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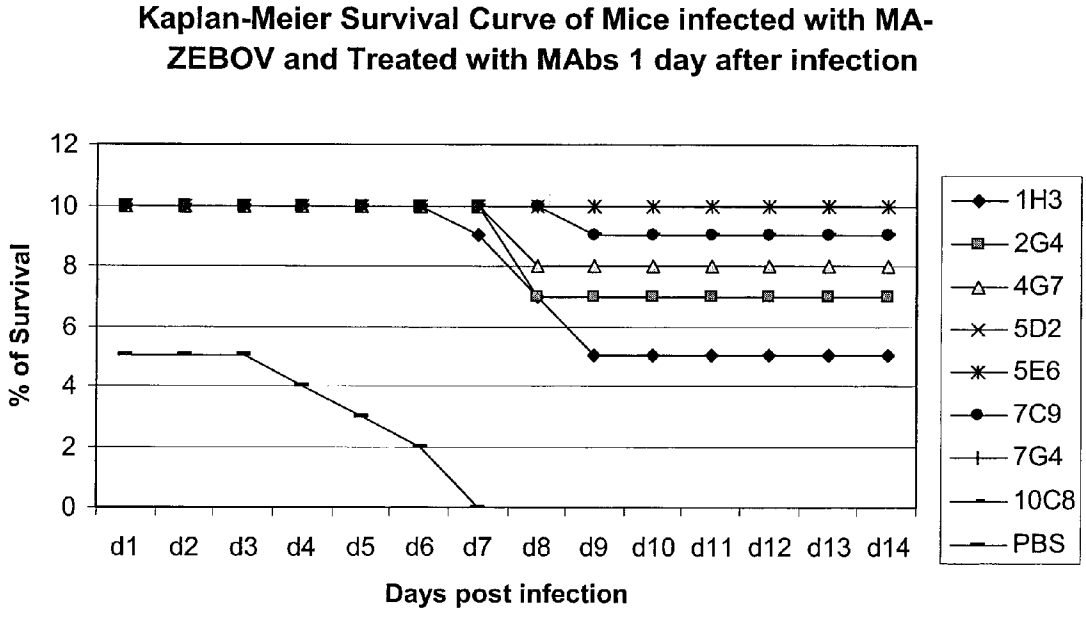

Fig. 1

(57) Abstract: Described herein are a number of Ebola and Marburg monoclonal antibodies.

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MONOCLONAL ANTIBODIES FOR EBOLA AND MARBURG VIRUSES

PRIOR APPLICATION INFORMATION

The instant application claims the benefit of US Provisional Patent Application 61/025,491, filed February 1, 2008.

BACKGROUND OF THE INVENTION

Ebola and Marburg viruses are highly pathogenic and virulent viruses causing rapidly fatal haemorrhagic fever in humans.

SUMMARY OF THE INVENTION

According to a first aspect of the invention, there is provided a monoclonal antibody comprising an amino acid sequence deduced from 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14), 10C8-light(SEQ ID No. 16), 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15).

According to a second aspect of the invention, there is provided a method of preparing a chimeric antibody comprising:

providing an expression vector comprising a nucleic acid molecule encoding a constant region domain of a human light chain or heavy chain genetically linked to a nucleic acid encoding a light chain variable region selected from the group consisting of 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14) and 10C8-light(SEQ ID No. 16) or a heavy chain variable region selected from the group consisting of 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15);

expressing the expression vector in a suitable host; and

recovering the chimeric antibody from said host.

According to a third aspect of the invention, there is provided a method of

preparing a recombinant antibodies comprising:

providing a nucleotide sequence selected from the group consisting of 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14), 10C8-light(SEQ ID No. 16), 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15);

modifying said nucleic acid sequence such that at least one but fewer than about 30 of the amino acid residues encoded by said nucleic acid sequence has been changed or deleted without disrupting antigen binding of said peptide; and

expressing and recovering said modified nucleotide sequence.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. Kaplan-Meier survival curve of mice infected with MA-ZEBOV and treated with MAbs 1 day after infection. Survival curve of MA-Ebola virus-infected mice treated with 100 µg of MAbs. Mice were intraperitoneally treated with 100 µg of each MAb on day 1. Control mice were given equal volumes of PBS.

Figure 2. Weight changes of GPA-Ebola infected guinea pigs treated with MAbs. Weight changes of virus-infected guinea pigs treated with cocktail of MAbs. Guinea pigs were intraperitoneally treated with either 5D2, 5E6, 7C9, 7G4 or 10C8 (3 mg/treatment) on day 1 and 4G7 + 1H3 + 2G4 [(2 mg +1 mg + 1 mg)/treatment] on day 2. Control guinea pig were given equal volume of PBS. The results are shown as the means and standard deviations of 6 guinea pigs.

Figure 3. Weight changes of GPA-Ebola infected guinea pigs treated with MAbs. Weight changes of virus-infected guinea pigs treated with cocktail of MAbs. Guinea pigs were intraperitoneally treated with either 5D2, 5E6, 7C9, 7G4 or 10C8 (3 mg/treatment) on day 1 and 4G7 + 1H3 + 2G4 [(2 mg + 1 mg + 1 mg)/treatment] on day 2. Control guinea pig were given equal volume of PBS. The results are shown as the group weight of 6 guinea pigs.

Figure 4. Immunoprecipitation. 293T cells were transfected with pCAGGS-ZEbovGP1,2 by using Fugene 6. After 48 hrs, cells were collected and washed 2X with cold PBS before being lysed with 2X RIPA buffer. After clarifying the cell

lysate, 100 µg protein was added to each McAb (5 µg) coupled protein A+G beads. The IP samples were run 10% SDS-PAGE and transferred to Hybond-P membrane. The blot was probed with mouse ant-EBOV-GP1.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned hereunder are incorporated herein by reference.

DEFINITIONS

As used herein, "neutralizing antibody" refers to an antibody, for example, a monoclonal antibody, capable of disrupting a formed viral particle or inhibiting formation of a viral particle or prevention of binding to or infection of mammalian cells by a viral particle.

As used herein, "diagnostic antibody" or "detection antibody" or "detecting antibody" refers to an antibody, for example, a monoclonal antibody, capable of detecting the presence of an antigenic target within a sample. As will be appreciated by one of skill in the art, such diagnostic antibodies preferably have high specificity for their antigenic target.

As used herein, "humanized antibodies" refer to antibodies with reduced immunogenicity in humans.

As used herein, "chimeric antibodies" refer to antibodies with reduced immunogenicity in humans built by genetically linking a non-human Variable region to human constant domains.

Described herein are a number of Ebola and Marburg monoclonal antibodies. Specifically, antigens were developed using a live replicating vector vesicular stomatitis virus described in PCT Application PCT/CA03/001125.

The VSV based vaccine delivery system was used to develop monoclonal antibodies in mice.

