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(54) **HUMAN EBOLA VIRUS SPECIES AND COMPOSITIONS AND METHODS THEREOF**

Publication Classification

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(57) **ABSTRACT**

Compositions and methods including and related to the Ebola Bundibugyo virus (EboBun) are provided. Compositions are provided that are operable as immunogens to elicit and immune response or protection from EboBun challenge in a subject such as a primate. Inventive methods are directed to detection and treatment of EboBun infection.

Related U.S. Application Data

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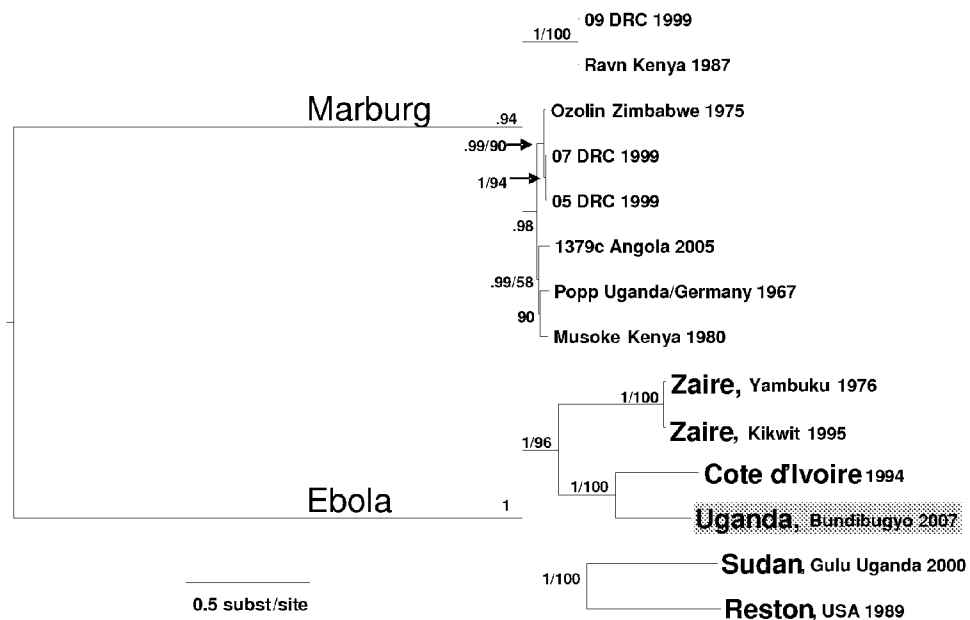


Fig. 1

FIG. 2

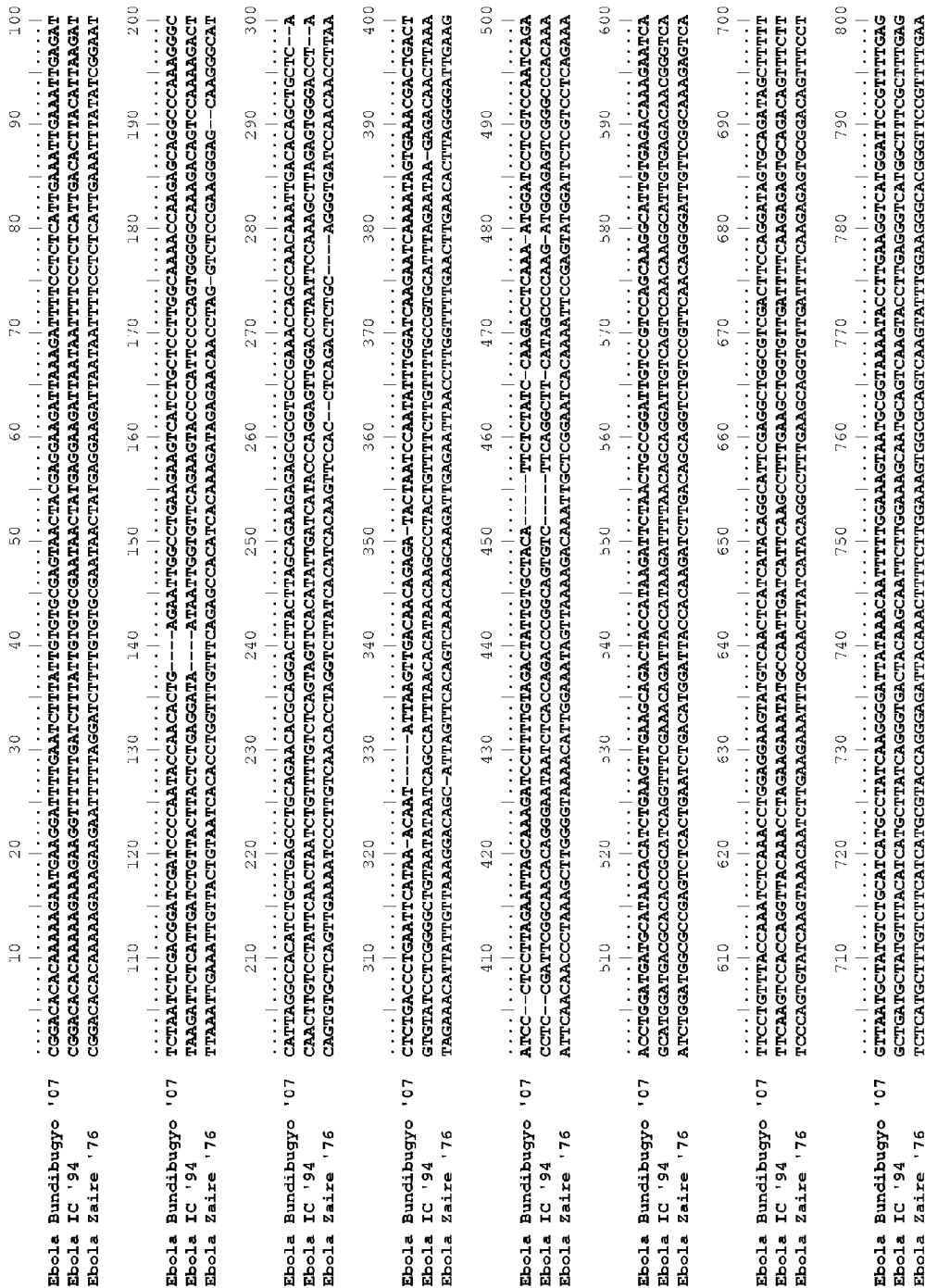


FIG. 2

Ebola Bundibugyo '07 2210 2220 2230 2240 2250 2260 2270 2280 2290 2300
 CGACCACAACGATGGTGCACAAATGAAAGCATCTCCCTCCGAAATCAGACGAGG-GTAGCACTGATACACTGACAGAAACAACAAGCCTGCCACTGC
 Ebola IC '94 TGGTCAAAATGAAGATGAATGATAGCATCCCTCCCTGGATCAGAGAAAB-ACAACACTGAGACACCAATACCCACCAAAAATPACCCTGC
 Ebola Zaire '76 GGAGGATGCCGACGACGAGCAGTCTAGCCTTCCGCTTGGAGTCAAGATGATGAGAGCAGGACGAGGAACTTCCAAACCCGACA-CCCACTGTCCG

 Ebola Bundibugyo '07 2310 2320 2330 2340 2350 2360 2370 2380 2390 2400
 ACCTCCCGCTCCGCTACCGAATCTCCGAGTATCTCCCTCAGAGAAATCCCGCACAGTCCAAATCAACAGCAATGAGGACAAATGTC
 Ebola IC '94 TCCACCAGCCTGTTTATCGAGTAAATCAGAAAGAGCCCTCCGCAAGAAAATCCAGAAACCAACCAACCAAGTGGTGTAGTGAATAACC
 Ebola Zaire '76 CCCACCGGCTCCCGTATACAGATACCTCTGAAAAGAAAGAACTCCCGCAAGACAGCAACAAGATCAGGACCACTCAAGAGCCAGGAACCAAGGAC

 Ebola Bundibugyo '07 2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
 AGGAAATGCTCAGTCGGGAAATCCATTGAGAAATGATCAACATATCTTGAACAACAAGGACCTTTTGTGATGCCATCCCTTACTACCATATGATGA
 Ebola IC '94 GACAAATAACCTCAGCAGCAATCAGTGGAAAGAAATGATCGACATCTCCAAACAAGGACCAATTTGATGCCATCCCTATACATACATGATGA
 Ebola Zaire '76 AGTGACAACCCAGTCAGAACACTCTTTTGGAGGAGATGATCCGCACATCTTAAGATCACAGGGGCCATTTGATGCTGTGTTTTGATTTATCATATGATGA

 Ebola Bundibugyo '07 2510 2520 2530 2540 2550 2560 2570 2580 2590 2600
 AAGGAGGCCCATATTTTCAGCACTAGTGGGAAAGATACATATCCAGACTCTTTGAAGATGATATCCACCCTGGCTCAGCGAAGGAGG
 Ebola IC '94 CGGAGGCGCGATGTTTATGCACTAGTGGAAAGAAATGATCCCTGATTTCTTGGAGGGAGCATCCACCCTGGCTCAGTGAAGAGAGGC
 Ebola Zaire '76 AGGATGACCTGTAGTTTTTCAGTACCAGTGTGATGGCAAGAGATACACGTATCCAGACTCCCTTGAAGAGGAAATATCCACCCTGGCTCAGTGAAGAGAGGC

 Ebola Bundibugyo '07 2610 2620 2630 2640 2650 2660 2670 2680 2690 2700
 CATGAACGAAAGACAATGATTAATCAAAACATGGATGGTGCAGGTTTTTACTGGCTGTGATGAATCATAAGAAATAAATTCATGGCAATCTCCAGCATCAC
 Ebola IC '94 CTTGAAATGAGGACAATAGGTTTTATCAAAATGATGATCAAAATTTACTGGCTGTGATGAATCAGAGAAACAATTCATGGCTATCCCTCAGCACCCAC
 Ebola Zaire '76 TATGAATGAAGAGAAATAGATTTGTTACATTTGGATGGTCAACAATTTATTTGGCCGGTGTGATGATCAAGAATAAATTCATGGCAATCTCCAGCAATCAT

 Ebola Bundibugyo '07 2710 2720 2730 2740 2750 2760 2770 2780 2790 2800
 AGGTGATCCGACCTTAARAATGAGCT---CCTAATCAAGTAC---CCATCCTCTGCGGAATGCCAGAACCTCCCTCCAAAACAGCTCCACATCGA
 Ebola IC '94 AAGTAATTTCTCAATGACAGATCA---TTGTAAGGTTATFACC---ACCATCCCTGCAACAAGCATGAAAACCACTCAACAACGCCCTTACCACAGG
 Ebola Zaire '76 CAGTGAATGAGCATGGAACAATGGGATGATTCGAACCGCAAAAATAGTAAACATTAAGTGTAGTCAAGGAAAGGAAAC-----AGGAAGAAATTTTGTGATGTC

 Ebola Bundibugyo '07 2810 2820 2830 2840 2850 2860 2870 2880 2890 2900
 GAACCTCCGACCGGTFACAGGCAAGACAGGCAACTTAATGATGTTCTGTTCCACCAACCGCAACCACTGATGATGCTTCCAGAC---AACTA
 Ebola IC '94 ATACCTTGGAGACATACCAAGATCAGCAGTGTCAACCCCGATCCAGATCCACCAACCAACCAACAAAT---AATCCAGACCAAAACCG
 Ebola Zaire '76 TAAGGTGGAATTTATTCACAATAAAGTGAAT---CTTATTTTGAATTAAGTAGCTTATTTACTACGCCGTTTTTCAAGTTCAATTTGAGTCTTT

FIG. 2

	2910	2920	2930	2940	2950	2960	2970	2980	2990	3000
Ebola Bundibugyo '07	CAACCCCTTAGC--CAACTCCACACACCAAGCACCCACCCATAACAACAACCCCAAAACCAA--CAACACATGATGTAAGTATGCTCTCACCCCAAGATGA	Ebola IC '94	CACACATCCAGAT--CAACCCAAACCTCAACACCCACCTCCG--CGATCCAGACCAAACTCCGCCCCAGACAAGCACCCACCCATCCCGAAGAAC	Ebola Zaire '76	AAATGCAAAATAGCGGTTAAGCCACAGTTAAGCCATAATGTAACTCAAT--ATTCTAACTAGCGATTTATCTAAATTAATTAATACATTAATGCTTTTATAACT		
	3010	3020	3030	3040	3050	3060	3070	3080	3090	3100
Ebola Bundibugyo '07	TCCCTGGACACCAACAACCCCTAACCTCCCAAGTTGTCATTAAGAAAAATAATATGATGAAGATTAATAAACCTTTCATCGAGGCTATTTCTTCTACGCTT	Ebola IC '94	CGCACGCCGAGAAATCGATCCCCAGCAATCAAAATGCGTTTATTAAGAAAAACAATATGATGAAGATTAATAAACCTTTCATCAACAATTTGCACAGACTTTGATC	Ebola Zaire '76	TACCTACTAGCCTGCCCAACATTTACAGCATCGTTTTTATAATTAAGAAAAAACTAATGATGAAGATTAATAAACCTTTCATCATCTTACCTCAATTTGAATTC		
	3110	3120	3130	3140	3150	3160	3170	3180	3190	3200
Ebola Bundibugyo '07	GGTTAGCACCAAGTATTCACAAACTATTTTACAATC-----CCTACCACAATATGACTTAAACAGACGCAAGGGTGTACTACAACCCACCAACCAACCA	Ebola IC '94	CTTAGGAGTTTATTTCTAGCTATCTACAAAACGGGT-----CCAAAAGGGAATGATTTCCACTAGGGCTCGAGCAATCAATGATCTCTCAATTAACCAATCA	Ebola Zaire '76	TCTAGCACTCGAAGCTTATTTGCTTCAATGTAATAAAGAAAGTGGTCTAACAAAGATGACAACTAGAACAAAAGGCGAGGGCCCATACTCGGGCCACCGACTC		
	3210	3220	3230	3240	3250	3260	3270	3280	3290	3300
Ebola Bundibugyo '07	CAGGCACACGATCGTGTGGCCGGAACCTTCCGGTGGATCTGTGACAAATGATGACAGCAAGATTCGATACCGATACCGATATCTCAATGAATGAATGAAC	Ebola IC '94	GAAACCAAGTACAGCTGGCCCTGAACTATCAGGATGATCTCCGAACTAAATGACAGCAAAATTCGCGGTAAGTAAATCTTCAACGACACTGAGCC	Ebola Zaire '76	AAAACGACAGAATGCCAGGCCCTGAGCTTTCCGGCTGGATCTGTAGCAGCTAAATGACCCGGAAGAAATCTCTGTAAGCGCACATCTCTCTGTATTTGAGAA		
	3310	3320	3330	3340	3350	3360	3370	3380	3390	3400
Ebola Bundibugyo '07	CTTACCTAGTATTAAGTCCCTCGATCCACTCCAAAATCAAAACCCCAAGTGTCAACCGCAGTGTCCAGACCCCAACTGACCCCAATTTGTAATCATGAT	Ebola IC '94	CCACATAAGCTCAGGCTCCGACTGCTCCAGACCCCAAAACAGCCGCCCTCCGACTCGCAACACCCAGACAGACCGGATCCGGTTTGCATCAACAAT	Ebola Zaire '76	CAATCCAGGATATGCTACCGATCCCAATGCAACAAACGAAACCCCGAAGCGGCAACACTCAACCCCAACCGGACCCCAATTTGCAATCATAGT		
	3410	3420	3430	3440	3450	3460	3470	3480	3490	3500
Ebola Bundibugyo '07	TTTGCAGAGTTGTGAAAATGCTAACATCTCTAACCCCTGTGCTACAAAACAACACCCCTTGCACACTGAATCCTAGCAACCGCATTTACTGACCTGGAAAG	Ebola IC '94	TTTGAAGACGTTACACAAGCACTAACATCAATTAACCAATGTCATACAAAACAGCGCTTTAACTTAGAGTCTCTCGAACAACCGCATCATAGATCTAGAGA	Ebola Zaire '76	TTTGAAGAGGTAGTACAAAATTTGGCTTCAATTTGGCTACTGTTGTGCAACAACCAACCATCCGATCAGAATCATTAAGAACACCGCATTTACGAGTCTTTGAGA		
	3510	3520	3530	3540	3550	3560	3570	3580	3590	3600
Ebola Bundibugyo '07	GTAGCCTGAARACCAAGTGTGAGATCACCAGATTTTCTGCACTAAATAGATCCTGTGCAAGATGGTGGCCAAAATATGATCTTCTAGTAAATGACGAC	Ebola IC '94	ATGGCTTAAAGCCCAATGTATGACATGGTAAAGTCAATTTCTGCAATGAATGATCTTGTGCTGATGGTGGTAAATAATGATCTCTGGTGGATGACAC	Ebola Zaire '76	ATGGTCTAAAGCCAGTTTATGATATGATGGCAAAAACAATCTCCCTCATTTGAAACAGGGTTTGTGCTGAGATGGTGTGCAAAAATATGATCTTCTGGTGGATGACAC		

FIG. 2

4410 4420 4430 4440 4450 4460 4470 4480 4490 4500
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

