesting that both are due to memory recall.

Example 2

Plasmablasts Induced by the Monovalent H1N1 2009 Vaccine Cross-React with the 2009/10 Seasonal Vaccine.

Since features of the plasmablast response to the pandemic H1N1 2009 vaccine were suggestive of memory recall, the extent to which plasmablasts could also be induced that were reactive against the seasonal influenza strain from the previous two years found in the 2009/10 TIV

(A/Brisbane/59/07) was examined. The HA of the pandemic H1N1 2009 strain diverged considerably from that of influenza A/Brisbane/59/07 with only 79% sequence homology (FIG. **8**). Despite this, most individuals, after vaccination with the pandemic H1N1 2009 vaccine, generated a large number of plasmablasts that reacted with the 2009/10 TIV (FIG. **9***a*). In order to enrich for plasmablasts, next these cells by flow were sorted by cytometry from 10 individuals at day 7 (FIG. **9***b*). A high proportion of sorted plasmablasts were antigen-specific (representative donor in FIG. **9***c*). This was similar to previous findings with seasonal influenza vaccination (Wrammert, 2008, supra). In addition, plasmablasts with specificity for A/Brisbane/59/07 HA as well as pandemic H1N1 2009 HA were detected in all sorted samples (FIG. **9***d*). Thus, the bulk of the humoral response to vaccination was against HA and that the pandemic H1N1 2009 vaccine induced a plasmablast response against both the homologous antigen and a heterologous antigen from the seasonal influenza strain of the preceding two years.

Example 3

The Pandemic H1N1 2009 Vaccine can Induce Antibodies that Bind the HA Stem

To examine the specificities of the antibody response to pandemic H1N1 2009 vaccine at the monoclonal level, single-cell RT-PCR of sorted individual plasmablasts was used to produce mAbs as previously described (Wrammert et 1., 2009, supra; Smith et al., 2009, *Nat Protoc* 4(3):372-384.). The advantage of this method lies in the ability to generate mAbs from B cells that are proliferating acutely in response to vaccination as opposed to resting memory B cells. Furthermore, bias is reduced by analyzing the whole vaccine-induced plasmablast response without preferentially selecting for particular sub-populations using an antigen bait. In total, 78 mAbs from 8 subjects were generated. By ELISA, 58% (45/78) bound to purified pandemic H1N1 2009 virus (FIG. **2***a*). Of these, 62% (28/45) bound to recombinant HA from the pandemic strain.

As ELISA is only capable of demonstrating binding of the antibody to antigen, functional assays were used to characterize HA-specific mAbs. The hemagglutination inhibition assay (HAI) measures the concentration of antibody required to inhibit the agglutination of red blood cells by the virus and is indicative of the capacity of the antibody to prevent viral attachment to cells. In contrast, neutralization assays show how effectively the antibody prevents viral infectivity by measuring the concentration required to block lytic infection of cultured cells. Out of the mAbs that demonstrated HA-specific binding, 89% (25/28) were shown to have functional activity against pandemic H1N1 2009 virus by HAI and/or neutralization assay (FIG. **2***b*).

It was previously shown that mAbs recognizing epitopes in the globular head of the influenza HA demonstrated binding by ELISA, positive HAI and neutralization of infectivity (Wrammert etl a., 2011, J. Exp. Med. 208(1): 181-193, 2011). In contrast, stem-binding mAbs showed binding by ELISA and neutralization, but negative HAI. In this set of mAbs, while there was generally good correlation between HAI and neutralization activities, three mAbs (05-2G02, 09-2A06 and 09-3A01) were found to have no HAI activity despite binding by ELISA and neutralization, a pattern suggestive of stem-binding mAbs. In order to confirm their HA binding site, their binding was compared with known stem-binding antibodies by competition ELISA (FIG. **2***c*). ELISA plates coated with influenza A/California/04/09 HA were pre-incubated with one of two known stem-binding mAbs (70-1F02 or 70-5B03) (Wrammert et al, 2011, supra). The putative stem-bind mAbs were biotinylated and added, according to a standard ELISA protocol, to either pre-incubated or non-pre-incubated plates. The amount of antibody binding in each plate was determined and percentage inhibition of each mAb was subsequently calculated using the ratio of binding in the pre-incubated plates to binding in non-pre-incubated plates.