Specifically, described herein are monoclonal antibodies 1H3, 2G4, 4G7, 5D2, 5E6, 7C9, 7G4 and 10C8. As discussed below, 1H3 comprises 1H3-heavy

chain (SEQ ID No. 1) and 1H3-light chain (SEQ ID No. 2); 2G4 comprises 2G4-heavy chain (SEQ ID No. 3) and 2G4-light chain (SEQ ID No. 4); 4G7 comprises 4G7-heavy chain (SEQ ID No. 5) and 4G7-light chain (SEQ ID No. 6); 5D2 comprises 5D2-heavy chain (SEQ ID No. 7) and 5D2-light chain (SEQ ID No. 8); 5E6 comprises 5E6-heavy chain (SEQ ID No. 9) and 5E6-light chain (SEQ ID No. 10); 7C9 comprises 7C9-heavy chain (SEQ ID No. 11) and 7C9-light chain (SEQ ID No. 12); 7G4 comprises 7G4-heavy chain (SEQ ID No. 13) and 7G4-light chain (SEQ ID No. 14); and 10C8 comprises 10C8-light chain (SEQ ID No. 16) and 10C8-heavy chain (SEQ ID No. 15).

These antibodies also appear to have high affinity and avidity to Ebola glycoproteins, which means that they could be used as highly sensitive diagnostic tools.

For example, as shown in Figure 1, mice infected with MA-ZEBOV and subsequently treated with the monoclonal antibodies described above showed increased survival compared to mice treated with PBS. Results are summarized in Tables 1 and 2.

Figures 2 and 3 show weight changes in guinea pigs treated with the monoclonal antibodies or mixtures thereof post infection. As can be seen, guinea pigs treated with the monoclonal antibodies showed consistent weight while those treated with PBS showed significant weight loss. Results are summarized in Table 3.

The nucleotide sequences of the heavy and light chains of 1H3, 2G4, 4G7, 5D2, 5E6, 7C9, 7G4 and 10C8 follow. As will be appreciated by one of skill in the art, the amino acid sequences of these antibodies can easily be deduced from the nucleotide sequences. Accordingly, in some embodiments, the invention is directed to amino acid sequences deduced from 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14), 10C8-light(SEQ ID No. 16), 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15).

mAb 1H3 heavy chain sequence: 373bp

TGGGGCAGAGCTTGTGAAGCCAGGGGCCTCAGTCAAGTTGTCCTGCACAGC
TTCTGGCTTCAACATTAAAGACACCTATATACATTGGGTGAAACAGGGGCCTG
AACAGGGCCTGGAGTGGATTGGAAGGATTGATCCTGCGAATGGTAATACTAA
ATATGACCCGAAGTTCCAGGGCAAGGCCACTATCACAGCAGACACATCCTCC
AATACAGCCTACCTGCAGCTCAGCGGCCTGACATCTGAGGACACTGCCGTCT
ATTACTGTGCTAGGGAGTCGAGGATATCTACTATGCTTACGACGGGGTACTTT
GACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCAGCCAAAACAACAG
CCCCATCG (SEQ ID No. 1)

mAb 1H3 light chain sequence: 303 bp

GCAATCATGTCTGCATCTCCAGGGGAGAAGGTCACCATGACCTGCAGTGCCA
GCTCAAGTGTAAGTTACATGTACTGGTACCAGCAGAAGCCAGGATCCTCCCC
CAGACTCCTGATTTATGACACATCCAACCTGGCTTCTGGAGTCCCTGTTCGCT
TCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCTCACAATCAGCCGAATGGA
GGCTGAAGATGCTGCCACTTATTACTGCCAGCAGTGGAGTAGTTACCCGTAC
ACGTTCGGAGGGGGGACCAAGCTGGAAATAAAACGGGCTGAT (SEQ ID No. 2)

mAb 2G4 heavy chain sequence: 364bp

TGGAGGAGGCTTGATGCAACCTGGAGGATCCATGAAACTCTCCTGTGTTGCC
TCAGGATTCACTTTCAGTAACTACTGGATGAACTGGGTCCGCCAGTCTCCAGA
GAAGGGGCTTGAGTGGGTTGCTGAAATTAGATTGAAATCTAATAATTATGCAA
CACATTATGCGGAGTCTGTGAAAGGGAGGTTCACCATTTCAAGAGATGATTCC
AAAAGGAGTGTCTACCTGCAAATGAATACCTTAAGAGCTGAAGACACTGGCAT
TTATTACTGTACCCGGGGGAATGGTAACTACAGGGCTATGGACTACTGGGGT
CAAGGAACCTCAGTCACCGTCTCCTCAGCCAAAACAACACCCCCATCA (SEQ ID No. 3)

mAb 2G4 light chain sequence: 306bp

GCCTCCCTATCTGTATCTGTGGGAGAAACTGTCTCCATCACATGTCGAGCAA
GTGAGAATATTTACAGTAGTTTAGCATGGTATCAGCAGAAACAGGGAAAATCT
CCTCAGCTCCTGGTCTATTCTGCAACAATCTTAGCAGATGGTGTGCCATCAAG
GTTCAGTGGCAGTGGATCAGGCACTCAGTATTCCCTCAAGATCAACAGCCTG
CAGTCTGAAGATTTTGGGACTTATTACTGTCAACATTTTTGGGGTACTCCGTA
CACGTTCGGAGGGGGGACCAAGCTGGAAATAAAACGGGCTGAT (SEQ ID No. 4)

mAb 4G7 heavy chain sequence: 358 bp

TGGACCTGAGCTGGAGATGCCTGGCGCTTCAGTGAAGATATCCTGCAAGGCT
TCTGGTTCCTCATTCACTGGCTTCAGTATGAACTGGGTGAAGCAGAGCAATG
GAAAGAGCCTTGAGTGGATTGGAAATATTGATACTTATTATGGTGGTACTACC
TACAACCAGAAATTCAAGGGCAAGGCCACATTGACTGTGGACAAATCCTCCA
GCACAGCCTACATGCAGCTCAAGAGCCTGACATCTGAGGACTCTGCAGTCTA

TTACTGTGCAAGATCGGCCTACTACGGTAGTACTTTTGCTTACTGGGGCCAAG
GGACTCTGGTCACTGTCTCTGCAGCCAAAACAACAGCCCCATCG (SEQ ID No. 5)

mAb 4G7 light chain sequence: 306 bp

GCCTCCCTATCTGCATCTGTGGGAGAAACTGTCACCATCACATGTCGAGCAA
GTGAGAATATTTACAGTTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCT
CCTCAGCTCCTGGTCTATAATGCCAAAACCTTAATAGAGGGTGTGCCATCAAG
GTTCAGTGGCAGTGGATCAGGCACACAGTTTTCTCTGAAGATCAACAGCCTG
CAGCCTGAAGATTTTGGGAGTTATTTCTGTCAACATCATTTTGGTACTCCATTC
ACATTCGGCTCGGGGACAGAGTTGGAAATAAAACGGGCTGAT (SEQ ID No. 6)

mAb 5D2 heavy chain sequence: 340bp

GGGACCTGGCCTGGTGAGACCTTCTCAGTCTCTGTCCCTCACCTGCACTGTC
ACTGGCTACTCAATCACCAGTGATTATGCCTGGAACTGGATCCGGCAGTTTC
CAGGAAACAAACTGGAGTGGCTGGGCTATATAACCAACACTGGTAGCACTGG
CTTCAACCCATCTCTCAAAAGTCGAATCTCTATCACTCGAGACACATCCAAGA
ACCAGTTCTTCCTGCAGTTGATTTCTGTGACTACTGAGGACACAGCCACATAT
CACTGTGCAAGGGGCCTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCT
CTGCAGCCAAAACAACAGCCCCATCG (SEQ ID No. 7)