4510 4520 4530 4540 4550 4560 4570 4580 4590 4600
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

4610 4620 4630 4640 4650 4660 4670 4680 4690 4700
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

4710 4720 4730 4740 4750 4760 4770 4780 4790 4800
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

4810 4820 4830 4840 4850 4860 4870 4880 4890 4900
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

4910 4920 4930 4940 4950 4960 4970 4980 4990 5000
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

5010 5020 5030 5040 5050 5060 5070 5080 5090 5100
Ebola Bundibugyo '07
Ebola IC '94
Ebola Zaire '76

TTATATGTTTCAAAAATACAAAGTGAAGATTAAAGAAAAGCATCCCTTTACTTTGAGAGGCTAAATCTTTTATACCTTAACTTTTAAAGTAAAGTT
CAAAAGACTTACAAAACAAGGGTGAAGATTAAAGAAAAGCCCTCCTTCAAGTTGCAAGGAGCTAAATCTTAAAACITCATCTAGACTAAGGATAAATC
TTAAGTAAACCC--AAACAAAAGTGAAGATTAAAGAAAAGCCCTCCTCGCTGAGAGAGTGTTCCTTATTAAACCTTCACTCTTTGTAACCGTTGAGCAA

.....
GATCCTACCCATGAGGAGGCAATTCCTACTACCCGCGCAATACATAGAGGCTGTCTACCCCAATGAGAACCGGTTAGTCTAGTATCAACAGT
GATTCCAATCAGCATGAGGAGAAATCATCTCCACCGCAGCACTGAATACATGGAGCTGTTTACCCCAATGAGAACCAATGAATCTGTGTCAGACAAC
AATGTTAAAAAATATGAGCGGGTTATATTGCTACTGTCTCTGAATATATGAGGCGCCATATACCCCTGTCAGGTCAAAATTCACAATTCCTAGAGT

.....
ACTGCCAGTGGTCCGAACCTTCCAGCACCGGATGATGATGAGTGAFAACCTCCCACTCACCCGACCAATTTGCTGATGATAACATCGATCAATCCAA
ACTGCCAGTGGCTTAATACACAACAACCTGGTGTGATGACAAAATGATCTCCTCTAAATTCACCTCCGACAGTTGCGATGATAATATGATCATCCGA
GGCAACAGCAATACAGGCTTCTGTGACACCGGAGTCAGTCAATGGGGACACTCCATCGAAATCCACTCAGGCGCAATTTGCCGATGACACCATCGACCAATGCCA

.....
GTCAATACCAACACAGTGTTCATCAGCCTTTATCTCGAGGCAATGGTGAATGATGATTCGGGGCGAAGGTACTAATGAGCAAAATCTCTATATGGCT
GCCACACGCTAAACAGTGTGGCTCTGCATTTATTTGAAAGCTATGTAATATCTGGCCGAAAGTGTGCTGAAAGTGAAGCAAAATCCCAATCTGGCT
GCCACACAGGCGAGTGTGTCATCAGCATCACTTCAGGCTTGAAGCTATGGTGAATGATGATTCGGGGCGCAAAAGTGTGTAATGAGCAAAATCTCCAAATTTGGCT

.....
CCCCTTGGGTGTGCTGATCAAAAACAATATAGTTTGGACTCAACTACAGCTGCAATTTGCTCGCATCGTACACCACTCACCTTTGGCAAAAACCTCC
TCCCTGGGTGTCTGACCCAGAGACATATAGCTTTGATTCACCCCTGCTGCCATATGCTAGCATCATATACCTCATCTATTTGGCAAAAACCTCA
TCCCTTAGGTGTGCTGATCAAAAAGACCTACAGCTTTGACTCAACTAGCGCGCCATCATGCTTGTCTCATACACTACCCCATTCACCCATTTCCGGCAAGGCAACC

.....
AATCCGCTTGTGAGATCAATCGACTTGGTCTGGATCCCGATCACCCTTGGCGCTTCTAAGAAATAGAAATCAAGCCCTTCTTCGAAGAGTTTGTGC
AATCCCTTGTGAGAAATCAACCGACTTGGTCTGGCATACCCATCGACTTCAAGAAATAGAAATCAAGCCCTTCTTCACAGAGTTTGTGC
AATCCACTTGTGAGATCAATCGGCTGGTCTGGAAATCCCGGATCATCCCTCAGGCTCCTCGGAAATTTGGAACACAGGCTTCTCCAGGAGTTCTGTTTC

.....
TGCTCCAGTTCAATTCGCCGAGTATTTACTTTGACCTGACGGCTTAAAGCTGATCACTCAACCTTCCCGGCAACCTTGGAGGATGATACTCC
TACCTCCTGTACAACCTGCCAATATCTCACTTTTGTGATCTGACAGGCTGAAGTGTATCACCCGACCTCCCGGCAACCTTGGACAGATGAAATCC
TTCCGCCAGTCCAACTACCCAGTATTTCACTTTGATTTGACAGCACTCAAACTGATCAACCCCACTGCTGTGCTGCAACATGGACCGGATGACACTCC

FIG. 2

Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	5910 5920 5930 5940 5950 5960 5970 5980 5990 6000 GTAA-TTGTATGGTATCAAATCTTATAAGAAAAGAACACCGATGAAGATTAACCGCCAGAGAGCCAGGCGCTTCCTTCAATCATCAATTAACTTGTCAA ACGCACTTCTTATGCCA-CAGCTTATATAAGAAAAGAACTGTGTAAGAAATAGGCAACCGATGAGGCTAFCCTTCAATCTTGTGATTGAGCTTAAAG ATCCAAGTACAGACATTCGGCTTCTTAAATTAAGAAAATAATCGCGATGAAGATTAAGCCAGCAGTGAAGGTAAATCTTCTCTCTAGATTATTGTTTT
Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	6010 6020 6030 6040 6050 6060 6070 6080 6090 6100 TAGACAACCTAGTTTGATTAATCTACTCT-TCCTAGTGTGACAACACCTTTGCTGTGTAATTAATTAATATACCAAGTCAATGTTTACATCAGGAAT TGAATACAGAGTTCTAFACTGTTCTTGTCCACCGGTAATTCAGCCAGGCTAAGACAGTAGCTA-ATCACAAGTCAATCGGAGCGGTCAAGGAAT CCAGAGTAGGGGTCCTCAGCTCCTTTTCAATCGTGTAAACCAAAATAAACCTCCACTAGAAGGATATTTGGGGCAACAA-CACAATGGGCGTTACAGGAAT
Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	6110 6120 6130 6140 6150 6160 6170 6180 6190 6200 TCTACAATTCGCCGTTGAACGCTTCAGAAAACATCATTTTTTGTGGTAATAATCTATTTCACAAAGTTTTCCCTATCCCAATGGGCGTAGTTCCAC TCTGCAATTCGCCGTTGAGGCTTCAGAAAACATCTTTTGTGGTAAATTAATTCCTATTCCTTAAGCTTTTCAATCCCGTTGGGGTTGTACAC ATTGCAGTTACCCTGCTGATCGAATTCAGAGGACATCATCTTTCTTTGGTAAATTAATCTTTCCTCCAAAGACATTTTCCATCCCACTTGGAGTCAATCCAC
Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	6210 6220 6230 6240 6250 6260 6270 6280 6290 6300 AACAACTCTCCAGTAAAGTGAATATAGATAAATTTGCTGCGGATTAATCTTCCACAACTGACTGAAATCGGTCGGGTAACTTAGAAGGTA AACAACTCTCAAGTGAATATGACAAGTTTGTGTCGCGAGACAACTCTTCACACTAGCCAAATGAAAGTCACTGAGGTTGAACTTGGAGGCA AATAGCACATTAACAGTTAGTAGTTCGACAACACTTCTTGTGAGACAACACTGCTCACCACAATAATCGAGTCAAGTTGGAGTCAATCTCGAAGGGA
Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	6310 6320 6330 6340 6350 6360 6370 6380 6390 6400 ATGGATTCACCACTGATGATGATACCAACAGCAACAGAGAGATGGGATTCGAGCTGCTGTTCCACCACAAAGTTGGTGAATCGAAAGCTGGGCTGTA ATGGATGCAACTGATGATGATACCAACAGCAACAGAGAGATGGGATTCGAGCTGCTGTTCCACCACAAAGTTGGTGAATCGAAAGCTGGGCTGTA ATGGATGGCAACTGACGTGCTCCTTCGCAACTAAAGAGATGGGCTTCAGGTCGGGTGCTCCCAACAAAGTTGTTAAATTAAGAGCTGGTGAATGGGCTGTA
Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	6410 6420 6430 6440 6450 6460 6470 6480 6490 6500 AAACTGCTAACACTGCACTCAAGAAAGCAGATGGTGGAGTGGCAATGCTAAGCCCTGAGGGTGAAGGGTTCCCTCGCTGCCCTTAGTTGTGTCAC GAACTGTTAACCCTGGCTATAAAGAAAGTTGATGATGAGTGCCTACAGAGCCCTGAGGGAGTGAAGGATTTCCCGGTTGCCCTAATGTACAC AAACTGCTAACATTTGAATCAAATAACCTGACGGGAGTGTGTACTACAGAGCCAGGAGATTCGGGGTTCCCGGGTTCGCCCTGAGTGTGTCAC
Ebola Bundibugyo '07 Ebola IC '94 Ebola Zaire '76	6510 6520 6530 6540 6550 6560 6570 6580 6590 6600 AAGTTTCGAAACAGGGCGTGGCTGAGGTTACGCTTTCCAAAGAGGGCGCTTTCTTCTCTGTATGATCGACTGGCAATCAACAATCATCTATCGAA AAAAGTCTCAGGAACCTGGACCATGCCAGGAGGACTGCCTTTTCAGAAAGAGGAGCTTCTTCTCTGTATGACCGACTCGCATCAACAATCATTTATCGGG AAAAGTATCAGAACGGGACCGTGTGCCCGGAGACTTTGCCCTTCCATAAAGAGGGTCTTCTTCTCTGTATGATCGACTGGCTTCACAGTTATCTACCGGAG

FIG. 2

9610 9620 9630 9640 9650 9660 9670 9680 9690 9700
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 9710 9720 9730 9740 9750 9760 9770 9780 9790 9800
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 9810 9820 9830 9840 9850 9860 9870 9880 9890 9900
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 9910 9920 9930 9940 9950 9960 9970 9980 9990 10000
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 10010 10020 10030 10040 10050 10060 10070 10080 10090 10100
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 10110 10120 10130 10140 10150 10160 10170 10180 10190 10200
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 10210 10220 10230 10240 10250 10260 10270 10280 10290 10300
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76
 10310 10320 10330 10340 10350 10360 10370 10380 10390 10400
 Ebola Bundibugyo '07
 Ebola IC '94
 Ebola Zaire '76

FIG. 2

10410 10420 10430 10440 10450 10460 10470 10480 10490 10500

 Ebola Bundibugyo '07 AACAGATCGATACATAATAGGGATTGTT--TCATACTAGCTCTCTGCNAACAATGGCTAAGGCAACAGGTAGGTAACAATGGTTTCCACTAATAA
 Ebola IC '94 AGTGAACAAGCTCATACTAATCAAGGCTAATCCCTGGCCCTCCCTGGAGTC--CACAAATGGCCAAAGGCTACTGGGAGGTACAACCTTATCTCCCAAGAA
 Ebola Zaire '76 AGACAACAATAATTGATACT-----CCAGACCAACGACCAAGCTGAGAAAACCAATGGCTAAGCTACGGGACGATACAATCTAATATATCGCCCAAAAA

 10510 10520 10530 10540 10550 10560 10570 10580 10590 10600

 Ebola Bundibugyo '07 GGACCTCGAGAGGGGCTTGTGAGTGAATGTCACCGTTTATGATGATCAGACTATCCAGGGTGGGGTGCATTTGGGTTGGATTTGATTTGAC
 Ebola IC '94 AGATCTTGAATAAGGGCTGGTCTGATGACCTTTCACCTCTCAGTGGCCCAAGGCTCCAGGGTGAAGGTTACCTGGGCTGGATTTGAATTTGAT
 Ebola Zaire '76 GGACCTGGAGAAAGGGTGTCTTAAGCGACCTCTGTAACTTCTAGTAGCCAAACTATTACAGGGTGAAGTTTATTGGGCTGGTATTTGAGTTTGGAT

 10610 10620 10630 10640 10650 10660 10670 10680 10690 10700

 Ebola Bundibugyo '07 ATGCCCAAGAAAGGATGGCTCTACTTCATCGGTTAAATAACTGCTGACTTCGCTCCATGGTTCGATGACAAGGAATTTATTTCCTCATTTATTCAA
 Ebola IC '94 GTTACACAGAAAGGGATGGCTTATTCACAGCTCAAGCCAGTGTATTTGCTCCAGCTGATGACCCAGGAATTTATTTCCACATCTCTTTTCAA
 Ebola Zaire '76 GTGACTCACAAAGGAATGGCCCTATTGCATAGACTGAAACTAATGACTTTGCCCTGCATGGTCAATGACAAGGAATCTTTCTTCATTTATTCAA

 10710 10720 10730 10740 10750 10760 10770 10780 10790 10800

 Ebola Bundibugyo '07 ATTCAAATCTACTATTAGTCTCCCTCTGGCATTACGAGTGTATTCGGCAGCTGGTATTCAAGACCAGTTAATTGACCAATCTCTGGTAGAACCCGTT
 Ebola IC '94 ACCCGAATCTACAAATGAGTGGCCACTTTGGCCACTGGGGTCACTAGCAGCAGGTTTCAAGATCAGCTAATGATCAATCGTTGATCGAACCCCTT
 Ebola Zaire '76 ATCCGAAATCCACAATGAAATCACCCGCTGTGGCATTGAGAGTCACTCCITTCGACAGGATACAGGACCCAGCTGATTTGACCAGTCTTTGATTTGAACCCCTT

 10810 10820 10830 10840 10850 10860 10870 10880 10890 10900

 Ebola Bundibugyo '07 GGCCGGAGCCCTGAGCTTAGTCTCCGATTGGCTTTACAAACAACAACCAATTTCAAATGGCCAGCCAGCAGCTAAAGAGCAACTGAGCTTGAAG
 Ebola IC '94 GCGAGGAGCCCTAGGCTTAAATGCTGATGGCTTCTACTACTGGAACAACCACTTTCAAATGGCCACACAACAGGCTAAGGCACTAAGCTTAAA
 Ebola Zaire '76 AGCAGGAGCCCTTGGCTGATCTGATCTGANTGGCTGTAAACCAACAACAATCAACCACTGCTCAACAGCTGCTCAAGGAACAATGAGCCATAAA

 10910 10920 10930 10940 10950 10960 10970 10980 10990 11000

 Ebola Bundibugyo '07 ATGCTATCAATAGTGGCTTAATATCTTGAATTTCAATCAATGGACGCACTAGATGCTGAACTACAATGGACTTTGAGCAGTATCGAAATTTG
 Ebola IC '94 ATGTTGTCCTGGTGGATCAACATCTCTAAAGTTTCACTCAACCACTAGTACTACATGTTGTAATTAACAATGGACTTCTCAGTAGCATTTGAAATTTG
 Ebola Zaire '76 ATGCTGCTGTTGATTCGATCCAAATATTCTCAAGTTTATTACAAATGGATGCTTACATGCTGTAACCAACCGGATTTGAGCAGTATTTGAAATTTG

 11010 11020 11030 11040 11050 11060 11070 11080 11090 11100

 Ebola Bundibugyo '07 GCACCTAGAAATCATACCAATATCATCAAGAACCAACATCGGGTTTCTGGTGAATTTACAGGAGCCCTGATTAATCTGCCATGAAATCAAAAGAAACCCAGG
 Ebola IC '94 GCACCAAAAGCCATACAAATATAATATCCCGGACAAATATGGGTTTTTTGGTAGAGTTGCAAGAGCCCTGACAAATCAGCCATGAACACCAGAAAACCCAGG
 Ebola Zaire '76 GAACTCAAAATCATACAAATCATATACTCGAACTAATCGGGTTTTCTGGTGGAGCTTCCAAAGAACCCCGCAAAATCGGCAATGAACCCGATGAAGCCCTGG

FIG. 2

11950 11960 11970 11980 11990 12000
.....
AATAGTTACATTGCCCGAGTATGTTTACCTTTTACGAACTTTATCCGGGGAGGCTTATGCCCTGTCGAACCAAAAGTGCAGCCCAATTTCTTA
GGTAGCAACATTGCCAGGGATTTTATAGTACCTACATTTCTTAGGACTCTATCAGGAATGGTTCCTGCAAAATGATCCAAATGCGATCAATTTTATA
AGTGGGACATTCGCCCAATGATTTTATAGTCCCGATTTCTCAAGGCACGTGTCAGGCAATGGATTTCTGCTGTGTAGCCCGCTGCCAACAGTTCTTA