Whether in competition with the previously described 70-1F02 or 70-5B03, all 3 potential stem-binding mAbs were inhibited by greater than 80%, which was comparable to the stem-binding mAbs used as positive controls (the reciprocal antibody of either 70-1F02 or 70-5B03 depending on which was used to pre-incubate). This contrasted with a previously described negative control (EM4C04), which was highly specific to pandemic H1N1 2009 HA and mapped to an epitope in the head region (Wrammert et al., 2011, supra). Thus, by competition ELISA, it was demonstrated that the mAbs 05-2G02, 09-2A06 and 09-3A01 all compete for binding to an epitope in the HA stem. The three stem-binding mAbs all used different V_H gene segments (FIG. **2***c* & FIG. **14**), compared with the pandemic H1N1 2009 infection where the majority of mAbs induced by the infection used the V_H1-69 gene segment, also shared by other reported stem-binding antibodies (Ekiert et al., 2009; *Science* 324(5924):246-251; Sui et al., 2009, *Nat Struct Mol Biol* 16(3):265-273). Here, only one mAb used the V_H1-69, although a second used the highly similar V_H1-18. Together our data suggest that stem-reactive antibodies can indeed be elicited by the pandemic H1N1 2009 vaccine, but occur at a lower frequency.

Example 4

Monoclonal Antibodies Elicited by Pandemic H1N1 2009 Vaccine Cross-React with Antigenically Divergent Strains

All HA-specific mAbs were tested for binding, HAI and neutralization capacity against a panel of antigens and virus strains, including antigenically similar strains such as the pandemic H1N1 1918 strain and antigenically diverse H1N1, H5N1 and H3N2 strains. Strikingly, the majority of mAbs that bound the HA head also demonstrated broad cross-reactivity (FIG. **3***a*) with three-quarters binding to both A/Brisbane/59/07 HA and 1918 HA. The majority (18 of 28) were able to bind all 3 H1N1 HAs whilst 6 out of 28 bound both pandemic H1N1 2009 and 1918 influenza HAs, in a similar manner to several antibodies previously described (Wrammert et al., 2011, supra; Xu et al., 2010, *Science* 328(5976):357-360). The high degree of cross-reactivity suggested that many of these plasmablasts had arisen by secondary expansion of cross-reactive memory B cells that presumably targeted conserved epitopes. Comparing the binding of these antibodies to the most recent seasonal H1N1 strain in circulation prior to the emergence of the pandemic, A/Brisbane/59/07, the patterns of cross-reactivity generally conform to three categories (FIG. **10**). Most (14/28) of the antibodies bound better to the pandemic H1N1 HA, suggesting ongoing adaptation through affinity maturation. Other antibodies bound equally well to both HAs (9/28) while the last category (5/28) bound better to the Brisbane HA, consistent with OAS (original antigenic sin).

Next, HAI and neutralization assays were performed using a more extensive panel of H1N1 virus strains including recent seasonal strains (A/Brisbane/10/07, A/Solomon Islands/3/06 and A/New Caledonia/20/99) and historic outbreak strains (A/New Jersey/76 and A/Fort Monmouth/1/47) (FIG. **3***b* & FIG. **11**), which displayed a broad range of sequence divergence compared to the pandemic H1N1 2009 virus. As expected from sequence homology (FIG. **8**), the highest degree of cross-reactivity by neutralization assay was seen with A/New Jersey/76, with 68% of mAbs cross-neutralizing. Of the more recent seasonal strains, up to 43% of mAbs demonstrated cross-reactivity between the seasonal strains and pandemic H1N1 2009 virus. In general, the fraction of cross-neutralizing antibodies paralleled sequence homology. Still, given the large antigenic differences measured by standard reference sera, the fraction of cross-neutralizing antibodies was much larger than expected.