mAb 5D2 light chain sequence: 321 bp

CTCACTTTGTCGGTTACCATTGGACAACCAGCCTCCATCTCTTGCAAGTCAAG
TCAGAGCCTCTTAGATAGTGATGGAAAGACATATCTGAATTGGTTGTTACAGA
GGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTAAACTGGACTC
TGGAGTCACTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTCACACTG
AAAATCAGCAGAGTGGAGGCTGAGGATTTGGGAGTTTATTATTGTTGGCAAG
GTACACACTCTCCATTCACGTTCGGCTCGGGGACAAAGTTGGAAATAAAACG
GGCTGAT (SEQ ID No. 8)

mAb 5E6 heavy chain sequence: 370 bp

TGGGGGAGGCTTAGTGAAGCCTGGAGGGTCCCTGAAACTCTCCTGTGCAGC
CTCTGGATCCGCTTTCAGTAGATATGACATGTCTTGGGTTCGCCAGACTCCG
GAGAAGAGGCTGGAGTGGGTCGCATACATTAGTCGTGGTGGTGGTTTCATCT
ACTATCCAGACACTGTGAAGGGCCGATTCACCATCTCCAGAGACAATGCCAA
GAACACCCTGTACCTGCAAATGAGCAGTCTGAAGTCTGACGACACAGCCATG
TATTACTGTGCAAGACACGTTTACTACGGTAGTAGCCCCCTCTATGCTATGGA
CTACTGGGGTCAAGGAACCTCAGTCACCGTCTCCTCAGCCAAAACAACAGCC
CCATCG (SEQ ID No. 9)

mAb 5E6 light chain sequence: 324 bp

TCAGCCTCTTTCTCCCTGGGAGCCTCAGCAAAACTCACGTGCACCTTGAGTA
GTCAGCACAGTACGTTCACCATTGAATGGTATCAGCAACAGCCACTCAAGCC
TCCTAAGTATGTGATGGAGCTTAAGAAAGATGGAAGCCACAGTACAGGTGAT

GGGATTCCTGATCGCTTCTCTGGATCCAGCTCTGGTGCTGATCGCTACCTTA
GCATTTCCAACATCCAGCCTGAAGATGAAGCAATATACATCTGTGGTGTGGGT
GATACAATTAATGAACAATTTGTGTATGTTTTCGGCGGTGGAACCAAGGTCAC
TGTCCTAGGT (SEQ ID No. 10)

mAb 7C9 heavy chain sequence: 358bp

TGGGGCAGAGCTTGTGAAGCCAGGGGCCTCAGTCAAGTTGTCCTGCACAGC
TTCTGGCTTCAACATTAAAGACACCTATATGCACTGGGTGAAGGAGAGGCCT
GACAAGGGCCTGGAGTGGATTGGAAGGATTGATCCAGCGAATGGTAATACTA
AATGTGACTCGAGGTTTCAGGGCAAGGCCACTATAACAGCAGACACATCCTC
CAACACAGCCTACCTGCAGCTCAGCAGCCTGACATCTGAGGACACTGCCGTC
TATTACTGTGCTAGAAGGATCTACTTTGGTAAGGGCTTTGACTTTTGGGGCCA
AGGCACCACTCTCACAGTCTCCTCAGCCAAAACAACAGCCCCATCG (SEQ ID
No. 11)

mAb 7C9 light chain sequence: 324 bp

TCCTCCCTGAGTGTGTCAGCAGGAGAGAAGGTCACTATGAGCTGCAAGTCCA
GTCAGAGTCTGTTTAACAGTGGAGATCAAAAGAACTACTTGGCCTGGTACCA
GCAGAAACCAGGGCAGCCTCCTAAACTGTTGATCTACGGGGCATCCACTAGG
GAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGGATCTGGAACCGATTTCA
CTCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAG
AATGATCAATTTTATCCTCCCACGTTCGGTGATGGGACCAAGCTGGACCTGAA
ACGGGCTGAT (SEQ ID No. 12)

mAb 7G4 heavy chain sequence: 367 bp

TGGAGGGGGCTTGGTACAGCCTGGGGGTTCTCTGAGACTCTCCTGTGCAACT
TCTGGCTTCACCTTTACTGATCACTACATGGGCTGGGTCCGCCAGCCTCCAG
GAAAGGCACTTGAGTGGTTGGCTTTTGTTAGATACAAAGCTAAGGGTTACACA
ACAGAGTACACTGCATCTGTGAAGGGTCGGTTCACCATCTCCAGAGATAATTC
CCAAAGCATCCTCTATCTTCAAATGAACACCCTGAGAACTGAGGACAGTGCCA
CTTATTACTGTGCAAGAGATAGAGGGGGTTACGTGGGAGCTATGGACTACTG
GGGTCAAGGAACCTCAGTCACCGTCTCCTCAGCCAAAACGACACCCCCATCT
(SEQ ID No. 13)

mAb 7G4 light chain sequence: 321 bp

CTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCTAG
TCAGAGCCTTGTACACAGGAATGGAAACACCTATTTCCATTGGTACCTGCAGA
AGCCAGGCCAGTCTCCAAAACTCCTGATCTACAAAGTTTCCAACCGATTTTCT
GGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACACTCA
AGATCAGCAGAGTGGAGGCTGAGGATCTGGGAGTTTATTTCTGCTCTCAAAG
TACACATGTTCCGTACACTTTCGGAGGGGGGACCAAGCTGGAAATAAAACGG
GCTGAT (SEQ ID No. 14)

mAb 10C8 heavy chain sequence: 352bp

TGGGGCAGAGCTTGTGAGGTCAGGGGCCTCAGTCAAGTTGTCCTGCACATCT
TCTGGCTTCAACATTAAAGACTACTTTCTACACTGGGTGAAACAGAGGCCTGA
ACAGGGCCTGGAGTGGATTGGATGGATTGATCCTGAGAATGGTGATACTGAA
TATGCCCCGAAGTTCCAGGACAAGGCCACTATGACTGCAGACACATCCTCCA
ACACAGCCTACCTGCACCTCAGCAGCCTGACATCTGAGGACACTGGCGTCTA
TTACTGTAATGCAGATGGTAACTACGGGAAGAACTACTGGGGCCAAGGCACC
ACTCTCACCGTCTCCTCAGCCAAAACAACAGCCCCATCG (SEQ ID No. 15)

mAb 10C8 light chain sequence: 324bp

CTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCTAG
TCAGAGCCTTGTACACAGTAATGGAAACACCTTTTTACATTGGTACCTGCAGA
AGCCAGGCCAGTCTCCAAAGCTCCTGATCTACAGAGTTTCCAACCGATTTTCT
GGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACACTCA
AGATCAGCAGAGTGGAGGCTGAGGATCTGGGAGTTTATTTCTGCTCTCAAAG
TACACATGTTCCTCCGTACACGTTCGGAGGGGGGACCAAGCTGGAAATAAAA
CGGGCTGAT (SEQ ID No. 16)

In another embodiment of the invention, one or more of the nucleic acid sequences described above encoding the antibody are subjected to humanization techniques or converted into chimeric human molecules for generating a variant antibody which has reduced immunogenicity in humans. Humanization techniques are well known in the art – see for example US Patent 6,309,636 and US Patent 6,407,213 which are incorporated herein by reference specifically for their disclosure on humanization techniques. Chimerics are also well known, see for example US Patent 6,461,824, US Patent 6,204,023, US Patent 6,020,153 and US Patent 6,120,767 which are similarly incorporated herein by reference.