12050 12060 12070 12080 12090 12100
.....
GATGAAATAGTAAAGTATGTTTGCAGGATGCACCGTTTTAAAGATACTATTTTAGGCATGTTGGAGTACACGATGACATGTTGGAAAAAATTTTGGAC
GAAGAAATGTCATATATACCTACAGATATCGCTTCCAAACTATTAAGTTCGCGGAGTGCATACGATCATGTGGATAGGATTTTGGAC
GATGAAATCATTAAGTACACATGCRAGATGCTCTCTTCTTGAATAATTAATCTCAAAAATGGGTCTCAAGAAAGACTGTGTTGATGAACACTTTCAAG

12150 12160 12170 12180 12190 12200
.....
CAAGATTAAGGCTTTGATTTATGATTAATGAAATTTCTGCAACAATTTTATTTAGTCCGATTTAGCAATCTAACCGCTAGAGCGGCTGAATCGAGG
AAAAATTCGCAATCTAATTTGCGACATGAGTTTACATCAAAATGTTTCACTGGTATGATCTTGGCAATCTAGCACGTAGAGGCGCAATAATAGAGG
AGAAAATCTTATCTCAATTCAGGGCAATGAAATTTTACATCAAAATGTTTCTGCTATGATCTGGCTATTTTAACTCGAAGGGTAGATTAATAATCGAGG

12250 12260 12270 12280 12290 12300
.....
GAATAACCGTTCAACATGGTTGCAATGACGATTAATAGACATTTCTCGGTACCGTGTATATTTCTGGAAAATACCGTGTCAATGTTCTCACTC
GAAATACGCTCAACATGGTTGCAATGATTTGGTAGATACCTAGGTTTAGGAAATTAATTTTGGAAAATACCAATATCACTACTACCAGTG
AAACTCTAGATCAACATGGTTGTTTCATGATGATTAATAGACAATCTTAGGCTATGCGGACTATGTTTTTTGGAAAGATCCCAAATTTCAATGTTACCACCTG

12350 12360 12370 12380 12390 12400
.....
AACACAGAGGGGATTCCTCATCGAGTAAGGACTGGTATCAGCATCAATCTTCAAAGAAGCGGTTCAAGGTCACACACATATCGTGTCCAGTTCCACTG
GATACAGGCTCCACATCGAGCAAGGACTGGTATCAAGATCGGTTTCAAGGAGCTATCAAGGCCAFACACACATCGTGTCCATCTCTACAG
AACACACAAGGAATCCCCATGCTGCTATGGACTGGTATCAGGCATCAGTATTCAAAGAAGCGGTTCAAGGGCATAACACACATGTTGTTCTGTTCTACTG

12450 12460 12470 12480 12490 12500
.....
CAGATGTTTTAATTAATGTTAAGGACATCAATAACCTGTTTCAATCCACACATCATGCGAGCATTTGGCAAAATTTAGAAGATCTATCTGTTCTGACTA
CAGATGCTTAAATCAATGTTAAGGACATPAATCACCTGTCGATTAATTAATCTTACTGATTTGCTGTGGCAAACTAGAGATTCAGTTCAATTCAGATTA
CCGACGTTTGATAATGTTGCAAAAGATTTAATTAATGTCGATTCACACAACTCTAATCTCAAAAATAGCAGAGATTTGAGGATCCAGTTTGTCTGATTA

12550 12560 12570 12580 12590 12600
.....
TCCCAACCTGAACAATCTTAATCTGTAFAAGGCAAGGATTAATCTCCGATACCTGGTTTCAAGGTTTCAAGGTTAATAGGTCATAAAGTTTTAGAACCA
CCCTTTACAGAAACAGTGTCTGACCTATACAAAGCAGGAGATTTAATCTCAATGCTAGGATTCAGAGGTTACAGAGTTACAAAATTCCTTTGAGCGG
TCCCAATTTAAGATTTGTTCTATGCTTTTACCAGAGCGGAGTTACTTACTCTCCATATTAGGGTCTGATAGGGTATGATTAATAAGTTCCTCCGAAACCA

FIG. 2

	13410	13420	13430	13440	13450	13460	13470	13480	13490	13500
Ebola Bundibugyo '07	TTATCCTACAGGTAATGTTCAAACTTTA	TGTCAGATGGCCTTATTTGGCAGATG	GGATAGTAAAGCCCTTTCCCTAGTAA	CACTGATGGTAAAGCCCTTTCCCTAG	TAAAGCCCTTTCCCTAGTAAAGCCCT	TTCCCTAGTAAAGCCCTTTCCCTAG	TAAAGCCCTTTCCCTAGTAAAGCCCT	TTCCCTAGTAAAGCCCTTTCCCTAG	TAAAGCCCTTTCCCTAGTAAAGCCCT	TTCCCTAGTAAAGCCCTTTCCCTAG
Ebola IC '94	ATATCCAACAGCAATGTTCAAACTTTG	TCAGAGCTTTGTCAGATGGTAAAGCC	CTTTGTCAGATGGTAAAGCCCTTTG	TCAGAGCTTTGTCAGATGGTAAAGCC	CTTTGTCAGATGGTAAAGCCCTTTG	TCAGAGCTTTGTCAGATGGTAAAGCC	CTTTGTCAGATGGTAAAGCCCTTTG	TCAGAGCTTTGTCAGATGGTAAAGCC	CTTTGTCAGATGGTAAAGCCCTTTG	TCAGAGCTTTGTCAGATGGTAAAGCC
Ebola Zaire '76	TTATCCGACTCGCAATGTTCAAACTTTG	TGAAGCTCTGTTAGCTGATGGTCTT	GTGTAAGCAATTTCCCTAGTAAAGCC	CTTTCCCTAGTAAAGCCCTTTCCCTA	GTGTAAGCAATTTCCCTAGTAAAGCC	CTTTCCCTAGTAAAGCCCTTTCCCTA	GTGTAAGCAATTTCCCTAGTAAAGCC	CTTTCCCTAGTAAAGCCCTTTCCCTA	GTGTAAGCAATTTCCCTAGTAAAGCC	CTTTCCCTAGTAAAGCCCTTTCCCTA
Ebola Bundibugyo '07	13510	13520	13530	13540	13550	13560	13570	13580	13590	13600
Ebola IC '94	CAGAGGAAAGCCCTCTTGCACCAAGG	CTGTCGGCACCACACAAGTACGATTT	CCGGTGGAGAAATGCCACTGTTAGAG	CGCAGCAGTTCGGTGGAGAAATGCCA	CTGTTAGAGCGCAGCAGTTCGGTGG	AGAAATGCCACTGTTAGAGCGCAGC	AGTTCGGTGGAGAAATGCCACTGTTA	GAGCGCAGCAGTTCGGTGGAGAAAT	GCCACTGTTAGAGCGCAGCAGTTCGG	TGGAGAAATGCCACTGTTAGAGCGCA
Ebola Zaire '76	CAAAAAGAAAGCCCTTTGCAATCAAG	CGCTTGGCATCACAAAGTGCATCACA	CAAGTGCATTTGGTGGAGAAATGCCA	CTGTTAGAGCGCAGCAGTTCGGTGG	AGAAATGCCACTGTTAGAGCGCAGC	AGTTCGGTGGAGAAATGCCACTGTTA	GAGCGCAGCAGTTCGGTGGAGAAAT	GCCACTGTTAGAGCGCAGCAGTTCGG	TGGAGAAATGCCACTGTTAGAGCGCA	ATTTCCCTAGTAAAGCCCTTTCCCTA
Ebola Bundibugyo '07	13610	13620	13630	13640	13650	13660	13670	13680	13690	13700
Ebola IC '94	AAAAATACAACTTGGCAATTTAGATTA	GTAGATGAGTTTACAGCTCCATTTAT	TGAATGAACTGATTTGTTGTTAAAG	AAATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA
Ebola Zaire '76	AGAAATACAACTTGGCAATTTAGATTA	GTAGATGAGTTTACAGCTCCATTTAT	TGAATGAACTGATTTGTTGTTAAAG	AAATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA	ATTTGTTGTTAAAGAAATTTGTTA
Ebola Bundibugyo '07	13710	13720	13730	13740	13750	13760	13770	13780	13790	13800
Ebola IC '94	TACGATACCGCAATGTTATACATGTA	GTAGTATTAATCCCTCCATGGAGTTT	CGCTAGAAATCGGGAAGATCCCGGA	AGCCCTAGCTCT	CACATATACCACAGTGTATATACATG	TAGTATTAATCCCTCCATGGAGTTT	CGCTAGAAATCGGGAAGATCCCGGA	AGCCCTAGCTCT	CACATATACCACAGTGTATATACATG	TAGTATTAATCCCTCCATGGAGTTT
Ebola Zaire '76	TACGATACCGCAATGTTATACATGTA	GTAGTATTAATCCCTCCATGGAGTTT	CGCTAGAAATCGGGAAGATCCCGGA	AGCCCTAGCTCT	CACATATACCACAGTGTATATACATG	TAGTATTAATCCCTCCATGGAGTTT	CGCTAGAAATCGGGAAGATCCCGGA	AGCCCTAGCTCT	CACATATACCACAGTGTATATACATG	TAGTATTAATCCCTCCATGGAGTTT
Ebola Bundibugyo '07	13810	13820	13830	13840	13850	13860	13870	13880	13890	13900
Ebola IC '94	TACCGTGGTCATTTGGGGGAAATGAG	GGACTCCAAACAGAACTCTGGACAG	CAATTCATGTGCACAACTTCATTAG	TTCAGATCAAGACTGGCTTTCA	TACCGTGGTCATTTGGGGGAAATGAG	GGACTCCAAACAGAACTCTGGACAG	CAATTCATGTGCACAACTTCATTAG	TTCAGATCAAGACTGGCTTTCA	TACCGTGGTCATTTGGGGGAAATGAG	GGACTCCAAACAGAACTCTGGACAG
Ebola Zaire '76	TACCGTGGTCATTTGGGGGAAATGAG	GGACTCCAAACAGAACTCTGGACAG	CAATTCATGTGCACAACTTCATTAG	TTCAGATCAAGACTGGCTTTCA	TACCGTGGTCATTTGGGGGAAATGAG	GGACTCCAAACAGAACTCTGGACAG	CAATTCATGTGCACAACTTCATTAG	TTCAGATCAAGACTGGCTTTCA	TACCGTGGTCATTTGGGGGAAATGAG	GGACTCCAAACAGAACTCTGGACAG
Ebola Bundibugyo '07	13910	13920	13930	13940	13950	13960	13970	13980	13990	14000
Ebola IC '94	AAATTGAGATCTGCGGTAATGGGTGAT	AAATGCAATGCAATCAGATTCCTTT	CCGTAATTCCTCTAGACAGATTC	CAATTCAGATTC	AAATTGAGATCTGCGGTAATGGGTGAT	AAATGCAATGCAATCAGATTCCTTT	CCGTAATTCCTCTAGACAGATTC	CAATTCAGATTC	AAATTGAGATCTGCGGTAATGGGTGAT	AAATGCAATGCAATCAGATTCCTTT
Ebola Zaire '76	AAATTGAGATCTGCGGTAATGGGTGAT	AAATGCAATGCAATCAGATTCCTTT	CCGTAATTCCTCTAGACAGATTC	CAATTCAGATTC	AAATTGAGATCTGCGGTAATGGGTGAT	AAATGCAATGCAATCAGATTCCTTT	CCGTAATTCCTCTAGACAGATTC	CAATTCAGATTC	AAATTGAGATCTGCGGTAATGGGTGAT	AAATGCAATGCAATCAGATTCCTTT
Ebola Bundibugyo '07	14010	14020	14030	14040	14050	14060	14070	14080	14090	14100
Ebola IC '94	CAATGCTGCTCGGTAGCAGCAGT	TAGCCAAAGTCCACAGTGCCTG	TGGCAATTCCTTAAACCAGATG	AGACTTTTGTGCAATTCAGGCTTT	TAATGCCGTAGAGTAGCTGCTAG	CCTAGCCAAAGTCCACAGTGCCTG	TGGCAATTCCTTAAACCAGATG	AGACTTTTGTGCAATTCAGGCTTT	CAATGCTGCTCGGTAGCAGCAGT	TAGCCAAAGTCCACAGTGCCTG
Ebola Zaire '76	CAATGCTGCTCGGTAGCAGCAGT	TAGCCAAAGTCCACAGTGCCTG	TGGCAATTCCTTAAACCAGATG	AGACTTTTGTGCAATTCAGGCTTT	TAATGCCGTAGAGTAGCTGCTAG	CCTAGCCAAAGTCCACAGTGCCTG	TGGCAATTCCTTAAACCAGATG	AGACTTTTGTGCAATTCAGGCTTT	CAATGCTGCTCGGTAGCAGCAGT	TAGCCAAAGTCCACAGTGCCTG

FIG. 2

14910	14920	14930	14940	14950	14960	14970	14980	14990	15000
Ebola Bundibugyo '07
Ebola IC '94	GACTCCTATTTAGAYAGGTTGAGGAAATCACTGCAGAGATGGAGTTTGTGTGTAGCTAGACCACTGTGATCAAGTTCAGAGATGTCTT	GAACCTATCCTTAGATCGATGAGGAAATACCGTGCNAAGTGGAGCCTGTGTGGTTAGTTAATCTCGACCACTGTGATCAAGTTCAGAGATG	GACACCGGTTTTGGACAGACTGAGGAAATCACTGCAAAAGTGGAGCCTATGTTTACTTTCATTCCTTGTGATAATATCCTGGGAGGAGGCTTTTA
Ebola Zaire '76	15010	15020	15030	15040	15050	15060	15070	15080	15090
Ebola Bundibugyo '07
Ebola IC '94	ACTCAGATAACCTTGACACTGTGGACTTAGCACAGATTCCTCGGAGTACACCTGGCCACACATAGAGGAAAGCCAGCTCATTTGGACCAACACTTCCTT	ACCCAAATAAATGACAGATTGACATTGACAGATTCGAGGGAATATTCATGGCTCATTATTTAGAGGGAAGACCCTTATTGGAGCCACACTCCCAT
Ebola Zaire '76	15110	15120	15130	15140	15150	15160	15170	15180	15190
Ebola Bundibugyo '07
Ebola IC '94	GCATGTAGAACAAATTAATGTGTTTGGTCAAAATCGTACGAAACAAATGCCCTAAATGTCAAAATCTAGAAAATCCAAAAGGAGGCCATTTGTGTCAAT	GTATACTAGAACAACTAATATGTCTCTGGCTCAAACTATGAGCATGCCCTAATGTGCCAAATGTCAAAAGTTCAGAAAACCCCTTAAAGGGAAACCTTTTGTGTTCTAT	GTATGATGGAGCAATTCAAAAGTGGTGTGGCTGAAACCCCTAGCAAAATGTCGGGAGTGTCCAAATGCAAAAGCAACCAGGTGGGAAACCAATTCGGGTGTCAGT
Ebola Zaire '76	15210	15220	15230	15240	15250	15260	15270	15280	15290
Ebola Bundibugyo '07
Ebola IC '94	TGCAATTAAGAAACAACTGATGTGATGATGATGCCCGGAAATCAGTTCAGCGGTTAAATTTGGACCAATTTGGACCAATGGGACCGGTGTFACATCGGGTCTCGAACAGAGGAC	TGCAATTAAGAAACAACTGATGTGATGATGATGCCCGGAAATCAGTTCAGCGGTTAAATTTGGACCAATTTGGACCAATGGGACCGGTGTFACATCGGGTCTCGAACAGAGGAC	GGCAGTCAAGAAACAACTATGTTGATGATGATGCCCGGAAACGGACTCCCGGAAATGAGCTGGGAAATGCAATCCCATACATTTGGATCAAGAGCAGAGAGAT
Ebola Zaire '76	15310	15320	15330	15340	15350	15360	15370	15380	15390
Ebola Bundibugyo '07
Ebola IC '94	AAGATTTGGCAGCCGCAATCAAGCCTAAGTGTCCCTCTGCTCCTACGTAAGCAAGCAATAGAGTTGATCATACTAGACTTAACATGGGTTACCACAAAGTGGTTG	AAGATTTGGCAGCCGCAATCAAGCCTAAGTGTCCCTCTGCTCCTACGTAAGCAAGCAATAGAGTTGATCATACTAGACTTAACATGGGTTACCACAAAGTGGTTG	AAGATTTGGCAGCCGCAATCAAGCCTAAGTGTCCCTCTGCTCCTACGTAAGCAAGCAATAGAGTTGATCATACTAGACTTAACATGGGTTACCACAAAGTGGTTG
Ebola Zaire '76	15410	15420	15430	15440	15450	15460	15470	15480	15490
Ebola Bundibugyo '07
Ebola IC '94	CCAATAGTGTGATTTGTAAACCCTTTGTAGAGCCAGGATAAACCCTGTAGTTGTCAGGAGATCTTCAAAATGACGCTTCTCATTTATTCAGGGAACAT	CCAATAGTGTGATTTGTAAACCCTTTGTAGAGCCAGGATAAACCCTGTAGTTGTCAGGAGATCTTCAAAATGACGCTTCTCATTTATTCAGGGAACAT	CCAATAGTGTGATTTGTAAACCCTTTGTAGAGCCAGGATAAACCCTGTAGTTGTCAGGAGATCTTCAAAATGACGCTTCTCATTTATTCAGGGAACAT
Ebola Zaire '76	CGAACAGTCACTTACTTAGTTAAACCCTTTCAATAGTAGCAGGATAAATTAAGTGTTCAGAACAACTTCAAAATGACGCTTCTCAATTCACATTCACAGGAAATAT	CGAACAGTCACTTACTTAGTTAAACCCTTTCAATAGTAGCAGGATAAATTAAGTGTTCAGAACAACTTCAAAATGACGCTTCTCAATTCACATTCACAGGAAATAT	CGAACAGTCACTTACTTAGTTAAACCCTTTCAATAGTAGCAGGATAAATTAAGTGTTCAGAACAACTTCAAAATGACGCTTCTCAATTCACATTCACAGGAAATAT
Ebola Bundibugyo '07
Ebola IC '94	CGTACATCGGTATATAAGCAATAGCAGCCCTCATTTCTTTCAGTGCAGTAATGATGATAGTATTCGCGGAGCATTTGGTGTGCGACAATACACTTCGGG	CGTACATCGGTATATAAGCAATAGCAGCCCTCATTTCTTTCAGTGCAGTAATGATGATAGTATTCGCGGAGCATTTGGTGTGCGACAATACACTTCGGG	CGTACATCGGTATATAAGCAATAGCAGCCCTCATTTCTTTCAGTGCAGTAATGATGATAGTATTCGCGGAGCATTTGGTGTGCGACAATACACTTCGGG
Ebola Zaire '76	TGTCATCGATATAAGTCAATATAGTCCACACTCAATTTATGCGAAATAGGATGAGTAAATTTCTGCTACTAGTGTGGTGTGCGACAATACACTTCGGG	TGTCATCGATATAAGTCAATATAGTCCACACTCAATTTATGCGAAATAGGATGAGTAAATTTCTGCTACTAGTGTGGTGTGCGACAATACACTTCGGG	TGTCATCGATATAAGTCAATATAGTCCACACTCAATTTATGCGAAATAGGATGAGTAAATTTCTGCTACTAGTGTGGTGTGCGACAATACACTTCGGG