The three stem-binding mAbs demonstrated the widest cross-reactivity by ELISA with detectable binding to all the H1 HAs tested plus HA from the H5N1 strain (A/Indonesia/05/2005)(FIG. **3***a*). Furthermore, 05-2G02 displayed even greater cross-reactivity by also binding H3, albeit weakly. Their ability to neutralize both H1N1 and H3N2 strains were tested (FIG. **3***c*). Once again, all three stem-binding mAbs demonstrated broad cross-reactivity with the capacity to neutralize all H1N1 strains tested. In addition, the exceptional breadth of 05-2G02 was again shown, with neutralizing activity against H3N2 as well as the H1N1 strains. Antibodies that neutralize influenza strains from both phylogenetic group 1 and group 2 are exceedingly rare and have only been reported once in the literature (Corti et al., 2011, Science 333: 850-856). These data demonstrate the high degree of cross-reactivity of mAbs generated following pandemic H1N1 2009 vaccination. This is true not only of the stem-reactive mAbs, one of which had unusually broad cross-reactivity against H1, H5 and H3, but also of the majority of non-stem-binding mAbs, which demonstrated substantial cross-reactivity within H1N1 strains in contrast to the more strain-specific mAbs generated following seasonal TIV (Wrammert et al., 2008, supra).

Example 5

Pandemic H1N1 2009 Vaccine Induces Monoclonal Antibodies with High Levels of Somatic Hypermutation

Together, the kinetics of the response, the dominance of IgG-secreting cells and the remarkable cross-reactivity of individual plasmablasts point to a memory origin for most clones. This was further supported by sequence analysis of virus-specific mAbs (FIG. **4***a*). When the somatic mutations per V_H gene were calculated, the majority of clones showed an exceptionally high number of mutations (median 21 range 8-41). This was significantly higher ($p<0.0001$) than the average IgG-producing memory B cell or germinal center B cell (median 11 range 1-35) but similar to the number found following the recall of the memory B cell response by the seasonal influenza vaccination (median 18.5 range 6-51). These were also similar to the results of a previous study of mAbs from patients infected with the pandemic H1N1 2009 virus, where high levels of somatic hypermutation were observed. When the HA-specific mAbs were analyzed alone (FIG. **4***b*), they displayed similar levels of mutation compared to the virus-specific mAbs as a whole. Furthermore, there was no obvious correlation between the number of mutations and the degree of cross-reactivity of each individual mAb (FIG. **3**).

Example 6

Presence of Memory B Cells Reactive to the Pandemic Strain Present Prior to its Emergence

It appeared possible that cross-reactive memory B cells capable of reacting to the pandemic H1N1 2009 vaccine were already present prior to vaccination. Thus, samples from pre-vaccination subjects were analyzed with a memory B cell assay (Crotty et al., *J Immunol Methods* 286(1-2): 111-122, 2004) (FIG. **5***a*). Using this technique, all subjects had detectable memory B cells reactive against pandemic H1N1 2009 HA prior to vaccination (median 0.4%, range 0.013%-1.98%). However, subclinical infections with influenza that induce seroconversion without symptoms do occur and go unreported (Papenburg, *Clin Infect Dis* 51(9):1033-1041, 2010). It was therefore possible that vaccinees had been exposed to the pandemic H1N1 2009 virus at some point between its emergence and their vaccination. In order to exclude this possibility, baseline samples were retrieved from a different healthy cohort taken in 2008/09 before the emergence of the novel pandemic strain (FIG. **5***b*). Once again the majority of these specimens contained detectable memory B cells which reacted against the pandemic H1N1 2009 HA. In summary, these data show that the pandemic H1N1 2009 vaccine preferentially activates cross-reactive memory B cells generated by encounters with HA from previous influenza strains, including broadly cross-reactive stem-specific Abs with neutralizing activity.