In one embodiment of the invention, chimeric antibodies are prepared by preparing an expression vector which comprises a nucleic acid encoding a constant region domain of a human light or heavy chain genetically linked to a nucleic acid encoding a light chain variable region selected from the group consisting of 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14) and 10C8-light(SEQ ID No. 16) or a heavy chain variable region selected from the group consisting of 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15). It is of note that all of these

sequences are described above.

In another embodiment of the invention, there are provided recombinant antibodies comprising at least one modified variable region, said region selected from the group consisting of 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14), 10C8-light(SEQ ID No. 16), 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15), in which at least one but fewer than about 30 of the amino acid residues of said variable region has been changed or deleted without disrupting antigen binding. It is of note that all of these sequences are described above.

In yet other embodiments, immunoreactive fragments of any of the above-described monoclonal antibodies, chimeric antibodies or humanized antibodies are prepared using means known in the art, for example, by preparing nested deletions using enzymatic degradation or convenient restriction enzymes.

It is of note that in all embodiments describing preparation of humanized antibodies, chimeric antibodies or immunoreactive fragments of monoclonal antibodies, these antibodies are screened to ensure that antigen binding has not been disrupted. This may be accomplished by any of a variety of means known in the art, but one convenient method would involve use of a phage display library. As will be appreciated by one of skill in the art, as used herein, 'immunoreactive fragment' refers in this context to an antibody fragment reduced in length compared to the wild-type or parent antibody which retains an acceptable degree or percentage of binding activity to the target antigen. As will be appreciated by one of skill in the art, what is an acceptable degree will depend on the intended use.

It is of note that as discussed herein, any of the above-described antibody or humanized variant thereof may be formulated into a pharmaceutical treatment for providing passive immunity for individuals suspected of or at risk of developing hemorrhagic fever comprising a therapeutically effective amount of said antibody. The pharmaceutical preparation may include a suitable excipient or carrier. See, for example, Remington: The Science and Practice of Pharmacy, 1995, Gennaro

ed. As will be apparent to one knowledgeable in the art, the total dosage will vary according to the weight, health and circumstances of the individual as well as the efficacy of the antibody.

While the preferred embodiments of the invention have been described above, it will be recognized and understood that various modifications may be made therein, and the appended claims are intended to cover all such modifications which may fall within the spirit and scope of the invention.

Table 1 Dose-dependent protective efficacy of McAbs in mice

Treatment[a]	Dose (μg/treatment)	Meantime to death[b]	No. of survivors/total
McAb 4G7	100	7.00 (n=1)	5/6
	50	7.00 (n=1)	5/6
	25	6.00 (n=3)	3/6
	12.5	6.80 (n=5)	1/6
	6.25	8.20 (n=5)	2/6
McAb 5D2	100	N/A[c]	6/6
	50	N/A[c]	6/6
	25	N/A[c]	6/6
	12.5	N/A[c]	6/6
	6.25	7.50 (n=2)	4/6
McAb 5E6	100	N/A[c]	6/6
	50	N/A[c]	6/6
	25	N/A[c]	6/6
	12.5	6.50 (n=2)	4/6
	6.25	6.67 (n=3)	3/6
McAb 7C9	100	N/A[c]	6/6
	50	N/A[c]	6/6
	25	7.00 (n=1)	5/6
	12.5	7.00 (n=1)	5/6
	6.25	6.50 (n=4)	2/6
McAb 7G4	100	N/A[c]	6/6
	50	7.50 (n=1)	4/6
	25	7.00 (n=1)	5/6
	12.5	7.60 (n=5)	1/6
	6.25	6.60 (n=5)	1/6
McAb 10C8	100	7.00 (n=1)	5/6
	50	7.00 (n=1)	5/6
	25	7.50 (n=4)	2/6
	12.5	7.00 (n=5)	1/6
	6.25	6.40 (n=5)	1/6
PBS		5.80 (n=5)	0/5

[a] Mice were intraperitoneally treated with antibodies 1 day after challenge with 1000 LD50 of the mouse-adapted Ebola virus.

[b] Data for animals that died (numbers of animals are shown in parentheses).

[c] N/A: not applicable.

Table 2. Time dependency of the protective efficacy of MAbs in mice

MAbs	Day of treatment[a]	Mean time to death[b]	No. of survivors/total
1H3	-4	6.70 ± 0.61 (n=10)	0/10
100 μg	-1	6.60 ± 0.61 (n=10)	0/15
	+1	8.10 ± 0.74 (n=9)	6/15
	+2	6.60 ± 0.80 (n=5)	5/10
	+3	6.40 ± 0.97 (n=10)	0/10
2G4	-4	7.40 ± 0.63 (n=10)	0/10
100 μg	-1	7.86 ± 0.74 (n=14)	1/15
	+1	8.00 (n=6)	9/15
	+2	7.30 ± 0.47 (n=3)	7/10
	+3	5.70 ± 1.13 (n=10)	0/10
4G7	-4	7.42 ± 0.46 (n=7)	3/10
100 μg	-1	7.08 ± 0.74 (n=14)	1/15
	+1	8.25 ± 0.43 (n=4)	11/15
	+2	n/a[c]	10/10
	+3	5.67 ± 1.34 (n=9)	1/10
5D2	-4	7.00 (n=1)	9/10
100 μg	-1	8.00 ± 1.00 (n=2)	13/15
	+1	n/a	15/15
	+2	7.00 (n=4)	6/10
	+3	6.30 ± 1.05 (n=10)	0/10
5E6	-4	7.00 (n=2)	8/10
100 μg	-1	8.25 ± 0.43 (n=4)	11/15
	+1	7.00 (n=1)	14/15
	+2	6.00 (n=1)	9/10
	+3	5.80 ± 1.03 (n=10)	0/10
7C9	-4	7.00 (n=1)	9/10
100 μg	-1	7.75 ± 0.43 (n=4)	11/15
	+1	8.00 ± 0.82 (n=3)	12/15
	+2	7.00 (n=1)	9/10
	+3	6.10 ± 0.67 (n=10)	0/10
7G4	-4	8.20 ± 0.71 (n=10)	0/10
100 μg	-1	8.07 ± 0.59 (n=14)	1/15
	+1	n/a	15/15
	+2	7.10 ± 0.57 (n=9)	1/10
	+3	6.70 ± 0.44 (n=10)	0/10
10C8	-4	7.83 ± 0.64 (n=6)	4/10
100 μg	-1	7.64 ± 1.17 (n=14)	1/15
	+1	8.50 ± 0.50 (n=2)	13/15
	+2	6.83 ± 0.37 (n=6)	4/10
	+3	6.30 ± 1.13 (n=10)	0/10
17F8[d]	-4	6.00 ± 1.10 (n=9)	1/10
100 μg	-1	6.13 ± 0.88 (n=15)	0/15
	+1	7.21 ± 0.86 (n=14)	1/15
	+2	6.10 ± 0.83 (n=10)	0/10
	+3	6.00 ± 1.13 (n=10)	0/10
PBS	-4	5.40 ± 1.43 (n=10)	0/10
	-1	6.60 ± 0.80 (n=5)	0/5
	+3	5.00 ± 0.60 (n=10)	0/10

[a] Mice were intraperitoneally treated with each MAb at indicated time before or after challenge with 1000 LD50 of the mouse-adapted Ebola virus.

[b] Data for animals that died (numbers of animals are shown in parentheses).

[c] N/A: not applicable.

[d] Control Mab: anti-MAR GP.