FIG. 2

18610 | 18620 | 18630 | 18640 | 18650 | 18660 | 18670 | 18680 | 18690 | 18700
|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 Ebola Bundibugyo '07 AAGAAAATTAAGTGTGGTTATGCAATTAATGACATCACAGATGGATA--TAATATAGTTAATCTTACCCTAA----ATGTTGAGTTAAGTAATTTGA
 Ebola IC '94 ATTAAGAAAAGT--TAATCTGCTTGGTTTAAATATATACTTAAATATATCG--ACAATATAGTTAAGCGTCTCATCA----CTCAAAATTTTCATTAACA-AA
 Ebola Zaire '76 ATAATAAACT--CTGCACCTCTTATAAATTAAGCTTTAAGCAAGGTCGGGCTCATATTTGTTATTAATAAATAATGTTGATCAATATCCCTGTCAGATGG

18710 | 18720 | 18730 | 18740 | 18750 | 18760 | 18770 | 18780 | 18790 | 18800
|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 Ebola Bundibugyo '07 AGTTATAATTAAGTATGATGCTTATACTAT----AAATAATAGCTATACCAAGTATACAAAGAAAGTTAAGATTTGATTTGATTTCAAATTAATTCACAGAA
 Ebola IC '94 AGAAGTACTCTGAGTATATTCACATATCAT----ATGATGATTAACAATAT--AAGCA--ACGCATGATCGGCTTCCCTTACTTATTTGTTGTTGTCACCGCAGT
 Ebola Zaire '76 AATAGTGTGTTGGTTGATAACACAACTCTTAAACAAAAATGATCTTTT--AAGATTAAGTTTTTATAAATATATCACTTTAATTTGTCGTTTTTAAAAA

18810 | 18820 | 18830 | 18840 | 18850 | 18860 | 18870 | 18880 | 18890 | 18900
|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 Ebola Bundibugyo '07 CT---TGATGATTAAT--AATAAAAAGTCTCAGTTGTTGGTTGT--TGAGTTGTAAAAACCTCCCGTTAA--AAATTTTATTTTCCACTTATAACTTAATAATAATC
 Ebola IC '94 CG-----TTGTACTACC--TCGAAAATCCAAAACAATAAATCGGTCTATCCCGCATTTAGTGTCTT--TAATTTAAGATCT--CAAAATCCAAAACACTGGGT
 Ebola Zaire '76 CGGTGATAGCCTTAATCTTTTGTGTAATAAAGAGATTAGGTGTAATAACCTTAAACATTTTGTCTAGTAAGCTACTATTT--CATACAGAATGATAAAATTT

18910 | 18920 | 18930 | 18940 | 18950 | 18960 | 18970 | 18980 | 18990 | 19000
|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 Ebola Bundibugyo '07 ATAGATCAGTATGAGTTGAGGCTATTCAAACCCTTAGAAAATTTGTCGATGTTTT---TTACCATGTCAAATCTTGAATTCAAATGATTTGGAGGCTT
 Ebola IC '94 TTATGTTGATGTAATCAATAATACCGAAATGCTTGATATTAATAAATAAAGCTTAAAGGATTTTCTTAAACCGTGATCTAGGTATATAGGAAAGCTC
 Ebola Zaire '76 AAAGAAAAGCAGGACTGTAAAATCAGAAAATACCTTCT--TTACAATAATAGCAGACTAGATAATAAATCTCGGTAAATGATAATTAAGACATTTGACCCAC

19010 | 19020 | 19030 | 19040 | 19050 | 19060 | 19070 | 19080 | 19090 | 19100
|.....|.....|.....|.....|.....|.....|.....|.....|.....|
 Ebola Bundibugyo '07 GTCGATAAATTCAGTAATTAACATTAAGTCAATTAAGTGTGGAACCTCATTTGGATATTTGATCGTACACAAA--TATCTTTACAAAATTTGTTTTCTCTTTTTTGT
 Ebola IC '94 GATCAGATGTCCTTACTCAGAAAAGAAAACGGAAGCCCTATTGSCCATTTAATCGTACACAAAATAATCTTTACCAAAATTTGTTTTCTCTTTTTTGT
 Ebola Zaire '76 GCTCATCAGAAAGGCTGCCAGATAAATACGTTGCAAAAGGATTCCTGGAAAATGGTCCACACAAAATTTAAAAATTAATCTATTTCTCTTTTTTGT

.....|...
 Ebola Bundibugyo '07 GTGTCCA
 Ebola IC '94 GTGTCCA
 Ebola Zaire '76 GTGTCCA

HUMAN EBOLA VIRUS SPECIES AND COMPOSITIONS AND METHODS THEREOF

RELATED APPLICATIONS

[0001] This application claims priority benefit of U.S. Provisional Application 61/108,175 filed 24 Oct. 2008; the contents of which are hereby incorporated by reference.

DEPOSIT STATEMENT

[0002] The invention provides the isolated human Ebola (hEbola) viruses denoted as Bundibugyo (EboBun) deposited with the Centers for Disease Control and Prevention (“CDC”; Atlanta, Ga., United States of America) on Nov. 26, 2007 and accorded an accession number 200706291. This deposit was not made to an International Depository Authority (IDA) as established under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, and is a non-Budapest treaty deposit. The deposited organism is not acceptable by American Type Culture Collection (ATCC), Manassas, Va., an International Depository Authority (IDA) as established under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. Samples of the stated Deposit Accession No. 200706291 will be made available to approved facilities for thirty years from the date of deposit, and for the lifetime of the patent issuing from, or claiming priority to this application.

FIELD OF THE INVENTION

[0003] The invention is related to compositions and methods directed to a novel species of human Ebola (hEbola) virus.

BACKGROUND OF THE INVENTION

[0004] The family Filoviridae consists of two genera, Marburgvirus and Ebolavirus, which have likely evolved from a common ancestor¹. The genus Ebolavirus includes four species: Zaire, Sudan, Reston and Côte d’Ivoire (Ivory Coast) ebolaviruses, which have, with the exception of Reston and Côte d’Ivoire ebolaviruses, been associated with large hemorrhagic fever (HF) outbreaks in Africa with high case fatality (53-90%)².

[0005] Viruses of each species have genomes that are at least 30-40% divergent from one another, a level of diversity that presumably reflects differences in the ecological niche they occupy and in their evolutionary history. Identification of the natural reservoir of ebolaviruses remains somewhat elusive, although recent PCR and antibody data suggest that three species of arboreal fruit bats may be carriers of Zaire ebolavirus³. No data has yet been published to suggest reservoirs for the Sudan, Reston and Côte d’Ivoire ebolavirus species. However, a cave-dwelling fruit bat has been recently implicated as a natural host for marburgvirus^{4, 5}, supporting the hypothesis that different bat species may be the reservoir hosts for the various filoviruses.

[0006] Filovirus outbreaks are sporadic, sometimes interspersed by years or even decades of no apparent disease activity. The last new species of ebolavirus was discovered 14 years ago (1994), in Cote d’Ivoire (Ivory Coast), and involved a single non-fatal case, a veterinarian who performed an autopsy on an infected chimpanzee found in the Tai Forest⁶. No further disease reports have been associated with Côte

d’Ivoire ebolavirus, in contrast to Zaire and Sudan ebolaviruses which have each caused multiple large outbreaks over the same time period.

[0007] In late November 2007, HF cases were reported in the townships of Bundibugyo and Kikyo in Bundibugyo District, Western Uganda. The outbreak continued through January 2008, and resulted in approximately 149 cases and 37 deaths⁷. Laboratory investigation of the initial 29 suspect-case blood specimens by classic methods (antigen capture, IgM and IgG ELISA) and a recently developed random-primed pyrosequencing approach identified this to be an Ebola HF outbreak associated with a new discovered ebolavirus species. These specimens were negative when initially tested with highly sensitive real-time RT-PCR assays specific for all known Zaire and Sudan ebolaviruses and Marburg viruses. This new species is referred to herein as “the Bundibugyo species”, abbreviated “EboBun”.

[0008] Accordingly, compositions and methods directed to the new Ebola virus species are described herein and the most closely related Ebola Ivory Coast species, which compositions and methods are useful for diagnosis and prevention of human Ebola virus infection; including related vaccine development, and prevention of hemorrhagic fever in a human population.

SUMMARY OF THE INVENTION

[0009] The present invention is based upon the isolation and identification of a new human Ebola virus species, EboBun. EboBun was isolated from the patients suffering from hemorrhagic fever in a recent outbreak in Uganda. The isolated virus is a member of the Filoviridae family, a family of negative sense RNA viruses. Accordingly, the invention relates to the isolated EboBun virus that morphologically and phylogenetically relates to known members filoviridae.

[0010] In one aspect, the invention provides the isolated EboBun virus deposited with the Centers for Disease Control and Prevention (“CDC”; Atlanta, Ga., United States of America) on Nov. 26, 2007 and accorded an accession number 200706291, as stated in the paragraph entitled “DEPOSIT STATEMENT” supra.

[0011] In another aspect, the invention provides an isolated hEbola EboBun virus comprising a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: a) a nucleotide sequence set forth in SEQ ID NO: 1; b) a nucleotide sequence that hybridizes to the sequence set forth in SEQ ID NO: 1 under stringent conditions; and c) a nucleotide sequence that has at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity to the SEQ ID NO: 1. In another aspect, the invention provides the complete genomic sequence of the hEbola virus EboBun.

[0012] In a related aspect, the invention provides nucleic acid molecules isolated from EboBun, or fragments thereof.

[0013] In another aspect, the invention provides proteins or polypeptides that are isolated from the EboBun, including viral proteins isolated from cells infected with the virus but not present in comparable uninfected cells; or fragments thereof. In one embodiment of the present invention, the amino acid sequences of the proteins or polypeptides are set forth in SEQ ID NOS: 2-9 and 59, or fragments thereof.

[0014] In a related aspect, the invention provides an isolated polypeptide encoded by the nucleic acid molecule of the inventive hEbola EboIC (Sequence ID No. 10) virus described above.

[0015] In another aspect, the invention provides an isolated hEbola EboIC virus comprising a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: a) a nucleotide sequence set forth in SEQ ID NO: 10; b) a nucleotide sequence that hybridizes to the sequence set forth in SEQ ID NO: 10 under stringent conditions; and c) a nucleotide sequence that has at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity to the SEQ ID NO: 10. In another aspect, the invention provides the complete genomic sequence of the hEbola virus EboIC.

[0016] In a related aspect, the invention provides nucleic acid molecules isolated from EboIC, or fragments thereof.

[0017] In another aspect, the invention provides proteins or polypeptides that are isolated from the EboIC, including viral proteins isolated from cells infected with the virus but not present in comparable uninfected cells; or fragments thereof. In one embodiment of the present invention, the amino acid sequences of the proteins or polypeptides are set forth in SEQ ID NOs: 11-19, or fragments thereof.

[0018] In a related aspect, the invention provides an isolated polypeptide encoded by the nucleic acid molecule of the inventive hEbola EboIC virus described above.

[0019] In other aspects, the invention relates to the use of the isolated hEbola virus for diagnostic and therapeutic methods based on EbBun, EboIC, or a combination thereof. In one embodiment, the invention provides a method of detecting in a biological sample an antibody immunospecific for the genus of West African Ebola Species constituting hEbola EbBun and EboIC virus using at least one the inventive isolated hEbola virus described herein, or any of the inventive proteins or polypeptides as described herein. In another specific embodiment, the invention provides a method of screening for an antibody which immunospecifically binds and neutralizes hEbola EboBun. Such an antibody is useful for a passive immunization or immunotherapy of a subject infected with hEbola.

[0020] In another aspect, the invention provides an isolated antibody or an antigen-binding fragment thereof which immunospecifically binds to the hEbola virus of the invention described above.

[0021] In other aspects, the invention provides methods for detecting the presence, activity or expression of the Glade of Bundibungyo-Ivory Coast hEbola virus in a biological material, such as cells, blood, saliva, urine, feces and so forth; and specifically at least one of EbBun or EboIC.

[0022] In a related aspect, the invention provides a method for detecting the presence of the inventive hEbola virus described above in a biological sample, the method includes (a) contacting the sample with an agent that selectively binds to a West African hEbola virus; and (b) detecting whether the compound binds to the West African hEbola virus in the sample.

[0023] In another aspect, the invention provides a method for detecting the presence of the inventive polypeptide described above, in a biological sample, said method includes (a) contacting the biological sample with an agent that selectively binds to the polypeptide; and (b) detecting whether the agent binds to the polypeptide in the sample. In another aspect, the invention provides a method for detecting the presence of a first nucleic acid molecule derived from the inventive hEbola virus described above in a biological sample, the method comprising: (a) contacting the biological

sample with an agent that selectively binds to the polypeptide; and (b) detecting whether the agent binds to the polypeptide in the sample.

[0024] In another aspect, the invention provides a method for propagating the hEbola virus in host cells comprising infecting the host cells with the inventive isolated hEbola virus described above, culturing the host cells to allow the virus to multiply, and harvesting the resulting virions. Also provided by the present invention are host cells infected with the inventive hEbola virus described above.

[0025] In another aspect, the invention provides a method of detecting in a biological sample the presence of an antibody that immunospecifically binds hEbola virus, the method comprising: (a) contacting the biological sample with the inventive host cell host described above; and (b) detecting the antibody bound to the cell.

[0026] In another aspect, the invention provides vaccine preparations, comprising the inventive hEbola virus, including recombinant and chimeric forms of the virus, nucleic acid molecules comprised by the virus, or protein subunits of the virus. The invention also provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of the inventive hEbola virus described above, and a pharmaceutically acceptable carrier. In one embodiment, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a protein extract of the inventive hEbola virus described above, or a subunit thereof; and a pharmaceutically acceptable carrier. In another, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or a complement thereof, and a pharmaceutically acceptable carrier. In another, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a nucleic acid molecule comprising any of inventive the nucleotide sequences as described above, or a complement thereof, and a pharmaceutically acceptable carrier.

[0027] In a related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of the inventive hEbola virus described above, and a pharmaceutically acceptable carrier. In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of a protein extract of the inventive hEbola virus described above or a subunit thereof, and a pharmaceutically acceptable carrier. In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or a complement thereof, and a pharmaceutically acceptable carrier. In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of a nucleic acid molecule comprising the inventive nucleotide sequence as described above or a complement thereof, and a pharmaceutically acceptable carrier. In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of any of the inventive polypeptides described above.

[0028] In another aspect, the present invention provides pharmaceutical compositions comprising antiviral agents of the present invention and a pharmaceutically acceptable carrier. In a specific embodiment, the antiviral agent of the invention is an antibody that immunospecifically binds hEbola

virus or any hEbola epitope. In another specific embodiment, the antiviral agent is a polypeptide or protein of the present invention or nucleic acid molecule of the invention.

[0029] In a related aspect, the invention provides a pharmaceutical composition comprising a prophylactically or therapeutically effective amount of an anti-hEbola EboBun agent and a pharmaceutically acceptable carrier.