Following infection with pandemic H1N1 2009 influenza virus, an earlier study showed that the humoral response was dominated by antibodies that bound to the conserved stem of HA and neutralized multiple influenza subtypes (Wrammet et al., 2008, supra). A vaccine that could induce these antibodies might provide heterosubtypic protection but seasonal influenza vaccines had not been shown to induce them (Hancock, 2009, supra; Wrammert et al., 2008, supra). The question therefore remained as to whether broadly cross-reactive stem-binding antibodies could, in fact, be generated following influenza vaccination. The current studies have shown that these antibodies could be induced by the monovalent inactivated pandemic H1N1 2009 vaccine. Healthy adults were vaccinated with the pandemic H1N1 2009 vaccine and mAbs generated from plasmablasts isolated at the peak of the response. These data suggest that, like the seasonal TIV, the pandemic vaccine induced an antibody response by stimulation of pre-existing memory B cells. However, in contrast to the seasonal vaccine, mAbs induced by the pandemic H1N1 2009 vaccine displayed striking cross-reactivity. Furthermore, although they were less frequent than with infection, stem-binding mAbs could readily be detected and one was even capable of neutralizing both H1N1 (phylogenetic group 1) and H3N2 (group 2) strains.

The approach used here for the cloning of mAbs from plasmablasts has two major advantages. Firstly, these were influenza-specific B cells proliferating in response to the challenge of a specific vaccine and not just resting memory B cells, which consist of a range of clones generated by a variety of previous antigenic challenges. Since plasmablasts generated in response to vaccine disappear within 14 days, those induced by seasonal influenza vaccine administered several weeks previously would not have directly contributed to the plasmablasts that were analyzed. Memory B cells against the HAs of seasonal strains may have been boosted by seasonal vaccination but would not have fundamentally changed in terms of repertoire. Secondly, while other techniques use antigen to preferentially enrich for B cells with the specificities of interest, analysis of all the proliferating plasmablasts allowed examination of the repertoire of influenza-specific antibodies with minimal bias. Using these techniques, the current studies showed that the B cell responses to the pandemic H1N1 2009 and seasonal vaccines were comparable in many ways (Wrammert et al., 2008, supra). Both vaccines induced large and rapid plasmablast responses with similar magnitudes and kinetics. In addition, both responses were predominantly made up of isotype switched IgG-producing plasmablasts and mAbs generated from these plasmablasts showed evidence of extensive somatic hypermutation. These features characterize a secondary response (Schittek and Rawjewsky, 1990, *Nature* 346(6286):749-751; McHeyzer-Williams et al., 1991, *Nature* 350(6318):502-505; and Aprin et al., 1997, *J Exp Med* 186(6):931-940) and imply that the response to the pandemic H1N1 2009 vaccine is derived from pre-existing memory B cells in a similar fashion to the seasonal vaccine. This was conclusively demonstrated by the presence of memory B cells specific for pandemic H1N1 2009 HA in individuals even prior to the emergence of the new virus, strongly implying they were induced by exposure to previous seasonal strains.

However, the antibody response to pandemic H1N1 2009 vaccine clearly differed in one important respect: the high degree of cross-reactivity. Unlike previous studies of seasonal TIV (Hancock et al., 2009, supra; Wrammert et al., 2008, supra), the current data suggest that cross-reactive antibodies against both the head and stem of HA were readily induced by the pandemic H1N1 2009 vaccine and made up a large proportion of the response. Cross-reactive antibodies against both the head and stem of HA from the seasonal TIV have been described in humans using a number of systems (Thorsby et al., 2008 *PLoS One* 3(12):e3942; Ekiert et al., 2009, *Science* 324(5924):246-251; Sui et al, 2009, *Nat Struct Mol Biol* 16(3):265-273; Cori et al., 2010, *J Clin Invest* 120(5):1663-1673). However, the antibodies that were identified previously were not effective. While different stem-binding antibodies have been identified following vaccination, these have primarily relied upon phage display libraries (Thorsby et al., 2008, supra; Ekiert et al., 2009, supra; Sui et al, 2009, supra) and immortalization of memory B cells (Corti et al, 2010, supra). A recent study has shown that the MF59 adjuvant can enhance the diversity and affinity of the antibody response to pandemic influenza vaccine (Khurana, 2011, *Sci Transl Med* 3(85): 85ra48).

The majority of the cross-reactive mAbs here were directed against the globular head of HA. However, three stem-binding mAbs were identified and shown to be broadly cross-reactive. One of them, 05-2G02, demonstrated an extraordinary breadth of neutralizing activity, with activity against all H1N1 strains tested as well as binding to H5N1 HA and neutralization of a H3N2 strain. The capacity to recognize HAs from both phylogenetic groups does not appear to be dependent on a unique antigen-binding structure. The antibodies provide important proof of concept that a universal vaccine capable of stimulating antibodies that neutralize all influenza subtypes.