Table3 Protective efficacy of MAbs in guinea pigs

Treatment	Day of treatment[a]	Meantime to death[b]	No. of survival/Tatal[c]
Cocktail of 5D2(3mg) + 4G7(2mg)+1H3(1mg)+2G4(1mg)	1 2	N/A[d]	6/6
Cocktail of 5E6(3mg) + 4G7(2mg)+1H3(1mg)+2G4(1mg)	1 2	N/A	6/6
Cocktail of 7C9(3mg) + 4G7(2mg)+1H3(1mg)+2G4(1mg)	1 2	N/A	6/6
Cocktail of 7G4(3mg) + 4G7(2mg)+1H3(1mg)+2G4(1mg)	1 2	N/A	6/6
Cocktail of 10C8(3mg) + 4G7(2mg)+1H3(1mg)+2G4(1mg)	1 2	9.00(n=1)	5/6
Cocktail of PBS + PBS	1 2	7.00(n=6)	0/6

[a] Guinea pigs were intraperiotoneally treated with the MAbs as showed dose in the table on the indicated days after challenge with 1000 LD_{50} of the guinea pig-adapted Ebola virus.
[b] Data for all animals that died(numbers of animals are shown in parentheses).
[c] Survival rate on day 28 after challenge.
[d] N/A: not applicable.

Table 4. Summary of ELISA Result of Anti-Ebola-GP McAbs

McAb	Isotype	Antigen					
		eVLPs	eGP1,2 ΔTm	sGP 1-295aa	Rf-GP1 sub-f-D 157-369aa	Mucin domain 333-458aa	GP1 1-501aa
1H3	IgG2a,κ	+	+	+	-	-	+
2G4	IgG2b,κ	+	+	-	-	-	-
4G7	IgG2a,κ	+	+	-	-	-	+
5D2	IgG2a,κ	+	+	-	+	+	+
5E6	IgG2a,λ	+	+	-	-	+	+
7C9	IgG2a,κ	+	+	-	+/-	+	+
7G4	IgG1, κ	+	+	-	-	+/-	+
10C8	IgG2a,κ	+	+	-	-	+/-	+

Antigens (0.3μg/well) were coated in 96 well microtitre plate then blocking with 2% skim milk. Serial dilutions of each MAb were applied to the plate followed by HRP-conjugated goat anti-mouse IgG. After incubabing with substrate, the asorbance awas read at OD405. Cut off was 2X background.

Table 5 Prolonged survival seen in McAb-treated Guinea pigs

Treatment[a]	Mean time to death[b]	Student's t-test
MAb 1H3	11.7 ± 2.18 (n=5)	$p = 0.0181$
MAb 2G4	11.5 ± 1.50 (n=2)	N/A[c]
MAb 4G7	10.5 ± 1.50 (n=2)	N/A[c]
MAb 5D2	9.4 ± 1.02 (n=5)	$p = 0.0244$
MAb 5E6	10.8 ± 1.47 (n=5)	$p = 0.0092$
MAb 7C9	9.6 ± 0.80 (n=5)	$p = 0.0056$
MAb 7G4	9.6 ± 0.80 (n=5)	$p = 0.0056$
MAb 10C8	9.4 ± 1.20 (n=5)	$p = 0.0428$
PBS	7.67± 0.75 (n=6)	N/A[c]

[a] Guinea pigs were intraperiotoneally treated with 5mg of the MAb as showed in the table on day 1 after challenge with 1000 LD_{50} of the guinea pig-adapted Ebola virus.

[b] Data for all animals that died (numbers of animals are shown in parentheses).

[c] N/A: not applicable.

Table 6 Protective efficacy of MAbs in guinea pigs

Treatment	Day of treatment [a]	Meantime to death [b]	No. of survival/Tatal [c]
Cocktail of 4G7(2mg) + 1H3(1.5mg)+2G4(1.5mg)	-1	11.17± 3.09 (n=3)	3/6
Cocktail of 4G7(2mg) + 1H3(1.5mg)+2G4(1.5mg)	+1	7.92 ± 0.42 (n=3)	3/6
Cocktail of 4G7(2mg) + 1H3(1.5mg)+2G4(1.5mg)	+2	N/A [d]	6/6
Cocktail of 4G7(2mg) + 1H3(1.5mg)+2G4(1.5mg)	+3	11.17± 3.09 (n=3)	4/6
PBS	+2	6.58 ± 0.59 (n=6)	3/6

[a] Guinea pigs were intraperiotoneally treated with the MAbs as showed dose in the table on the indicated days before or after challenge with 1000 LD50 of the guinea pig-adapted Ebola virus.

[b] Data for all animals that died(numbers of animals are shown in parentheses).

[c] Survival rate on day 28 after challenge.

[d] N/A: not applicable.

Table 7 Epitopes bound by ZEbov GP McAbs

mAb name	Ebola GPs with epitope	epitope sequence	epitope position
1H3(IgG2a/κ):	sGP[a]	SNTTGKLIWKVNPEI	267- 280aa
2G4(IgG2b/κ):	GP2[a]	REAIVNA**Q**PKCNPNL	502-516aa
4G7(IgG2a/κ):	GP2[a]	REAIVNA**Q**PKCNPNL	502-516aa
5D2 (IgG2a/κ):	GP1[b,c,d]	DPGTNTTTEDHKIMA	329-343aa
5E6 (IgG2a/λ):	GP1[b,c,d]	ATQVEQHHRRTDNDS	401-415aa
7C9(IgG2a,κ):	GP1[b.c]	unknown	unknown
7G4(IgG1, κ):	GP1[b,c]	unknown	unknown
10C8(IgG2a,κ):	GP1[b.c]	unknown	unknown

a: determined by using recombinant vesicular stamatitis virus(VSV) containing ZEbov GP gene to identify the amino acid changes in antigenic variants that escape antibody neutralization;
b: determined by Western blot reactivity with Ebola Zaire 1976 or VLPs,
c: determined by ELISA using recombinant GP1 protein;
d: determined by ELISA using peptide library.

CLAIMS

1. A monoclonal antibody comprising an amino acid sequence deduced from 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14), 10C8-light(SEQ ID No. 16), 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15).

2. A method of preparing a chimeric antibody comprising:

providing an expression vector comprising a nucleic acid molecule encoding a constant region domain of a human light chain or heavy chain genetically linked to a nucleic acid encoding a light chain variable region selected from the group consisting of 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14) and 10C8-light(SEQ ID No. 16) or a heavy chain variable region selected from the group consisting of 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15);

expressing the expression vector in a suitable host; and

recovering the chimeric antibody from said host.

3. A method of preparing a recombinant antibodies comprising:

providing a nucleotide sequence selected from the group consisting of 1H3-light (SEQ ID No. 2); 2G4-light (SEQ ID No. 4); 4G7-light (SEQ ID No. 6); 5D2-light (SEQ ID No. 8); 5E6-light (SEQ ID No. 10); 7C9-light (SEQ ID No. 12); 7G4-light (SEQ ID No. 14), 10C8-light(SEQ ID No. 16), 1H3-heavy (SEQ ID No. 1); 2G4-heavy (SEQ ID No. 3); 4G7-heavy (SEQ ID No. 5); 5D2-heavy (SEQ ID No. 7), 5E6-heavy (SEQ ID No. 9), 7C9-heavy (SEQ ID No. 11), 7G4-heavy (SEQ ID No. 13) and 10C8-heavy (SEQ ID No. 15);

modifying said nucleic acid sequence such that at least one but fewer than about 30 of the amino acid residues encoded by said nucleic acid sequence has

been changed or deleted without disrupting antigen binding of said peptide; and expressing and recovering said modified nucleotide sequence.