[0030] The invention also provides kits containing compositions and formulations of the present invention. Thus, in another aspect, the invention provides a kit comprising a container containing the inventive immunogenic formulation described above. In another aspect, the invention provides a kit comprising a container containing the inventive vaccine formulation described above. In another, the invention provides a kit comprising a container containing the inventive pharmaceutical composition described above. In another, the invention provides a kit comprising a container containing the inventive vaccine formulation described above. In another, the invention provides a method for identifying a subject infected with the inventive hEbola virus described above, comprising: (a) obtaining total RNA from a biological sample obtained from the subject; (b) reverse transcribing the total RNA to obtain cDNA; and (c) amplifying the cDNA using a set of primers derived from a nucleotide sequence of the inventive hEbola virus described above.

[0031] The invention further relates to the use of the sequence information of the isolated virus for diagnostic and therapeutic methods.

[0032] In another aspect, the present invention provides methods for screening antiviral agents that inhibit the infectivity or replication of hEbola virus or variants thereof.

[0033] The invention further provides methods of preparing recombinant or chimeric forms of hEbola.

BRIEF DESCRIPTION OF THE DRAWINGS

[0034] FIG. 1 represents a Phylogenetic tree comparing full-length genomes of Ebolavirus and Marburg virus by Bayesian analysis;

[0035] FIG. 2 represents an alignment of genomes of novel hEbola EboBun (SEQ ID NO: 1) referred to below as “Ebola Bundibugyo” or “EboBun”, and hEbola Zaire (SEQ ID NO: 20); referred to below as “Ebola Zaire ’76” or “EboZ” and hEbola Ivory Coast (SEQ ID NO: 10) also referred to below as “EboIC”.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0036] It is to be understood that the present invention is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

[0037] Due to the sequence divergence of EboBun relative to all previously recognized ebolaviruses, the present invention has utility in design of diagnostic assays to monitor Ebola HF disease in humans and animals, and develop effective antivirals and vaccines.

[0038] The EboBun virus of the present invention is genetically distinct, differing by more than 30% at the genome level from all other known ebolavirus species. The unique nature of this virus created challenges for traditional filovirus molecular based diagnostic assays and genome sequencing approaches. Instead, over 70% of the virus genome was

sequenced using a recently developed random-primed pyrosequencing approach which allowed the rapid development of molecular detection assay which were deployed in the disease outbreak response. This random-primed pyrosequencing draft sequence allowed faster completion of the whole genome sequence using traditional primer walking approach and confirmation that the EboBun virus represented a new ebolavirus species.

Definitions

[0039] The definitions herein provided are operative throughout the entire description of the invention set forth herein, including the Summary of the Invention.

[0040] The term “an antibody or an antibody fragment that immunospecifically binds a polypeptide of the invention” as used herein refers to an antibody or a fragment thereof that immunospecifically binds to the polypeptide encoded by the nucleotide sequence of SEQ ID NO: 1 (EboBun), or a fragment thereof, and does not non-specifically bind to other polypeptides. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention may cross-react with other antigens. Preferably, an antibody or a fragment thereof that immunospecifically binds to a polypeptide of the invention does not cross-react with other antigens. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention can be identified by, for example, immunoassays or other techniques known to those skilled in the art, or otherwise as described herein.

[0041] An “isolated” or “purified” peptide or protein is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language “substantially free of cellular material” includes preparations of a polypeptide/protein in which the polypeptide/protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, a polypeptide/protein that is substantially free of cellular material includes preparations of the polypeptide/protein having less than about 30%, 20%, 10%, 5%, 2.5%, or 1% (by dry weight) of contaminating protein. When the polypeptide/protein is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation.

[0042] When polypeptide/protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the polypeptide/protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than polypeptide/protein fragment of interest. In a preferred embodiment of the present invention, polypeptides/proteins are isolated or purified.

[0043] An “isolated” nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Moreover, an “isolated” nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. In a preferred embodiment of the invention, nucleic acid molecules encoded

ing polypeptides/proteins of the invention are isolated or purified. The term "isolated" nucleic acid molecule does not include a nucleic acid that is a member of a library that has not been purified away from other library clones containing other nucleic acid molecules.

[0044] The term "portion" or "fragment" as used herein includes the specified fragment lengths, and all integers in between, inclusive of the specified end points in a specified range, and inclusive of any length up to the full length of a protein, polypeptide, or nucleic acid.

[0045] The term "having a biological activity of the protein" or "having biological activities of the polypeptides of the invention" refers to the characteristics of the polypeptides or proteins having a common biological activity, similar or identical structural domain, and/or having sufficient amino acid identity to the polypeptide encoded by the nucleotide sequence of SEQ ID NO: 1 (EboBun). Such common biological activities of the polypeptides of the invention include antigenicity and immunogenicity.

[0046] The term "under stringent condition" refers to hybridization and washing conditions under which nucleotide sequences having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% identity to each other remain hybridized to each other. Such hybridization conditions are described in, for example but not limited to, Current Protocols in Molecular Biology, John Wiley & Sons, NY (1989), 6.3.1-6.3.6; Basic Methods in Molecular Biology, Elsevier Science Publishing Co., Inc., NY (1986), pp. 75-78, and 84-87; and Molecular Cloning, Cold Spring Harbor Laboratory, NY (1982), pp. 387-389, and are well known to those skilled in the art. A preferred, non-limiting example of stringent hybridization conditions is hybridization in 6× sodium chloride/sodium citrate (SSC), 0.5% SDS at about 68° C. followed by one or more washes in 2×SSC, 0.5% SDS at room temperature. Another preferred, non-limiting example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C., followed by one or more washes in 0.2×SSC, 0.1% SDS at about 50-65° C.

[0047] The term "variant" as used herein refers either to a naturally occurring genetic mutant of hEbola EboBun, or hEbola EboIC, or a recombinantly prepared variation of these hEbola species, each of which contain one or more mutations in its genome compared to the hEbola of SEQ ID NO: 1 or 10. The term "variant" may also refer either to a naturally occurring variation of a given peptide or a recombinantly prepared variation of a given peptide or protein in which one or more amino acid residues have been modified by amino acid substitution, addition, or deletion.

[0048] "Homology" refers to sequence similarity or, alternatively, sequence identity, between two or more polynucleotide sequences or two or more polypeptide sequences.

[0049] The terms "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of identical nucleotide matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps in the sequences being compared in order to optimize alignment between two sequences, and therefore achieve a more meaningful comparison of the two sequences.

[0050] Percent identity between polynucleotide sequences may be determined using one or more computer algorithms or programs known in the art or described herein. For example, percent identity can be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the

MEGALIGN version 3.12e sequence alignment program. This program is part of the LASERGENE software package, a suite of molecular biological analysis programs (DNASTAR, Madison, Wis.). CLUSTAL V is described in Higgins, D. G. and P. M. Sharp (1989; CABIOS 5:151-153) and in Higgins, D. G. et al. (1992; CABIOS 8:189-191). For pairwise alignments of polynucleotide sequences, the default parameters are set as follows: Ktuple=2, gap penalty=5, window=4, and "diagonals saved"=4. The "weighted" residue weight table is selected as the default.

[0051] Alternatively, a suite of commonly used and freely available sequence comparison algorithms which can be used is provided by the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) (Altschul, S. F. et al. (1990) J. Mol. Biol. 215:403-410), which is available from several sources, including the NCBI, Bethesda, Md., and on the NCBI World Wide Web site available on the Internet. The BLAST software suite includes various sequence analysis programs including "blastn," that is used to align a known polynucleotide sequence with other polynucleotide sequences from a variety of databases. Also available is a tool called "BLAST 2 Sequences" that is used for direct pairwise comparison of two nucleotide sequences. "BLAST 2 Sequences" can be accessed and used interactively on the Internet via the NCBI World Wide Web site as well. The "BLAST 2 Sequences" tool can be used for both blastn and blastp (discussed below). BLAST programs are commonly used with gap and other parameters set to default settings. For example, to compare two nucleotide sequences, one may use blastn with the "BLAST 2 Sequences" tool Version 2.0.12 (Apr. 21, 2000) set at default parameters. Such default parameters may be, for example: Matrix: BLOSUM62; Reward for match: 1; Penalty for mismatch: -2; Open Gap: 5 and Extension Gap: 2 penalties; Gap×drop-off: 50; Expect: 10; Word Size: 11; Filter: on.

[0052] Percent identity may be measured over the length of an entire defined sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined sequence, for instance, a fragment of at least 20, at least 30, at least 40, at least 50, at least 70, at least 100, or at least 200 contiguous nucleotides. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures, or sequence listing, may be used to describe a length over which percentage identity may be measured.

[0053] The phrases "percent identity" and "% identity", as applied to polypeptide sequences, refer to the percentage of identical residue matches between at least two polypeptide sequences aligned using a standardized algorithm. Methods of polypeptide sequence alignment are well known. Some alignment methods take into account conservative amino acid substitutions. Such conservative substitutions, explained in more detail above, generally preserve the charge and hydrophobicity at the site of substitution, thus preserving the structure (and therefore function) of the polypeptide. The phrases "percent similarity" and "% similarity", as applied to polypeptide sequences, refer to the percentage of residue matches, including identical residue matches and conservative substitutions, between at least two polypeptide sequences aligned using a standardized algorithm. In contrast, conservative substitutions are not included in the calculation of percent identity between polypeptide sequences.

[0054] Percent identity between polypeptide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGA-LIGN version 3.12e sequence alignment program (described and referenced above). For pairwise alignments of polypeptide sequences using CLUSTAL V, the default parameters are set as follows: Ktuple=1, gap penalty=3, window=5, and “diagonals saved”=5. The PAM250 matrix is selected as the default residue weight table.

[0055] Alternatively the NCBI BLAST software suite may be used. For example, for a pairwise comparison of two polypeptide sequences, one may use the “BLAST 2 Sequences” tool Version 2.0.12 (Apr. 21, 2000) with blastp set at default parameters. Such default parameters may be, for example: Matrix: BLOSUM62; Open Gap: 11 and Extension Gap: 1 penalties; Gap×drop-off: 50; Expect: 10; Word Size: 3; Filter: on.

[0056] Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance, a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or sequence listing, may be used to describe a length over which percentage identity may be measured.

[0057] The term “agent” encompasses any chemical, biochemical, or biological molecule; such as small molecules, proteins, polypeptides, antibodies, nucleic acid molecules including DNA or RNA, and the like.

Methods and Compositions Related to the Inventive hEbola

[0058] The present invention is based upon the isolation and identification of a new human Ebola virus species, EboBun and the sequencing of the only other known West African Ebola species EboIC. EboBun was isolated from the patients suffering from hemorrhagic fever in a recent outbreak in Uganda. The isolated virus is a member of the Filoviridae family, a family of negative sense RNA viruses. Accordingly, the invention relates to the isolated EboBun or EBOIC virus that morphologically and phylogenetically relates to known members filoviridae.

[0059] In another aspect, the invention provides an isolated hEbola virus including a nucleic acid molecule with a nucleotide sequence that is preferably: a) a nucleotide sequence set forth in SEQ ID NO: 1; b) a nucleotide sequence that hybridizes to the sequence set forth in SEQ ID NO: 1 under stringent conditions; or c) a nucleotide sequence that has at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity to the SEQ ID NO: 1. In one embodiment of the present invention, the hEbola virus is killed. In another, the virus is attenuated. In another, the infectivity of the attenuated hEbola virus is reduced. In another, the infectivity is reduced by at least 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 250-fold, 500-fold, or 10,000-fold. In another, the replication ability of the attenuated hEbola virus is reduced. In another, the replication ability of the attenuated virus is reduced by at least 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 250-fold, 500-fold, 1,000-fold, or 10,000-fold. In another, the protein synthesis ability of the attenuated virus is reduced. In another, the protein synthesis ability is reduced by at least 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 250-fold, 500-fold, 1,000-fold, or

10,000-fold. In another, the assembling ability of the attenuated hEbola virus is reduced. In another, the assembling ability of the attenuated virus is reduced by at least 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 250-fold, 500-fold, 1,000-fold, or 10,000-fold. In another, the cytopathic effect of the attenuated hEbola virus is reduced. In another, the cytopathic effect is reduced by at least 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 250-fold, 500-fold, 1,000-fold, or 10,000-fold.

[0060] In another aspect, the invention provides the complete genomic sequence of the hEbola virus EboBun or EboIC. In a specific embodiment, the virus includes a nucleotide sequence of SEQ ID NOS: 1 or 10, respectively.

[0061] In a related aspect, the invention provides nucleic acid molecules isolated from EboBun, EboIC, or fragments thereof. In one embodiment of the present invention, the isolated nucleic acid molecule includes the nucleotide sequence of SEQ ID NOS: 1 or 10, or a complement thereof. In another, the nucleic acid molecule includes a nucleotide sequence having at least 4, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 4600, 4700, 4800, or 4900 contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 1, or a complement thereof; with the proviso that the nucleotide sequence is not comprised by the nucleotide sequence set forth in SEQ ID NO: 20 (Ebola Zaire nucleotide sequence); or at least 5000, 5500, 5600, 5700, 5800, 5900, 6000, 6100, 6200, 6300, 6400, 6500, or 6600 contiguous nucleotides of the nucleotide sequence of SEQ ID NOS: 1 or 10, or a complement thereof. In another embodiment, the isolated nucleic acid molecule includes a nucleotide sequence that encodes the EboBun amino acid sequence of SEQ ID NOS: 2-9 or 59, the EboIC amino acid sequence of SEQ ID NOS: 11-19, or a complement of the nucleotide sequence that encodes the EboBun amino acid sequences of SEQ ID NOS: 2-9 or 59 or the EboIC amino acid sequences of SEQ ID NOS: 11-19. In another, the isolated nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS: 1 or 10 or a complement thereof, wherein the nucleic acid molecule encodes an amino acid sequence which has a biological activity exhibited by a polypeptide encoded by the nucleotide sequence of SEQ ID NOS: 1 or 10. In another, nucleic acid molecule is RNA. In another, nucleic acid molecule is DNA.

[0062] In another aspect, the invention provides proteins or polypeptides that are isolated from the EboBun, including viral proteins isolated from cells infected with the virus but not present in comparable uninfected cells. In one embodiment of the present invention, the amino acid sequences of the proteins or polypeptides are set forth in SEQ ID NOS: 2-9, 59, or 11-19, or fragments thereof. In one embodiment, polypeptides or proteins of the present invention have a biological activity of the protein (including antigenicity and/or immunogenicity) encoded by the sequence of SEQ ID NOS: 1 or 10. In another, the polypeptides or the proteins of the present invention have a biological activity of at least one protein having the amino acid sequence (including antigenicity and/or immunogenicity) set forth in SEQ ID NOS: 2-9, 59, or 11-19, or a fragment thereof.

[0063] In a related aspect, the invention provides an isolated polypeptide encoded by the nucleic acid molecule of the invention described above. In one embodiment of the present invention, the isolated polypeptide includes the amino acid

sequence selected from the group consisting of: a) an amino acid sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, or 9; 11, 12, 13, 14, 15, 16, 17, 18 or 19; and b) an amino acid sequence that has 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% homology to the amino acid sequence according to a). In another, the isolated polypeptide comprises the amino acid sequence having at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 210, 220, 230, 240 or 250 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 5 or 18 (VP24); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 210, 220, 230, 240, 250, 260, 270, 280 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 6 or 17 (VP30); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 310, or 320 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 8 or 13 (VP40); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 310, 320, 330, or 340 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 7 or 12 (VP35); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 310, 320, 330, 340, 350, 360, or 370 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 4 or 15 (SGP); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 310, 320, 330, 340, 350, 360, or 370 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 59 or 16 (SSGP); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 450, 500, 550, 600, 610, 620, 630, 640, 650, 660, or 670 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 9 or 14 (GP); 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 450, 500, 550, 600, 650, 700, 710, 720, or 730 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 3 or 11 (NP); or 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000, 2050, 2100, 2150, 2160, 2170, 2180, 2190, or 2200 contiguous amino acid residues of the amino acid sequence of SEQ ID NOs: 2 or 19 (L).

[0064] In other aspects, the invention relates to the use of an isolated West African hEbola virus for diagnostic and therapeutic methods. In one embodiment, the invention provides a method of detecting in a biological sample an antibody immunospecific for the hEbola virus using the inventive isolated hEbola virus described herein, or any of the inventive proteins or polypeptides as described herein. In another specific embodiment, the invention provides a method of screening for an antibody which immunospecifically binds and neutralizes hEbola EboBun or EboIC or a combination thereof. Such an antibody is useful for a passive immunization or immunotherapy of a subject infected with hEbola.

[0065] In another aspect, the invention provides an isolated antibody or an antigen-binding fragment thereof which immunospecifically binds to a West African genus hEbola virus of the invention described above, and illustratively including EboBun or EboIC. In one embodiment of the present invention, the isolated antibody or an antigen-binding fragment thereof neutralizes a West African genus hEbola virus. In another, the isolated antibody or an antigen-binding fragment thereof immunospecifically binds to the inventive polypeptide described above. The invention further provides antibodies that specifically bind a polypeptide of the inven-

tion encoded by the nucleotide sequence of SEQ ID NOs: 1 (EboBun) or 10 (EboIC), a fragment thereof, or encoded by a nucleic acid comprising a nucleotide sequence that hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NOs: 1 (EboBun) or 10 (EboIC) and/or any hEbola EboBun epitope, having one or more biological activities of a polypeptide of the invention. These polypeptides include those shown in SEQ ID NOs: 2-9, 59, and 11-19. Such antibodies include, but are not limited to, polyclonal, monoclonal, bi-specific, multi-specific, human, humanized, chimeric antibodies, single chain antibodies, Fab fragments, F(ab')₂ fragments, disulfide-linked Fvs, intrabodies and fragments containing either a VL or VH domain or even a complementary determining region (CDR) that specifically binds to a polypeptide of the invention.