It is also clear that cross-reactive stem-binding antibodies are very rare after vaccination with seasonal strains. Studies that have found stem-binding memory B cell clones have required high throughput techniques to screen large numbers of cells (Corte et al., 2006, supra). In the work disclosed herein, stem-reactive antibodies were readily found with 3 out of 28 HA-specific mAbs generated from 8 vaccinees showing stem-reactivity. This implies that the pandemic H1N1 2009 vaccine induces these antibodies more frequently as a consequence of the major change in epitopes from the HA head while the stem remains relatively conserved. In addition, while 2 stem-specific mAbs came from one subject and one from another, several subjects had none, suggesting that some individuals might have a stronger propensity for developing cross-reactive antibodies by nature of their underlying B cell repertoire and their previous antigenic history. In animal models, sequential immunization with different HAs can preferentially stimulate broadly cross-reactive antibodies (Wang et al, 2010, *PLoS Pathog* 6(2):e1000796), a phenomenon recapitulated in nature with the emergence of a pandemic strain.

The low frequency of broadly cross-reactive stem-binding antibodies following the pandemic H1N1 2009 vaccine contrasts with the antibody responses seen following natural infection. Earlier studies demonstrated that broadly cross-reactive antibodies that bound to the HA stem region dominated the humoral response in patients infected with pandemic H1N1 2009, with as many as half of these neutralizing mAbs recognizing the same epitope (Wrammert et al., 2008, supra). These stem-binding mAbs shared a common V_H gene rearrangement which was not observed following vaccination. Immunization with the subunit pandemic H1N1 2009 vaccine, which primarily consists of HA and NA, induces a quantitatively and qualitatively different immune response. Specifically, subunit vaccines cannot infect cells, therefore preferentially utilizing extrinsic antigen presentation pathways as well as inducing less potent inflammatory and innate responses. Infection also results in greater antigen load and duration, leading to increased recruitment of precursors and signals for differentiation.

Unlike the humoral response to the seasonal vaccine, cross-reactive clones against the pandemic H1N1 2009 vaccine could be readily detected from acutely responding plasmablasts. The current studies also showed that they were derived from memory B cells that recognized conserved epitopes across virus strains. Thus, it might be that broadly cross-reactive antibodies are produced by low-frequency memory B cells reactive against conserved but subdominant epitopes (FIG. **6**). In the context of seasonal influenza, these are not recruited into the response, remaining relatively quiescent due to competition by the more numerous B cells specific for immunodominant epitopes exposed in the globular HA head. However, following a major change in the HA, most of these immunodominant epitopes are replaced with novel structures. With their disappearance, cross-reactive memory B cells against conserved epitopes in both the head and stem no longer need to compete with memory cells specific for the previous strains. Thus, cross-reactive antibodies make up a greater proportion of the humoral immune response following antigenic shift.

This also offers an explanation as to why the preceding seasonal H1N1 strain almost completely disappeared following the emergence of the pandemic H1N1 2009 virus (Palese P & Wang T T (2011), MBio 2(5)). The current studies in individuals infected or vaccinated with pandemic H1N1 2009 have shown that in either situation large numbers of cross-reactive antibodies with activity against A/Brisbane/59/07 are generated (Wrammert et al, 2008, supra). Thus, most individuals who have encountered the pandemic H1N1 2009 strain will also have developed protective immunity against A/Brisbane/59/07 leading to a rapid decrease in the number of susceptible hosts.

The data herein show that broadly cross-reactive stem-binding antibodies can be induced by the pandemic H1N1 2009 vaccine, thus demonstrating that productive infection is not required. Furthermore, stem-binding antibodies with the capacity to neutralize a broad range of influenza subtypes can be induced by vaccination. However, the frequency of these stem-binding antibodies following the pandemic H1N1 2009 vaccine was low and not all vaccinees were found to generate them. In order for a truly universal vaccine to be effective, it must induce cross-reactive antibodies to a high level in all recipients to provide robust heterosubtypic immunity.