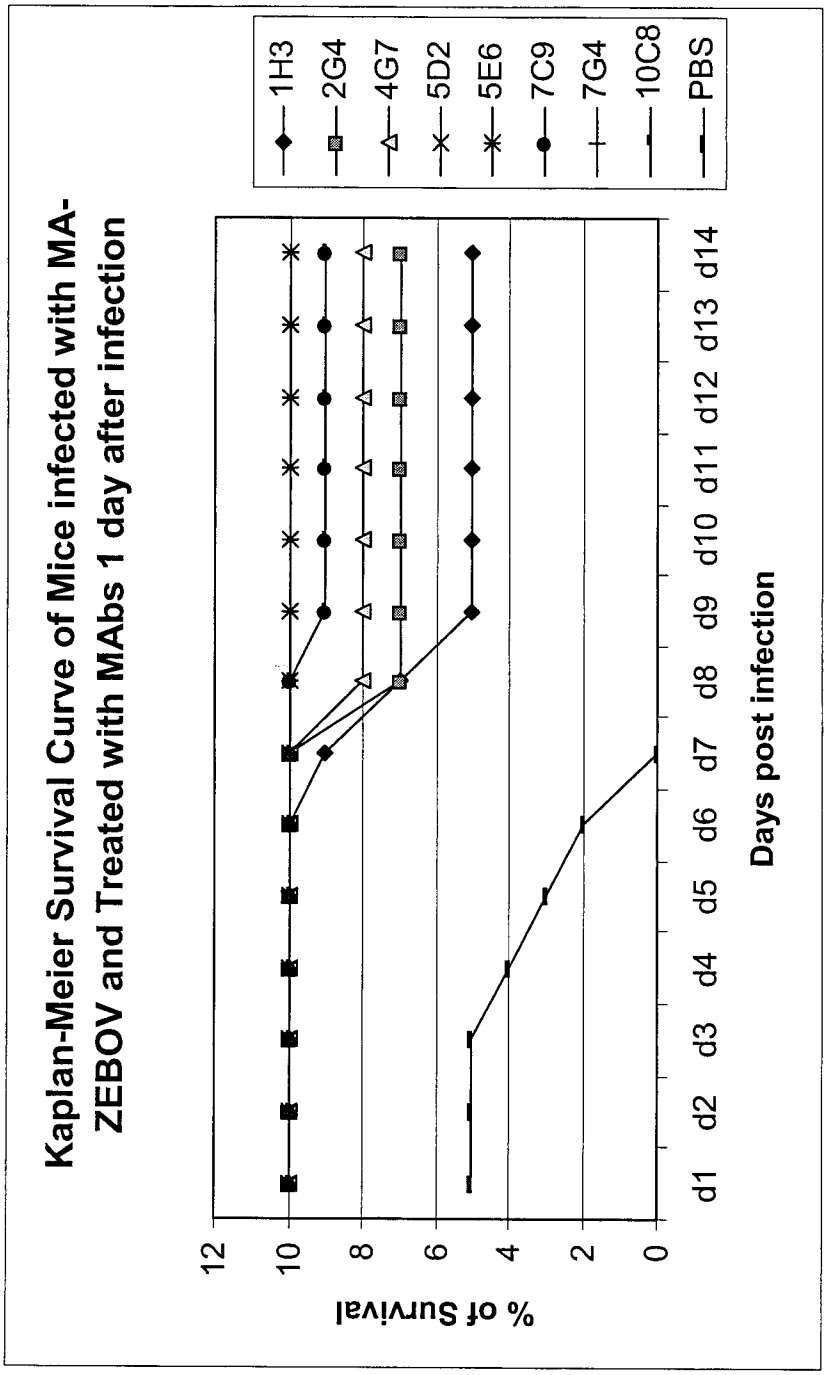
Kaplan-Meier Survival Curve of Mice infected with MA-ZEBOV and Treated with MAbs 1 day after infection
1H3
2G4
4G7
5D2
5E6
7C9
7G4
10C8
PBS
% of Survival
0
2
4
6
8
10
12
d1 d2 d3 d4 d5 d6 d7 d8 d9 d10 d11 d12 d13 d14
Days post infection

Fig. 1

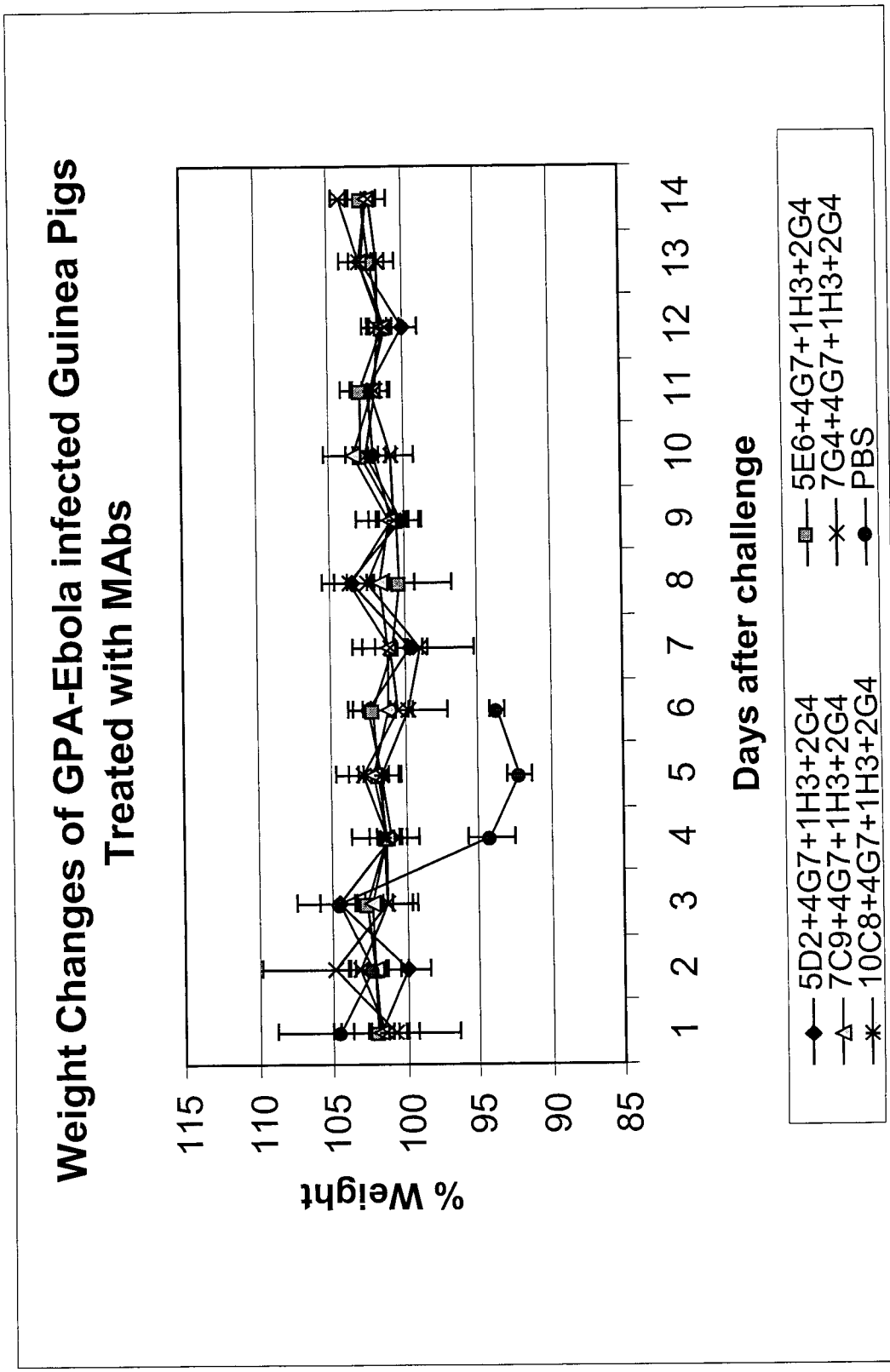
Weight Changes of GPA-Ebola infected Guinea Pigs
Treated with MAbs
% Weight
115
110
105
100
95
90
85
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Days after challenge
5D2+4G7+1H3+2G4
7C9+4G7+1H3+2G4
10C8+4G7+1H3+2G4
5E6+4G7+1H3+2G4
7G4+4G7+1H3+2G4
PBS