[0066] In other aspects, the invention provides methods for detecting the presence, activity or expression of the hEbola virus of the invention in a biological material, such as cells, blood, saliva, urine, and so forth. The increased or decreased activity or expression of the hEbola virus in a sample relative to a control sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the presence, activity or expression of the hEbola virus. In one embodiment of the present invention, the detecting agents are the antibodies or nucleic acid molecules of the present invention. Antibodies of the invention can also be used to treat hemorrhagic fever.

[0067] In a related aspect, the invention provides a method for detecting the presence of the inventive hEbola virus described above in a biological sample, the method comprising: (a) contacting the sample with an agent that selectively binds to the hEbola virus; and (b) detecting whether the compound binds to the hEbola virus in the sample. In one embodiment of the present invention, the biological sample is selected from the group consisting of cells; blood; serum; plasma; feces; rectal, vaginal and conjunctival swabs. In another, the agent that binds to the virus is an antibody. In another, the agent that binds to the virus is a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or a complement thereof. In another, the agent that binds to the virus is a nucleic acid molecule comprising a nucleotide sequence having at least 4, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 4600, 4700, 4800, 4900, 5000, 5500, 5600, 5700, 5800, 5900, 6000, 6100, 6200, 6300, 6400, 6500, or 6600 contiguous nucleotides of the nucleotide sequence of SEQ ID NOs: 1 or 10, or a complement thereof.

[0068] In another aspect, the invention provides a method for detecting the presence of the inventive polypeptide described above, in a biological sample, the method comprising: (a) contacting the biological sample with an agent that selectively binds to the polypeptide; and (b) detecting whether the agent binds to the polypeptide in the sample. In one embodiment of the present invention, the biological sample is selected from the group consisting of cells; blood; serum; plasma; feces; rectal, vaginal and conjunctival swabs. In another, the agent that binds to the polypeptide is an antibody or an antigen-binding fragment thereof.

[0069] In another aspect, the invention provides a method for detecting the presence of a first nucleic acid molecule derived from the inventive hEbola virus described above in a biological sample, the method includes (a) contacting the biological sample with an agent that selectively binds to the

nucleic acid; and (b) detecting whether the agent binds to the nucleotide in the sample. In one embodiment of the present invention, the agent that binds to the first nucleic acid molecule is a second nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or a complement thereof. In another, the second nucleic acid molecule comprises at least 4, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 4600, 4700, 4800, 4900, 5000, 5500, 5600, 5700, 5800, 5900, 6000, 6100, 6200, 6300, 6400, 6500, or 6600 contiguous nucleotides of the nucleotide sequence of SEQ ID NOs: 1 or 10, or a complement thereof.

[0070] In another aspect, the invention provides a method for propagating the hEbola virus in host cells comprising infecting the host cells with an inventive isolated West African hEbola virus described above, culturing the host cells to allow the virus to multiply, and harvesting the resulting virions. Also provided by the present invention are host cells infected with the inventive hEbola virus described above. In one embodiment of the present invention, the host cell is a primate cell.

[0071] In another aspect, the invention provides a method of detecting in a biological sample the presence of an antibody that immunospecifically binds hEbola virus, the method includes: (a) contacting the biological sample with the inventive host cell described above; and (b) detecting the antibody bound to the cell.

[0072] In another aspect, the invention provides vaccine preparations, including the inventive hEbola virus, including recombinant and chimeric forms of the virus, nucleic acid molecules comprised by the virus, or protein subunits of the virus. In one embodiment, the vaccine preparations of the present invention includes live but attenuated hEbola virus with or without pharmaceutically acceptable carriers, including adjuvants. In another, the vaccine preparations of the invention comprise an inactivated or killed hEbola Ebola virus, EboIC virus, or a combination thereof, with or without pharmaceutically acceptable carriers, including adjuvants. Such attenuated or inactivated viruses may be prepared by a series of passages of the virus through the host cells or by preparing recombinant or chimeric forms of virus. Accordingly, the present invention further provides methods of preparing recombinant or chimeric forms of the inventive hEbola viruses described herein.

[0073] In another specific embodiment, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of the inventive hEbola virus described above, and a pharmaceutically acceptable carrier. In another, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a protein extract of the inventive hEbola virus described above, or a subunit thereof; and a pharmaceutically acceptable carrier. In another aspect, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 1 or 10, or a complement thereof, and a pharmaceutically acceptable carrier. In another, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a nucleic acid molecule comprising any of inventive the nucleotide sequences as described above, or a complement thereof, and a pharmaceutically acceptable carrier. In another aspect, the invention provides a vaccine for-

mulation comprising a therapeutically or prophylactically effective amount of a protein extract of the inventive hEbola virus described above, or a subunit thereof; and a pharmaceutically acceptable carrier. In another aspect, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 1 or 10, or a complement thereof, and a pharmaceutically acceptable carrier. In another, the invention provides a vaccine formulation comprising a therapeutically or prophylactically effective amount of a nucleic acid molecule comprising any of inventive the nucleotide sequences as described above, or a complement thereof, and a pharmaceutically acceptable carrier.

[0074] In yet another specific embodiment, the vaccine preparations of the present invention comprise a nucleic acid or fragment of the hEbola virus, e.g., the virus having Accession No. 200706291, or nucleic acid molecules having the sequence of SEQ ID NOs: 1 or 10, or a fragment thereof. In another, the vaccine preparations comprise a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NOs: 1 or 10 or a fragment thereof. In a specific embodiment, the vaccine preparations comprise polypeptides of the invention as shown in SEQ ID NOs: 2-9, 59, or 11-19, or encoded by the nucleotide sequence of SEQ ID NOs: 1 or 10, or a fragment thereof.

[0075] Furthermore, the present invention provides methods for treating, ameliorating, managing or preventing hemorrhagic fever by administering the vaccine preparations or antibodies of the present invention alone or in combination with adjuvants, or other pharmaceutically acceptable excipients. Furthermore, the present invention provides methods for treating, ameliorating, managing, or preventing hemorrhagic fever by administering the inventive compositions and formulations including the vaccine preparations or antibodies of the present invention alone or in combination with antivirals [e.g., amantadine, rimantadine, gancyclovir, acyclovir, ribavirin, penciclovir, oseltamivir, foscamet zidovudine (AZT), didanosine (ddI), lamivudine (3TC), zalcitabine (ddC), stavudine (d4T), nevirapine, delavirdine, indinavir, ritonavir, vidarabine, nelfinavir, saquinavir, relenza, tamiflu, pleconaril, interferons, etc.], steroids and corticosteroids such as prednisone, cortisone, fluticasone and glucocorticoid, antibiotics, analgesics, bronchodilators, or other treatments for respiratory and/or viral infections.

[0076] In a related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of the inventive hEbola virus described above, and a pharmaceutically acceptable carrier.

[0077] In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of a protein extract of the inventive hEbola virus described above or a subunit thereof, and a pharmaceutically acceptable carrier.

[0078] In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 1, 10, a combination thereof, or a complement thereof, and a pharmaceutically acceptable carrier.

[0079] In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of a nucleic acid molecule comprising the

inventive nucleotide sequence as described above or a complement thereof, and a pharmaceutically acceptable carrier.

[0080] In another related aspect, the invention provides an immunogenic formulation comprising an immunogenically effective amount of any of the inventive polypeptides described above.

[0081] In another aspect, the present invention provides pharmaceutical compositions comprising antiviral agents of the present invention and a pharmaceutically acceptable carrier. In a specific embodiment, the antiviral agent of the invention is an antibody that immunospecifically binds hEbola virus or any hEbola epitope. In another specific embodiment, the antiviral agent is a polypeptide or protein of the present invention or nucleic acid molecule of the invention.

[0082] In a related aspect, the invention provides a pharmaceutical composition comprising a prophylactically or therapeutically effective amount of an anti-hEbola EboBun agent and a pharmaceutically acceptable carrier. In one embodiment of the present invention, the anti-hEbola EboBun agent is an antibody or an antigen-binding fragment thereof which immunospecifically binds to the hEbola virus of Deposit Accession No. 200706291, or polypeptides or protein derived therefrom. In another, the anti-hEbola agent is a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 1, 10, a combination thereof, or a fragment thereof. In another, the anti-hEbola agent is a polypeptide encoded by a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 1, 10, a combination thereof, or a fragment thereof having a biological activity of the polypeptide.

[0083] The invention also provides kits containing compositions and formulations of the present invention. Thus, in another aspect, the invention provides a kit comprising a container containing the inventive immunogenic formulation described above.

[0084] In another aspect, the invention provides a kit includes a container containing the inventive vaccine formulation described above.

[0085] In another aspect, the invention provides a kit including a container containing the inventive pharmaceutical composition described above.

[0086] In another aspect, the invention provides a kit including a container containing the inventive vaccine formulation described above.

[0087] In another aspect, the invention provides a method for identifying a subject infected with the inventive hEbola virus described above, including: (a) obtaining total RNA from a biological sample obtained from the subject; (b) reverse transcribing the total RNA to obtain cDNA; and (c) amplifying the cDNA using a set of primers derived from a nucleotide sequence of the inventive hEbola virus described above.

[0088] In one embodiment of the present invention, the set of primers are derived from the nucleotide sequence of the genome of the hEbola virus of Deposit Accession No. 200706291. In another, the set of primers are derived from the nucleotide sequence of SEQ ID NOs: 1 or 10 or any of the inventive nucleotide sequences as described above, or a complement thereof.

[0089] The invention further relates to the use of the sequence information of the isolated virus for diagnostic and therapeutic methods. In a specific embodiment, the invention provides nucleic acid molecules which are suitable for use as primers consisting of or including the nucleotide sequence of

SEQ ID NOs: 1 or 10, or a complement thereof, or at least a portion of the nucleotide sequence thereof. In another specific embodiment, the invention provides nucleic acid molecules which are suitable for hybridization to the inventive hEbola nucleic acid; including, but not limited to PCR primers, Reverse Transcriptase primers, probes for Southern analysis or other nucleic acid hybridization analysis for the detection of hEbola nucleic acids, e.g., consisting of or including the nucleotide sequence of SEQ ID NOs: 1, 10 a combination thereof, a complement thereof, or a portion thereof. The invention further encompasses chimeric or recombinant viruses encoded in whole or in part by the nucleotide sequences.

[0090] In another aspect, the present invention provides methods for screening antiviral agents that inhibit the infectivity or replication of hEbola virus or variants thereof.

[0091] The invention further provides methods of preparing recombinant or chimeric forms of hEbola.

[0092] In another aspect, the invention provides vaccine preparations including the hEbola virus, including recombinant and chimeric forms of the virus, or subunits of the virus. The present invention encompasses recombinant or chimeric viruses encoded by viral vectors derived from the genome of the inventive hEbola virus described herein or natural variants thereof. In a specific embodiment, a recombinant virus is one derived from the hEbola virus of Deposit Accession No. 200706291. It is recognized that natural variants of the inventive hEbola viruses described herein comprise one or more mutations, including, but not limited to, point mutations, rearrangements, insertions, deletions etc., to the genomic sequence. It is recognized that the mutations may or may not result in a phenotypic change.

[0093] In another specific embodiment, a chimeric virus of the invention is a recombinant hEbola EboBun or EboIC virus which further comprises a heterologous nucleotide sequence. In accordance with the invention, a chimeric virus may be encoded by a nucleotide sequence in which heterologous nucleotide sequences have been added to the genome or in which endogenous or native nucleotide sequences have been replaced with heterologous nucleotide sequences.

[0094] According to the present invention, the chimeric viruses are encoded by the viral vectors of the invention which further comprise a heterologous nucleotide sequence. In accordance with the present invention a chimeric virus is encoded by a viral vector that may or may not include nucleic acids that are non-native to the viral genome. In accordance with the invention a chimeric virus is encoded by a viral vector to which heterologous nucleotide sequences have been added, inserted or substituted for native or non-native sequences. In accordance with the present invention, the chimeric virus may be encoded by nucleotide sequences derived from different species or variants of hEbola virus. In particular, the chimeric virus is encoded by nucleotide sequences that encode antigenic polypeptides derived from different species or variants of hEbola virus.

[0095] A chimeric virus may be of particular use for the generation of recombinant vaccines protecting against two or more viruses (Tao et al., *J. Virol.* 72, 2955-2961; Durbin et al., 2000, *J. Virol.* 74, 6821-6831; Skiadopoulou et al., 1998, *J. Virol.* 72, 1762-1768 (1998); Teng et al., 2000, *J. Virol.* 74, 9317-9321). For example, it can be envisaged that a virus vector derived from the hEbola virus expressing one or more proteins of variants of hEbola virus including hEbola EboBun, or vice versa, will protect a subject vaccinated with

such vector against infections by both the native hEbola and the variant. Attenuated and replication-defective viruses may be of use for vaccination purposes with live vaccines as has been suggested for other viruses. (See, for example, PCT WO 02/057302, at pp. 6 and 23; and United States Patent Application Publication 2008/0069838 incorporated by reference herein).

[0096] In accordance with the present invention the heterologous sequence to be incorporated into the viral vectors encoding the recombinant or chimeric viruses of the invention include sequences obtained or derived from different species or variants of hEbola.

[0097] In certain embodiments, the chimeric or recombinant viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more sequences, intergenic regions, termini sequences, or portions or entire ORF have been substituted with a heterologous or non-native sequence. In certain embodiments of the invention, the chimeric viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more heterologous sequences have been inserted or added to the vector.

[0098] The selection of the viral vector may depend on the species of the subject that is to be treated or protected from a viral infection. If the subject is human, then an attenuated hEbola virus can be used to provide the antigenic sequences.

[0099] In accordance with the present invention, the viral vectors can be engineered to provide antigenic sequences which confer protection against infection by the inventive hEbola and natural variants thereof. The viral vectors may be engineered to provide one, two, three or more antigenic sequences. In accordance with the present invention the antigenic sequences may be derived from the same virus, from different species or variants of the same type of virus, or from different viruses.

[0100] The expression products and/or recombinant or chimeric virions obtained in accordance with the invention may advantageously be utilized in vaccine formulations. The expression products and chimeric virions of the present invention may be engineered to create vaccines against a broad range of pathogens, including viral and bacterial antigens, tumor antigens, allergen antigens, and auto antigens involved in autoimmune disorders. One way to achieve this goal involves modifying existing hEbola genes to contain foreign sequences in their respective external domains. Where the heterologous sequences are epitopes or antigens of pathogens, these chimeric viruses may be used to induce a protective immune response against the disease agent from which these determinants are derived. In particular, the chimeric virions of the present invention may be engineered to create vaccines for the protection of a subject from infections with hEbola virus and variants thereof.

[0101] Thus, the present invention further relates to the use of viral vectors and recombinant or chimeric viruses to formulate vaccines against a broad range of viruses and/or antigens. The present invention also encompasses recombinant viruses including a viral vector derived from the hEbola or variants thereof which contains sequences which result in a virus having a phenotype more suitable for use in vaccine formulations, e.g., attenuated phenotype or enhanced antigenicity. The mutations and modifications can be in coding regions, in intergenic regions and in the leader and trailer sequences of the virus.

[0102] The invention provides a host cell including a nucleic acid or a vector according to the invention. Plasmid or

viral vectors containing the polymerase components of hEbola virus are generated in prokaryotic cells for the expression of the components in relevant cell types (bacteria, insect cells, eukaryotic cells). Plasmid or viral vectors containing full-length or partial copies of the hEbola genome will be generated in prokaryotic cells for the expression of viral nucleic acids in vitro or in vivo. The latter vectors optionally contain other viral sequences for the generation of chimeric viruses or chimeric virus proteins, optionally lack parts of the viral genome for the generation of replication defective virus, and optionally contain mutations, deletions or insertions for the generation of attenuated viruses. In addition, the present invention provides a host cell infected with hEbola virus of Deposit Accession No. 200706291,

[0103] Infectious copies of West African hEbola (being wild type, attenuated, replication-defective or chimeric) are optionally produced upon co-expression of the polymerase components according to the state-of-the-art technologies described above.

[0104] In addition, eukaryotic cells, transiently or stably expressing one or more full-length or partial hEbola proteins are optionally used. Such cells are preferably made by transfection (proteins or nucleic acid vectors), infection (viral vectors) or transduction (viral vectors) and are useful for complementation of mentioned wild type, attenuated, replication-defective or chimeric viruses.

[0105] The viral vectors and chimeric viruses of the present invention optionally modulate a subject's immune system by stimulating a humoral immune response, a cellular immune response or by stimulating tolerance to an antigen. As used herein, a subject means: humans, primates, horses, cows, sheep, pigs, goats, dogs, cats, avian species and rodents.