Example 7

Detailed Information Regarding Antibodies that Bind Influenza Virus

Table 1 (FIG. **12**) provides detailed information, including sequence information, about each of the antibodies that were confirmed to bind influenza. Each antibody is identified in Col. A by antibody name and an indication of whether the heavy or light chain is being described. Heavy chains are indicated by H and light chains are indicated by L at the end of the identifier in Col. A. For example, line 1 of Table 1 (FIG. **12**) discloses 005-2G02H, which is a heavy chain for one of the antibodies, and line 2 of Table 1 (FIG. **12**) discloses 005-2G02L, which is the light chain for the same antibody. Accordingly, each pair of rows (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, 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, and 140/141) represent paired heavy and light chains from a cloned human antibody. Col. G provides the V region amino acid sequence, column O provides the full translated V region amino acid sequence. Col. H provides the FR1 amino acid sequence. Col. I provides the CDR1 amino acid sequence. Col. J provides the FR2 amino acid sequence. Col. K provides the CDR2 amino acid sequence. Col. L provides the FR3 amino acid sequence. Col. M provides the CDR3 amino acid sequence. Col. N provides the nucleotide sequence. Column P provides the FR4 amino acid sequence. FIG. **14** provides the V gene, J gene D gene allele, and provides the V mutations, CDR lengths and AA junction sequence ("AA junction" sequences are disclosed in FIGS. **14**A and **14**B as SEQ ID NOS 1401-1540, respectively, in order of appearance).

Example 8

Materials and Methods

Patients and Vaccines:

All studies were approved by an institutional review board). Twenty-four healthy adult volunteers were given the monovalent pandemic H1N1 2009 vaccine. Subject 2 was given the seasonal 2009/10 TIV only 4 days before receiving pandemic H1N1 2009 vaccine and was excluded from all cross-reactivity assays. Memory B cell and mutational analysis data were derived from clinical studies of 2008/09 and 2009/10 season TIV vaccinees. Peripheral blood mononuclear cells (PBMCs) were isolated using Vacutainer tubes (BD for immediate use or cryopreserved. Plasma samples were saved at −80° C. for subsequent analysis. All vaccines were obtained from Sanofi Pasteur Inc.

Viruses and Antigens:

The pandemic H1N1 2009 influenza virus (A/California/04/09) was utilized. Other influenza virus stocks used for the assays were obtained from the Centers for Disease Control (CDC), grown in eggs and purified as described (Wrammert et al., 2008, supra). Recombinant HA proteins were provided by the CDC and by the Biodefense and Emerging Infections research repository.

ELISPOT and Memory B Cell Assay:

Direct ELISPOT to enumerate the number of either total IgG-secreting, pandemic H1N1 influenza virus-specific, vaccine-specific and recombinant HA-specific plasmablasts present in the PBMC samples was performed as previously described (Crotty et al., 2003, J Immunol 171(10):4969-4973).

Flow Cytometry Analysis and Cell Sorting.

Analytical and cell sorting flow cytometry analysis was performed as described (Wrammert et al., 2008, supra).

Generation of mAbs and Variable Gene Repertoire Analysis.

As previously detailed (Wrammert et al., 2008, supra; Smith et al., 2009, Nat Protoc 4(3):372-384; Wardemann et al., 2003, Science 301(5638):1374-1377), V_H and Vκ genes were PCR-amplified from the transcripts of single ASCs and then sequenced. These variable genes were then cloned into IgG1 or Igκ expression vectors and co-transfected into the 293A cell line for expression. Variable genes were analyzed for identity and mutations using in-house analysis software and the IMGT search engine (Ehrenmann et al., 2010, Nucleic Acids Res 38(Database issue):D301-307; Lefranc et al., 2009, Nucleic Acids Res 37(Database issue):D1006-1012). Background mutation rate by this method is ~1 base-exchange per 1,000 bases sequenced (based on sequences of constant region gene segments). Comparisons were made to previously published data (Wrammert et al., 2008, supra; Zheng et al., 2005, J Clin Invest 113(8):1188-1201; Zeng et al., 2005b, J Exp Med 201(9):1467-1478). Antibody sequences were deposited on GENBANK®.