Fig. 2

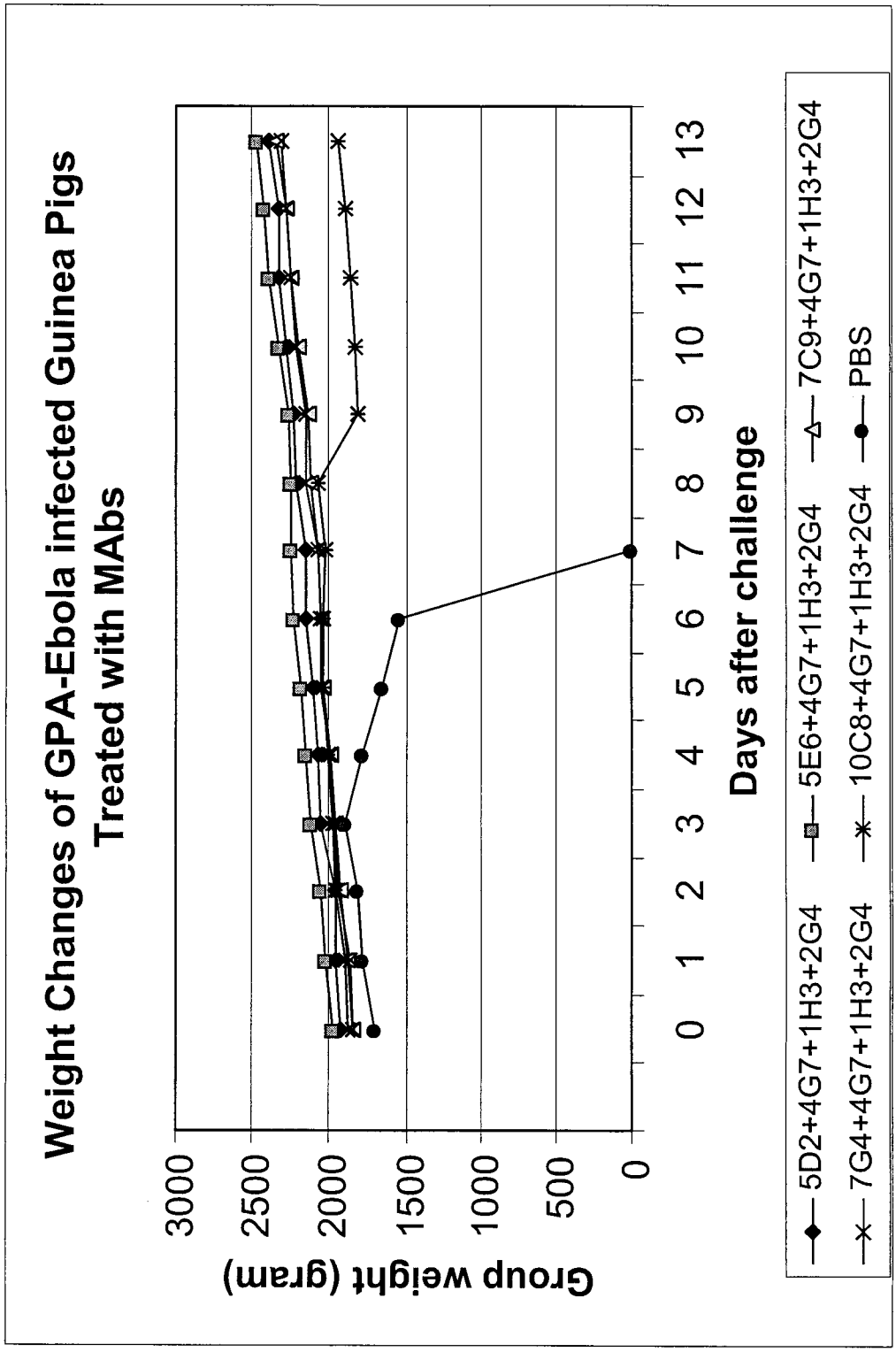
Weight Changes of GPA-Ebola infected Guinea Pigs
Treated with MAbs
Group weight (gram)
3000
2500
2000
1500
1000
500
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13
Days after challenge
5D2+4G7+1H3+2G4
5E6+4G7+1H3+2G4
7C9+4G7+1H3+2G4
7G4+4G7+1H3+2G4
10C8+4G7+1H3+2G4
PBS