Formulation of Vaccines and Antivirals

[0106] In a preferred embodiment, the invention provides a proteinaceous molecule or hEbola virus specific viral protein or functional fragment thereof encoded by a nucleic acid according to the invention. Useful proteinaceous molecules are for example derived from any of the genes or genomic fragments derivable from the virus according to the invention, preferably the GP, L, NP, sGP, VP24, VP30, VP35, and VP 40 proteins described herein. Such molecules, or antigenic fragments thereof, as provided herein, are for example useful in diagnostic methods or kits and in pharmaceutical compositions such as subunit vaccines. Particularly useful are polypeptides encoded by the nucleotide sequence of SEQ ID NOs: 1 or 10; or antigenic fragments thereof for inclusion as antigen or subunit immunogen, but inactivated whole virus can also be used. Particularly useful are also those proteinaceous substances that are encoded by recombinant nucleic acid fragments of the hEbola genome, of course preferred are those that are within the preferred bounds and metes of ORFs, in particular, for eliciting hEbola specific antibody or T cell responses, whether in vivo (e.g. for protective or therapeutic purposes or for providing diagnostic antibodies) or in vitro (e.g. by phage display technology or another technique useful for generating synthetic antibodies).

[0107] It is recognized that numerous variants, analogues, or homologues of EboBun polypeptides are within the scope of the present invention including amino acid substitutions, alterations, modifications, or other amino acid changes that increase, decrease, or do not alter the function or immunogenic propensity of the inventive immunogen or vaccine. Several post-translational modifications are similarly envi-

sioned as within the scope of the present invention illustratively including incorporation of a non-naturally occurring amino acid(s), phosphorylation, glycosylation, sulfation, and addition of pendent groups such as biotinylation, fluorophores, lumiphores, radioactive groups, antigens, or other molecules.

[0108] Methods of expressing and purifying natural or recombinant peptides and proteins are well known in the art. Illustratively, peptides and proteins are recombinantly expressed in eukaryotic cells. Exemplary eukaryotic cells include yeast, HeLa cells, 293 cells, COS cells, Chinese hamster ovary cells (CHO), and many other cell types known in the art. Both eukaryotic and prokaryotic expression systems and cells are available illustratively from Invitrogen Corp., Carlsbad, Calif. It is appreciated that cell-free expression systems are similarly operable.

[0109] In a preferred embodiment an immunogenic polypeptide is a full length EboBun protein. Preferably, an immunogen is a full length EboBun protein of SEQ ID NOs: 2-9 or 59, or EboIc SEQ ID NOs: 11-19, or a fragment thereof as described herein. Preferably, an immunogen is has a minimum of 5 amino acids. As used herein an immunogen is preferably a polypeptide. In the context of an immunogenic polypeptide the terms immunogen, polypeptide, and antigen are used interchangeably.

[0110] Modifications and changes can be made in the structure of the inventive immunogens that are the subject of the application and still obtain a molecule having similar or improved characteristics as the wild-type sequence (e.g., a conservative amino acid substitution). For example, certain amino acids are optionally substituted for other amino acids in a sequence without appreciable loss of immunogenic activity. Because it is the interactive capacity and nature of a polypeptide that defines that polypeptide's biological functional activity, certain amino acid sequence substitutions can be made in a polypeptide sequence and nevertheless obtain a polypeptide with like or improved properties. Optionally, a polypeptide is used that has less or more immunogenic activity compared to the wild-type sequence.

[0111] In making such changes, the hydropathic index of amino acids is preferably considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a polypeptide is generally understood in the art. It is known that certain amino acids can be substituted for other amino acids having a similar hydropathic index or score and still result in a polypeptide with similar biological activity. Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics. Those indices are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cysteine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

[0112] It is believed that the relative hydropathic character of the amino acid determines the secondary structure of the resultant polypeptide, which in turn defines the interaction of the polypeptide with other molecules, such as enzymes, substrates, receptors, antibodies, antigens, and the like. It is known in the art that an amino acid can be substituted by another amino acid having a similar hydropathic index and still obtain a functionally equivalent immunogen. In such changes, the substitution of amino acids whose hydropathic

indices are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

[0113] As outlined above, amino acid substitutions are generally based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take various of the foregoing characteristics into consideration are well known to those of skill in the art and include (original residue: exemplary substitution): (Ala: Gly, Ser), (Arg: Lys), (Asn: Gln, His), (Asp: Glu, Cys, Ser), (Gln: Asn), (Glu: Asp), (Gly: Ala), (His: Asn, Gln), (Ile: Leu, Val), (Leu: Ile, Val), (Lys: Arg), (Met: Leu, Tyr), (Ser: Thr), (Thr: Ser), (Tyr: Trp, Phe), and (Val: Ile, Leu). Embodiments of this disclosure thus contemplate functional or biological equivalents of a polypeptide and immunogen as set forth above. In particular, embodiments of the polypeptides and immunogens optionally include variants having about 50%, 60%, 70%, 80%, 90%, and 95% sequence identity to the polypeptide of interest.

[0114] The invention provides vaccine formulations for the prevention and treatment of infections with hEbola virus. In certain embodiments, the vaccine of the invention comprises recombinant and chimeric viruses of the hEbola virus. In certain embodiments, the virus is attenuated.

[0115] In another embodiment of this aspect of the invention, inactivated vaccine formulations are prepared using conventional techniques to "kill" the chimeric viruses. Inactivated vaccines are "dead" in the sense that their infectivity has been destroyed. Ideally, the infectivity of the virus is destroyed without affecting its immunogenicity. In order to prepare inactivated vaccines, the chimeric virus may be grown in cell culture or in the allantois of the chick embryo, purified by zonal ultracentrifugation, inactivated by formaldehyde or β -propiolactone, and pooled. The resulting vaccine is usually inoculated intramuscularly or intranasally.

[0116] Inactivated viruses are optionally formulated with a suitable adjuvant in order to enhance the immunological response. Such adjuvants illustratively include but are not limited to mineral gels, e.g., aluminum hydroxide; surface active substances such as lysolecithin, pluronic polyols, polyanions; peptides; oil emulsions; and potentially useful human adjuvants such as BCG and *Corynebacterium parvum*.

[0117] In another aspect, the present invention also provides DNA vaccine formulations including a nucleic acid or fragment of the inventive hEbola virus, e.g., the virus having Accession No. 200706291, or nucleic acid molecules having the sequence of SEQ ID NOs: 1 or 10, or a fragment thereof. In another specific embodiment, the DNA vaccine formulations of the present invention comprise a nucleic acid or fragment thereof encoding the antibodies which immunospecifically bind hEbola viruses. In DNA vaccine formulations, a vaccine DNA comprises a viral vector, such as that derived from the hEbola virus, bacterial plasmid, or other expression vector, bearing an insert including a nucleic acid molecule of the present invention operably linked to one or more control elements, thereby allowing expression of the vaccinating proteins encoded by the nucleic acid molecule in a vaccinated subject. Such vectors can be prepared by recombinant DNA technology as recombinant or chimeric viral vectors carrying a nucleic acid molecule of the present invention.

[0118] A nucleic acid as used herein refers to single- or double-stranded molecules which are optionally DNA,

including the nucleotide bases A, T, C and G, or RNA, including the bases A, U (substitutes for T), C, and G. The nucleic acid may represent a coding strand or its complement. Nucleic acids are optionally identical in sequence to the sequence which is naturally occurring or include alternative codons which encode the same amino acid as that which is found in the naturally occurring sequence. Furthermore, nucleic acids optionally include codons which represent conservative substitutions of amino acids as are well known in the art.

[0119] As used herein, the term “isolated nucleic acid” means a nucleic acid separated or substantially free from at least some of the other components of the naturally occurring organism, for example, the cell structural components commonly found associated with nucleic acids in a cellular environment and/or other nucleic acids. The isolation of nucleic acids is illustratively accomplished by techniques such as cell lysis followed by phenol plus chloroform extraction, followed by ethanol precipitation of the nucleic acids. The nucleic acids of this invention are illustratively isolated from cells according to methods well known in the art for isolating nucleic acids. Alternatively, the nucleic acids of the present invention are optionally synthesized according to standard protocols well described in the literature for synthesizing nucleic acids. Modifications to the nucleic acids of the invention are also contemplated, provided that the essential structure and function of the peptide or polypeptide encoded by the nucleic acid are maintained.

[0120] The nucleic acid encoding the peptide or polypeptide of this invention is optionally part of a recombinant nucleic acid construct comprising any combination of restriction sites and/or functional elements as are well known in the art which facilitate molecular cloning and other recombinant DNA manipulations. Thus, the present invention further provides a recombinant nucleic acid construct including a nucleic acid encoding a polypeptide of this invention.

[0121] Generally, it may be more convenient to employ as the recombinant polynucleotide a cDNA version of the polynucleotide. It is believed that the use of a cDNA version will provide advantages in that the size of the gene will generally be much smaller and more readily employed to transfect the targeted cell than will a genomic gene, which will typically be up to an order of magnitude larger than the cDNA gene. However, the inventor does not exclude the possibility of employing a genomic version of a particular gene where desired.

[0122] As used herein, the terms “engineered” and “recombinant” cells are synonymous with “host” cells and are intended to refer to a cell into which an exogenous DNA segment or gene, such as a cDNA or gene has been introduced. Therefore, engineered cells are distinguishable from naturally occurring cells which do not contain a recombinantly introduced exogenous DNA segment or gene. A host cell is optionally a naturally occurring cell that is transformed with an exogenous DNA segment or gene or a cell that is not modified. A host cell preferably does not possess a naturally occurring gene encoding RSV G protein. Engineered cells are, thus, cells having a gene or genes introduced through the hand of man. Recombinant cells illustratively include those having an introduced cDNA or genomic DNA, and also include genes positioned adjacent to a promoter not naturally associated with the particular introduced gene.

[0123] To express a recombinant encoded polypeptide in accordance with the present invention one optionally pre-

pares an expression vector that comprises a polynucleotide under the control of one or more promoters. To bring a coding sequence “under the control of” a promoter, one positions the 5' end of the translational initiation site of the reading frame generally between about 1 and 50 nucleotides “downstream” of (i.e., 3' of) the chosen promoter. The “upstream” promoter stimulates transcription of the inserted DNA and promotes expression of the encoded recombinant protein. This is the meaning of “recombinant expression” in the context used here.

[0124] Many standard techniques are available to construct expression vectors containing the appropriate nucleic acids and transcriptional/translational control sequences in order to achieve protein or peptide expression in a variety of host-expression systems. Cell types available for expression include, but are not limited to, bacteria, such as *E. coli* and *B. subtilis* transformed with recombinant phage DNA, plasmid DNA or cosmid DNA expression vectors.

[0125] Certain examples of prokaryotic hosts illustratively include *E. coli* strain RR1, *E. coli* LE392, *E. coli* B, *E. coli* 1776 (ATCC No. 31537) as well as *E. coli* W3110 (F-, lambda-, prototrophic, ATCC No. 273325); bacilli such as *Bacillus subtilis*; and other enterobacteria such as *Salmonella typhimurium*, *Serratia marcescens*, and various *Pseudomonas* species.

[0126] In general, plasmid vectors containing replicon and control sequences that are derived from species compatible with the host cell are used in connection with these hosts. The vector ordinarily carries a replication site, as well as marking sequences that are capable of providing phenotypic selection in transformed cells. For example, *E. coli* is often transformed using pBR322, a plasmid derived from an *E. coli* species. Plasmid pBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells. The pBR322 plasmid, or other microbial plasmid or phage may also contain, or be modified to contain, promoters that can be used by the microbial organism for expression of its own proteins.

[0127] In addition, phage vectors containing replicon and control sequences that are compatible with the host microorganism are optionally used as transforming vectors in connection with these hosts. For example, the phage lambda is optionally utilized in making a recombinant phage vector that can be used to transform host cells, such as *E. coli* LE392.

[0128] Further useful vectors include pIN vectors and pGEX vectors, for use in generating glutathione S-transferase (GST) soluble fusion proteins for later purification and separation or cleavage. Other suitable fusion proteins are those with β -galactosidase, ubiquitin, or the like.

[0129] Promoters that are most commonly used in recombinant DNA construction include the β -lactamase (penicillinase), lactose and tryptophan (trp) promoter systems. While these are the most commonly used, other microbial promoters have been discovered and utilized, and details concerning their nucleotide sequences have been published, enabling those of skill in the art to ligate them functionally with plasmid vectors.

[0130] For expression in *Saccharomyces*, the plasmid YRp7, for example, is commonly used. This plasmid contains the trp1 gene, which provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example ATCC No. 44076 or PEP4-1. The presence of the trp1 lesion as a characteristic of the yeast host cell genome

then provides an effective environment for detecting transformation by growth in the absence of tryptophan.

[0131] Suitable promoting sequences in yeast vectors illustratively include the promoters for 3-phosphoglycerate kinase or other glycolytic enzymes, such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase. In constructing suitable expression plasmids, the termination sequences associated with these genes are also preferably ligated into the expression vector 3' of the sequence desired to be expressed to provide polyadenylation of the mRNA and termination.

[0132] Other suitable promoters, which have the additional advantage of transcription controlled by growth conditions, illustratively include the promoter region for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, and the aforementioned glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization.

[0133] In addition to microorganisms, cultures of cells derived from multicellular organisms are also operable as hosts. In principle, any such cell culture is operable, whether from vertebrate or invertebrate culture. In addition to mammalian cells, these include insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus); and plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing one or more coding sequences.

[0134] In a useful insect system, *Autographica californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The isolated nucleic acid coding sequences are cloned into non-essential regions (for example the polyhedron gene) of the virus and placed under control of an AcNPV promoter (for example, the polyhedron promoter). Successful insertion of the coding sequences results in the inactivation of the polyhedron gene and production of non-occluded recombinant virus (i.e., virus lacking the proteinaceous coat coded for by the polyhedron gene). These recombinant viruses are then used to infect *Spodoptera frugiperda* cells in which the inserted gene is expressed (e.g., U.S. Pat. No. 4,215,051).

[0135] Examples of useful mammalian host cell lines include VERO and HeLa cells, Chinese hamster ovary (CHO) cell lines, W138, BHK, COS-7, 293, HepG2, NIH3T3, RIN and MDCK cell lines. In addition, a host cell is preferably chosen that modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the encoded protein.

[0136] Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins. Appropriate cell lines or host systems are preferably chosen to ensure the correct modification and processing of the foreign protein expressed. Expression vectors for use in mammalian cells ordinarily include an origin of replication (as necessary), a promoter located in front of the gene to be expressed, along with any necessary ribosome binding sites, RNA splice sites, polyadenylation site, and transcriptional terminator sequences. The origin of replica-

tion is preferably provided either by construction of the vector to include an exogenous origin, such as may be derived from SV40 or other viral (e.g., Polyoma, Adeno, VSV, BPV) source, or may be provided by the host cell chromosomal replication mechanism. If the vector is integrated into the host cell chromosome, the latter is often sufficient.

[0137] The promoters are optionally derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Further, it is also possible, and may be desirable, to utilize promoter or control sequences normally associated with the desired gene sequence, provided such control sequences are compatible with the host cell systems.

[0138] A number of viral based expression systems are operable herein, for example, commonly used promoters are derived from polyoma, Adenovirus 2, Adenovirus 5, cytomegalovirus and Simian Virus 40 (SV40). The early and late promoters of SV40 virus are useful because both are obtained easily from the virus as a fragment which also contains the SV40 viral origin of replication. Smaller or larger SV40 fragments are also operable, particularly when there is included the approximately 250 bp sequence extending from the HindIII site toward the BglII site located in the viral origin of replication.

[0139] In cases where an adenovirus is used as an expression vector, the coding sequences are preferably ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene is then optionally inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing proteins in infected hosts.

[0140] Specific initiation signals may also be required for efficient translation of the claimed isolated nucleic acid coding sequences. These signals include the ATG initiation codon and adjacent sequences. Exogenous translational control signals, including the ATG initiation codon, may additionally need to be provided. One of ordinary skill in the art would readily be capable of determining this need and providing the necessary signals. It is well known that the initiation codon must be in-frame (or in-phase) with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons are optionally of a variety of origins, both natural and synthetic. The efficiency of expression is optionally enhanced by the inclusion of appropriate transcription enhancer elements or transcription terminators.

[0141] In eukaryotic expression, one will also typically desire to incorporate into the transcriptional unit an appropriate polyadenylation site if one was not contained within the original cloned segment. Typically, the poly A addition site is placed about 30 to 2000 nucleotides "downstream" of the termination site of the protein at a position prior to transcription termination.

[0142] For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines that stably express constructs encoding proteins are engineered. Rather than using expression vectors that contain viral origins of replication, host cells are preferably transformed with vectors controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a

selectable marker. Following the introduction of foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched medium, and then are switched to a selective medium. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci, which in turn can be cloned and expanded into cell lines.