ELISA, HA1 and Neutralization Assays.

Whole virus, recombinant HA, vaccine-specific ELISA, HA1 and neutralization assays were performed as previously described (Wrammert et al., 2008, supra). For competition ELISA an additional pre-incubation with unlabeled competitor antibodies to the HA-stalk epitope at a 10-fold molar excess was then performed prior to application of the mAbs to the plate. Competitors consisted of one of two known stem-binding mAbs (70-1F02 or 70-5B03) or a negative control antibody specific for the HA globular head (EM-4C04). Competition level was calculated as the percentage inhibition of the half-maximal binding concentration of test antibody relative to the absorbance without competitor.

In view of the many possible embodiments to which the principles of the disclosed invention may be applied, it should be recognized that the illustrated embodiments are only preferred examples of the invention and should not be taken as limiting the scope of the invention. Rather, the scope of the invention is defined by the following claims. We therefore claim as our invention all that comes within the scope and spirit of these claims.

SEQUENCE LISTING

The patent contains a lengthy "Sequence Listing" section. A copy of the "Sequence Listing" is available in electronic form from the USPTO web site (http://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US10208107B2). An electronic copy of the "Sequence Listing" will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

We claim:

1. A non-naturally occurring chimeric antibody, wherein the antibody comprises a heavy chain variable domain and a light chain variable domain,

wherein the heavy chain variable domain comprises the amino acid sequence set forth as SEQ ID NO: 23, the amino acid sequence set forth as SEQ ID NO: 25, and the amino acid sequence set forth as SEQ ID NO: 27 and the light chain variable domain comprises the amino acid sequence set forth as SEQ ID NO: 33, the amino acid sequence KAS, and the amino acid sequence set forth as SEQ ID NO: 37, and

wherein the antibody specifically binds hemagglutinin (HA) of H1N1 and H5N1.

2. The non-naturally occurring chimeric antibody of claim **1**, wherein the antibody specifically binds HA of H3N2.

3. The non-naturally occurring antibody of claim **1**, wherein the heavy chain variable domain comprises an amino acid sequence set forth as SEQ ID NO: 21.

4. The non-naturally occurring chimeric antibody of claim **1**, wherein the light chain variable domain comprises an amino acid sequence set forth as SEQ ID NO: 31.

5. The non-naturally occurring chimeric antibody of claim **1**, wherein the antibody is an IgG, IgM or IgA.

6. The non-naturally occurring chimeric antibody of claim **1**, wherein the antibody is labeled.

7. The non-naturally occurring chimeric antibody of claim **6**, wherein the label is a fluorescent, enzymatic, or radioactive label.

8. A composition comprising an effective amount of the non-naturally occurring chimeric antibody and a pharmaceutically acceptable carrier, wherein the antibody comprises a heavy chain variable domain and a light chain variable domain,

wherein the heavy chain variable domain comprises the amino acid sequence set forth as SEQ ID NO: 23, the amino acid sequence set forth as SEQ ID NO: 25, and the amino acid sequence set forth as SEQ ID NO: 27 and the light chain variable domain comprises the amino acid sequence set forth as SEQ ID NO: 33, the amino acid sequence KAS, and the amino acid sequence set forth as SEQ ID NO: 37, and

wherein the antibody specifically binds hemagglutinin (HA) of H1N1 and H5N1.

9. The composition of claim **8**, wherein the pharmaceutically acceptable carrier is a physiological saline or balanced salt solution.

10. The composition of claim **8**, wherein the pharmaceutically acceptable carrier comprises a buffering agent.

11. The composition of claim **8**, wherein the pharmaceutically acceptable carrier comprises sodium acetate, sodium chloride, potassium chloride, calcium chloride, or sodium lactate.

12. The composition of claim **8**, wherein the pharmaceutically acceptable carrier comprises aqueous dextrose or glycerol.

13. The composition of claim **8**, wherein the pharmaceutically acceptable carrier comprises sorbitan monolaurate.

* * * * *