Fig. 3

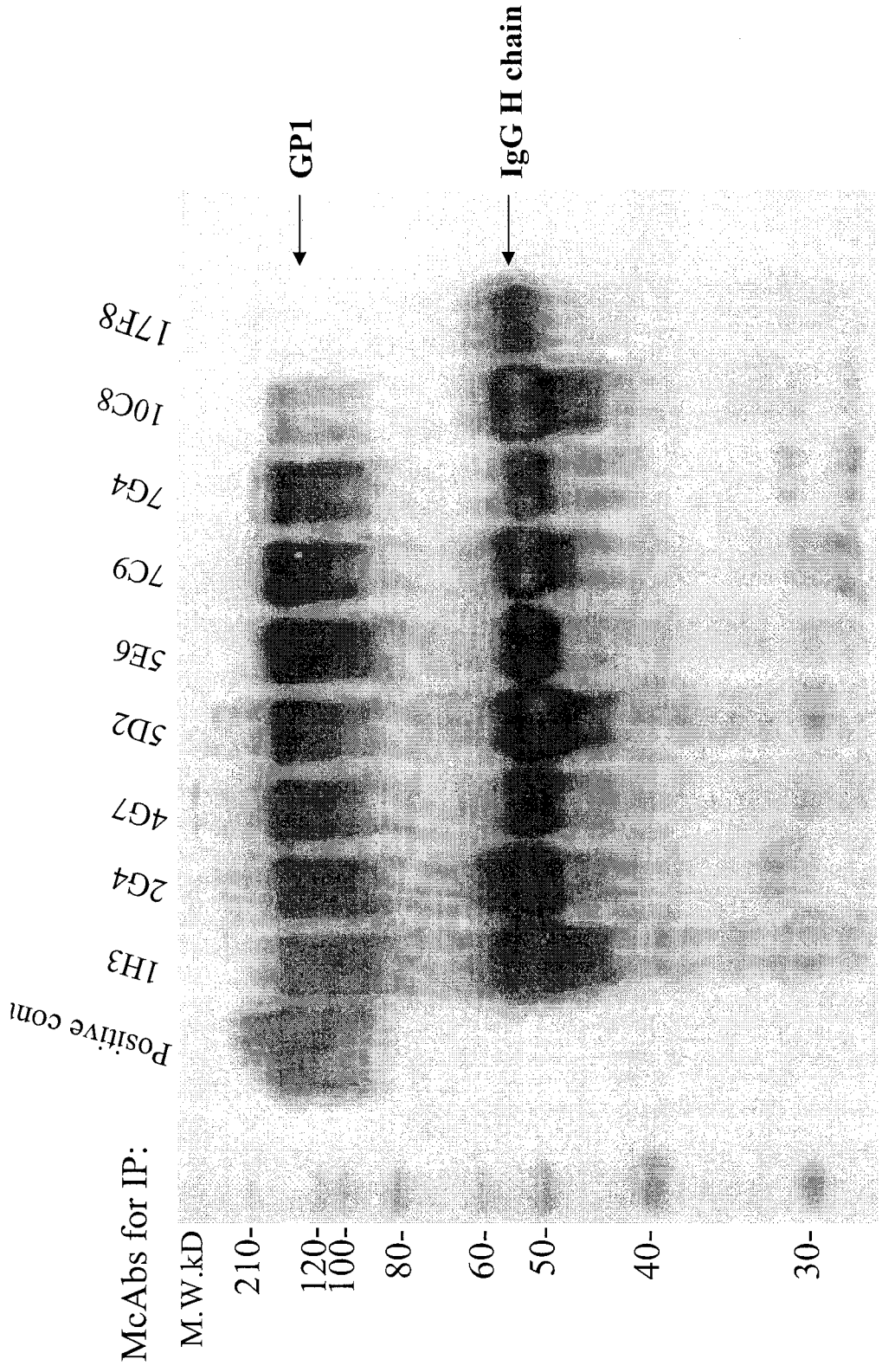
GP1
IgG H chain
McAbs for IP:
Positive con
1H3
2G4
4G7
5D2
5E6
7C9
7G4
10C8
17F8
M.W.kD
210-
120-
100-
80-
60-
50-
40-
30-

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2009/000070

A. CLASSIFICATION OF SUBJECT MATTER

IPC: ***C07K 16/10*** (2006.01) , ***C07K 16/46*** (2006.01) , ***C12N 15/09*** (2006.01) , ***C12P 21/08*** (2006.01) , ***C12N 15/13*** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: ***C07K 16/10*** (2006.01) , ***C07K 16/46*** (2006.01) , ***C12N 15/09*** (2006.01) , ***C12P 21/08*** (2006.01) , ***C12N 15/13*** (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)

Scopus, Pubmed, Delphion, Canadian Patent Database, GQPAT, Derwent GeneSeq, RefSeq, GenBank, ENSEMBL mRNA, NCBI Probe DB, NCBI IGBLAST, DrugBank Pro nucleotide sequences, PDB Nucleotides, GQ Gene. Keywords: Ebola, Marburg, monoclonal antibody. SEQ ID NOs: 1-16. Authors: Jones, Qiu, Feldmann.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 04/018649 (HART, M.K. et al.) 4 March 2004 (04-03-2004)	1-3
A	TAKADA, A. et al., "Protective efficacy of neutralizing antibodies against Ebola virus infection", Vaccine, 2007, Vol. 25, pp. 993-999, ISSN: 0264-410X	1-3
A	SHAHHOSSEINI, S. et al., "Production and characterization of monoclonal antibodies against different epitopes of Ebola virus antigens", Journal of Virological Methods, 2007, Vol. 143, pp. 29-37, ISSN: 0166-0934	1-3

[ ] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 April 2009 (14-04-2009)	9 June 2009 (09-06-2009)

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
Place du Portage I, C114 - 1st Floor, Box PCT
50 Victoria Street
Gatineau, Quebec K1A 0C9
Facsimile No.: 001-819-953-2476

Authorized officer

Ali Abdallah (819) 994-4253

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2009/000070

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [ ] Claim Nos. :
because they relate to subject matter not required to be searched by this Authority, namely :

2. [ ] Claim Nos. :
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

See Supplemental Page

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2009/000070

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO 04/018649	04-03-2004	AU 2003265883A1	11-03-2004
		AU 2003265883A8	11-03-2004
		DE 60317800D1	10-01-2008
		EP 1539238A2	15-06-2005
		EP 1539238A4	21-12-2005
		EP 1539238B1	28-11-2007
		US 6875433B2	05-04-2005
		US 7335356B2	26-02-2008
		US 2004053865A1	18-03-2004
		US 2007298042A1	27-12-2007
		WO 2004018649A3	17-06-2004

Continuation of Box III:

This International Searching Authority found multiple inventions in this international application, as follows:

Group 1: Claims 1-3 (all partially) are directed to a monoclonal antibody (1H3) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 1 and SEQ ID NO: 2, respectively, and a method of preparing a chimeric and a recombinant antibody using said 1H3 monoclonal antibody.

Group 2: Claims 1-3 (all partially) are directed to a monoclonal antibody (2G4) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 3 and SEQ ID NO: 4, respectively, and a method of preparing a chimeric and a recombinant antibody using said 2G4 monoclonal antibody.

Group 3: Claims 1-3 (all partially) are directed to a monoclonal antibody (4G7) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 5 and SEQ ID NO: 6, respectively, and a method of preparing a chimeric and a recombinant antibody using said 4G7 monoclonal antibody.

Group 4: Claims 1-3 (all partially) are directed to a monoclonal antibody (5D2) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 7 and SEQ ID NO: 8, respectively, and a method of preparing a chimeric and a recombinant antibody using said 5D2 monoclonal antibody.

Group 5: Claims 1-3 (all partially) are directed to a monoclonal antibody (5E6) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 9 and SEQ ID NO: 10, respectively, and a method of preparing a chimeric and a recombinant antibody using said 5E6 monoclonal antibody.

Group 6: Claims 1-3 (all partially) are directed to a monoclonal antibody (7C9) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 11 and SEQ ID NO: 12, respectively, and a method of preparing a chimeric and a recombinant antibody using said 7C9 monoclonal antibody.

Group 7: Claims 1-3 (all partially) are directed to a monoclonal antibody (7G4) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 13 and SEQ ID NO: 14, respectively, and a method of preparing a chimeric and a recombinant antibody using said 7G4 monoclonal antibody.

Group 8: Claims 1-3 (all partially) are directed to a monoclonal antibody (10C8) comprising a heavy chain and a light chain amino acid sequence deduced from SEQ ID NO: 15 and SEQ ID NO: 16, respectively, and a method of preparing a chimeric and a recombinant antibody using said 10C8 monoclonal antibody.

The only linking feature between all groups is: a monoclonal antibody specific for Ebola virus.

Based on *a posteriori* considerations, monoclonal antibodies specific for Ebola virus are well known in the art (see e.g.WO 04/018649 (HART, M.K. et al.) 4 March 2004; TAKADA, A. et al., Vaccine, 2007, Vol. 25, pp. 993-999; or SHAHHOSSEINI, S. et al., Journal of Virological Methods, 2007, Vol. 143, pp. 29-37). As such, no single inventive feature links the subject matter of the multiple inventions outlined above.