[0143] A number of selection systems are illustratively used, including, but not limited to, the herpes simplex virus thymidine kinase, hypoxanthine-guanine phosphoribosyltransferase and adenine phosphoribosyltransferase genes, in tk⁻, hgp^{rt}- or ap^{rt}- cells, respectively. Also, antimetabolite resistance is optionally used as the basis of selection for dhfr, which confers resistance to methotrexate; gpt, which confers resistance to mycophenolic acid; neo, which confers resistance to the aminoglycoside G-418; and hyg^r, which confers resistance to hygromycin. It is appreciated that numerous other selection systems are known in the art that are similarly operable in the present invention.

[0144] The nucleic acids encoding the peptides and polypeptides of this invention are optionally administered as nucleic acid vaccines. For the purposes of vaccine delivery, a nucleic acid encoding a peptide or polypeptide of this invention is preferably in an expression vector that includes viral nucleic acid including, but not limited to, vaccinia virus, adenovirus, retrovirus and/or adeno-associated virus nucleic acid. The nucleic acid or vector of this invention is optionally in a liposome or a delivery vehicle which can be taken up by a cell via receptor-mediated or other type of endocytosis. The nucleic acid vaccines of this invention are preferably in a pharmaceutically acceptable carrier or administered with an adjuvant. The nucleic acids encoding the peptides and polypeptides of this invention can also be administered to cells *in vivo* or *ex vivo*.

[0145] It is contemplated that the isolated nucleic acids of the disclosure are optionally "overexpressed", i.e., expressed in increased levels relative to its natural expression in cells of its indigenous organism, or even relative to the expression of other proteins in the recombinant host cell. Such overexpression is assessed by a variety of methods illustratively including radio-labeling and/or protein purification. However, simple and direct methods are preferred, for example, those involving SDS/PAGE and protein staining or immunoblotting, followed by quantitative analyses, such as densitometric scanning of the resultant gel or blot. A specific increase in the level of the recombinant protein or peptide in comparison to the level in natural in transfected cells is indicative of overexpression, as is a relative abundance of the specific protein in relation to the other proteins produced by the host cell and, e.g., visible on a gel.

[0146] Various heterologous vectors are described for DNA vaccinations against viral infections. For example, the vectors described in the following references, incorporated herein by reference, may be used to express hEbola sequences instead of the sequences of the viruses or other pathogens described; in particular, vectors described for hepatitis B virus (Michel, M. L. et al., 1995, DAN-mediated immunization to the hepatitis B surface antigen in mice: Aspects of the humoral response mimic hepatitis B viral infection in humans, *Proc. Natl. Aca. Sci. USA* 92:5307-5311; Davis, H. L. et al., 1993, DNA-based immunization induces continuous secretion of hepatitis B surface antigen and high levels of circulating antibody, *Human Molec. Genetics* 2:1847-1851),

HIV virus (Wang, B. et al., 1993, Gene inoculation generates immune responses against human immunodeficiency virus type 1, *Proc. Natl. Acad. Sci. USA* 90:4156-4160; Lu, S. et al., 1996, Simian immunodeficiency virus DNA vaccine trial in Macques, *J. Virol.* 70:3978-3991; Letvin, N. L. et al., 1997, Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination, *Proc Natl Acad Sci USA.* 94(17):9378-83), and influenza viruses (Robinson, H. L. et al., 1993, Protection against a lethal influenza virus challenge by immunization with a haemagglutinin-expressing plasmid DNA, *Vaccine* 11:957-960; Ulmer, J. B. et al., Heterologous protection against influenza by injection of DNA encoding a viral protein, *Science* 259:1745-1749), as well as bacterial infections, such as tuberculosis (Tascon, R. E. et al., 1996, Vaccination against tuberculosis by DNA injection, *Nature Med.* 2:888-892; Huygen, K. et al., 1996, Immunogenicity and protective efficacy of a tuberculosis DNA vaccine, *Nature Med.*, 2:893-898), and parasitic infection, such as malaria (Sedegah, M., 1994, Protection against malaria by immunization with plasmid DNA encoding circumsporozoite protein, *Proc. Natl. Acad. Sci. USA* 91:9866-9870; Doolan, D. L. et al., 1996, Circumventing genetic restriction of protection against malaria with multi-gene DNA immunization: CD8+T cell-interferon .delta., and nitric oxide-dependent immunity, *J. Exper. Med.*, 1183:1739-1746).

[0147] Many methods are optionally used to introduce the vaccine formulations described above. These include, but are not limited to, oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, and intranasal routes. Alternatively, in a preferred embodiment the chimeric virus vaccine formulation is introduced via the natural route of infection of the pathogen for which the vaccine is designed. The DNA vaccines of the present invention are optionally administered in saline solutions by injections into muscle or skin using a syringe and needle (Wolff J. A. et al., 1990, Direct gene transfer into mouse muscle *in vivo*, *Science* 247:1465-1468; Raz, E., 1994, Intradermal gene immunization: The possible role of DNA uptake in the induction of cellular immunity to viruses, *c. Natl. Acad. Sci. USA* 91:9519-9523). Another way to administer DNA vaccines operable herein is called the "gene gun" method, whereby microscopic gold beads coated with the DNA molecules of interest is fired into cells (Tang, D. et al., 1992, Genetic immunization is a simple method for eliciting an immune response, *Nature* 356:152-154). For general reviews of the methods for DNA vaccines, see Robinson, H. L., 1999, DNA vaccines: basic mechanism and immune responses (Review), *Int. J. Mol. Med.* 4(5):549-555; Barber, B., 1997, Introduction: Emerging vaccine strategies, *Seminars in Immunology* 9(5):269-270; and Robinson, H. L. et al., 1997, DNA vaccines, *Seminars in Immunology* 9(5):271-283.

Attenuation of hEbola Virus or Variants Thereof

[0148] The hEbola virus or variants thereof of the invention are optionally genetically engineered to exhibit an attenuated phenotype. In particular, the viruses of the invention exhibit an attenuated phenotype in a subject to which the virus is administered as a vaccine. Attenuation can be achieved by any method known to a skilled artisan. Without being bound by theory, the attenuated phenotype of the viruses of the invention is caused, e.g., by using a virus that naturally does not replicate well in an intended host species, for example, by reduced replication of the viral genome, by reduced ability of the virus to infect a host cell, or by reduced ability of the viral

proteins to assemble to an infectious viral particle relative to the wild type species of the virus.

[0149] The attenuated phenotypes of hEbola virus or variants thereof are optionally tested by any method known to the artisan. A candidate virus, for example, is optionally tested for its ability to infect a host or for the rate of replication in a cell culture system. In certain embodiments, growth curves at different temperatures are used to test the attenuated phenotype of the virus. For example, an attenuated virus is able to grow at 35° C., but not at 39° C. or 40° C. In certain embodiments, different cell lines are used to evaluate the attenuated phenotype of the virus. For example, an attenuated virus may only be able to grow in monkey cell lines but not the human cell lines, or the achievable virus titers in different cell lines are different for the attenuated virus. In certain embodiments, viral replication in the respiratory tract of a small animal model, including but not limited to, hamsters, cotton rats, mice and guinea pigs, is used to evaluate the attenuated phenotypes of the virus. In other embodiments, the immune response induced by the virus, including but not limited to, the antibody titers (e.g., assayed by plaque reduction neutralization assay or ELISA) is used to evaluate the attenuated phenotypes of the virus. In a specific embodiment, the plaque reduction neutralization assay or ELISA is carried out at a low dose. In certain embodiments, the ability of the hEbola virus to elicit pathological symptoms in an animal model is tested. A reduced ability of the virus to elicit pathological symptoms in an animal model system is indicative of its attenuated phenotype. In a specific embodiment, the candidate viruses are tested in a monkey model for nasal infection, indicated by mucus production.

[0150] The viruses of the invention are optionally attenuated such that one or more of the functional characteristics of the virus are impaired. In certain embodiments, attenuation is measured in comparison to the wild type species of the virus from which the attenuated virus is derived. In other embodiments, attenuation is determined by comparing the growth of an attenuated virus in different host systems. Thus, for a non-limiting example, hEbola virus or a variant thereof is attenuated when grown in a human host if the growth of the hEbola or variant thereof in the human host is reduced compared to the non-attenuated hEbola or variant thereof.

[0151] In certain embodiments, the attenuated virus of the invention is capable of infecting a host, is capable of replicating in a host such that infectious viral particles are produced. In comparison to the wild type species, however, the attenuated species grows to lower titers or grows more slowly. Any technique known to the skilled artisan can be used to determine the growth curve of the attenuated virus and compare it to the growth curve of the wild type virus.

[0152] In certain embodiments, the attenuated virus of the invention (e.g., a recombinant or chimeric hEbola) cannot replicate in human cells as well as the wild type virus (e.g., wild type hEbola) does. However, the attenuated virus can replicate well in a cell line that lacks interferon functions, such as Vero cells.

[0153] In other embodiments, the attenuated virus of the invention is capable of infecting a host, of replicating in the host, and of causing proteins of the virus of the invention to be inserted into the cytoplasmic membrane, but the attenuated virus does not cause the host to produce new infectious viral particles. In certain embodiments, the attenuated virus infects the host, replicates in the host, and causes viral proteins to be inserted in the cytoplasmic membrane of the host with the

same efficiency as the wild type hEbola. In other embodiments, the ability of the attenuated virus to cause viral proteins to be inserted into the cytoplasmic membrane into the host cell is reduced compared to the wild type virus. In certain embodiments, the ability of the attenuated hEbola virus to replicate in the host is reduced compared to the wild type virus. Any technique known to the skilled artisan can be used to determine whether a virus is capable of infecting a mammalian cell, of replicating within the host, and of causing viral proteins to be inserted into the cytoplasmic membrane of the host.

[0154] In certain embodiments, the attenuated virus of the invention is capable of infecting a host. In contrast to the wild type hEbola, however, the attenuated hEbola cannot be replicated in the host. In a specific embodiment, the attenuated hEbola virus can infect a host and can cause the host to insert viral proteins in its cytoplasmic membranes, but the attenuated virus is incapable of being replicated in the host. Any method known to the skilled artisan can be used to test whether the attenuated hEbola has infected the host and has caused the host to insert viral proteins in its cytoplasmic membranes.

[0155] In certain embodiments, the ability of the attenuated virus to infect a host is reduced compared to the ability of the wild type virus to infect the same host. Any technique known to the skilled artisan can be used to determine whether a virus is capable of infecting a host.

[0156] In certain embodiments, mutations (e.g., missense mutations) are introduced into the genome of the virus, for example, into the sequence of SEQ ID NOs: 1 or 10, or to generate a virus with an attenuated phenotype. Mutations (e.g., missense mutations) can be introduced into the structural genes and/or regulatory genes of the hEbola. Mutations are optionally additions, substitutions, deletions, or combinations thereof. Such variant of hEbola can be screened for a predicted functionality, such as infectivity, replication ability, protein synthesis ability, assembling ability, as well as cytopathic effect in cell cultures. In a specific embodiment, the missense mutation is a cold-sensitive mutation. In another embodiment, the missense mutation is a heat-sensitive mutation. In another embodiment, the missense mutation prevents a normal processing or cleavage of the viral proteins.

[0157] In other embodiments, deletions are introduced into the genome of the hEbola virus, which result in the attenuation of the virus.

[0158] In certain embodiments, attenuation of the virus is achieved by replacing a gene of the wild type virus with a gene of a virus of a different species, of a different subgroup, or of a different variant. In another aspect, attenuation of the virus is achieved by replacing one or more specific domains of a protein of the wild type virus with domains derived from the corresponding protein of a virus of a different species. In certain other embodiments, attenuation of the virus is achieved by deleting one or more specific domains of a protein of the wild type virus.

[0159] When a live attenuated vaccine is used, its safety should also be considered. The vaccine preferably does not cause disease. Any techniques known in the art for improving vaccine safety are operable in the present invention. In addition to attenuation techniques, other techniques are optionally be used. One non-limiting example is to use a soluble heterologous gene that cannot be incorporated into the virion membrane. For example, a single copy of the soluble version

of a viral transmembrane protein lacking the transmembrane and cytosolic domains thereof is used.

[0160] Various assays are optionally used to test the safety of a vaccine. For example, sucrose gradients and neutralization assays are used to test the safety. A sucrose gradient assay is optionally used to determine whether a heterologous protein is inserted in a virion. If the heterologous protein is inserted in the virion, the virion is preferably tested for its ability to cause symptoms in an appropriate animal model since the virus may have acquired new, possibly pathological, properties.

5.4 Adjuvants and Carrier Molecules

[0161] hEbola-associated antigens are administered with one or more adjuvants. In one embodiment, the hEbola-associated antigen is administered together with a mineral salt adjuvant or mineral salt gel adjuvant. Such mineral salt and mineral salt gel adjuvants include, but are not limited to, aluminum hydroxide (ALHYDROGEL, REHYDRAGEL), aluminum phosphate gel, aluminum hydroxyphosphate (ADJU-PHOS), and calcium phosphate.

[0162] In another embodiment, hEbola-associated antigen is administered with an immunostimulatory adjuvant. Such class of adjuvants include, but are not limited to, cytokines (e.g., interleukin-2, interleukin-7, interleukin-12, granulocyte-macrophage colony stimulating factor (GM-CSF), interferon- γ interleukin-1 β (IL-1 β), and IL-1 β peptide or Sclavo Peptide), cytokine-containing liposomes, triterpenoid glycosides or saponins (e.g., QuilA and QS-21, also sold under the trademark STIMULON, ISCOPREP), Muramyl Dipeptide (MDP) derivatives, such as N-acetyl-muramyl-L-threonyl-D-isoglutamine (Threonyl-MDP, sold under the trademark TERMURTIDE), GMDP, N-acetyl-nor-muramyl-L-alanyl-D-isoglutamine, N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-s-n-glycero-3-hydroxyphosphoryloxy)-ethylamine, muramyl tripeptide phosphatidylethanolamine (MTP-PE), unmethylated CpG dinucleotides and oligonucleotides, such as bacterial DNA and fragments thereof, LPS, monophosphoryl Lipid A (3D-MLA sold under the trademark MPL), and polyphosphazenes.

[0163] In another embodiment, the adjuvant used is a particular adjuvant, including, but not limited to, emulsions, e.g., Freund's Complete Adjuvant, Freund's Incomplete Adjuvant, squalene or squalene oil-in-water adjuvant formulations, such as SAF and MF59, e.g., prepared with block-copolymers, such as L-121 (polyoxypropylene/polyoxyethylene) sold under the trademark PLURONIC L-121, Liposomes, Virosomes, cochleates, and immune stimulating complex, which is sold under the trademark ISCOM.

[0164] In another embodiment, a microparticulate adjuvant is used. Microparticulate adjuvants include, but are not limited to, biodegradable and biocompatible polyesters, homo- and copolymers of lactic acid (PLA) and glycolic acid (PGA), poly(lactide-co-glycolides) (PLGA) microparticles, polymers that self-associate into particulates (poloxamer particles), soluble polymers (polyphosphazenes), and virus-like particles (VLPs) such as recombinant protein particulates, e.g., hepatitis B surface antigen (HbsAg).

[0165] Yet another class of adjuvants that are optionally used include mucosal adjuvants, including but not limited to heat-labile enterotoxin from *Escherichia coli* (LT), cholera holotoxin (CT) and cholera Toxin B Subunit (CTB) from *Vibrio cholerae*, mutant toxins (e.g., LTK63 and LTR72), microparticles, and polymerized liposomes.

[0166] In other embodiments, any of the above classes of adjuvants are optionally used in combination with each other or with other adjuvants. For example, non-limiting examples of combination adjuvant preparations used to administer the hEbola-associated antigens of the invention include liposomes containing immunostimulatory protein, cytokines, T-cell and/or B-cell peptides, or microbes with or without entrapped IL-2 or microparticles containing enterotoxin. Other adjuvants known in the art are also included within the scope of the invention (see Vaccine Design: The Subunit and Adjuvant Approach, Chap. 7, Michael F. Powell and Mark J. Newman (eds.), Plenum Press, New York, 1995, which is incorporated herein in its entirety).

[0167] The effectiveness of an adjuvant is illustratively determined by measuring the induction of antibodies directed against an immunogenic polypeptide containing a hEbola polypeptide epitope, the antibodies resulting from administration of this polypeptide in vaccines which are also comprised of the various adjuvants.

[0168] The polypeptides are optionally formulated into the vaccine as neutral or salt forms. Pharmaceutically acceptable salts include the acid additional salts (formed with free amino groups of the peptide) and which are formed with inorganic acids, such as, for example, hydrochloric or phosphoric acids, or organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with free carboxyl groups are optionally derived from inorganic bases, such as, for example, sodium potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine and the like.

[0169] The vaccines of the invention are preferably multivalent or univalent. Multivalent vaccines are made from recombinant viruses that direct the expression of more than one antigen.

[0170] Many methods are operable herein to introduce the vaccine formulations of the invention; these include but are not limited to oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal routes, and via scarification (scratching through the top layers of skin, e.g., using a bifurcated needle).

[0171] The patient to which the vaccine is administered is preferably a mammal, most preferably a human, but is also optionally a non-human animal including but not limited to lower primates, cows, horses, sheep, pigs, fowl (e.g., chickens), goats, cats, dogs, hamsters, mice and rats.

Preparation of Antibodies

[0172] Antibodies that specifically recognize a polypeptide of the invention, such as, but not limited to, polypeptides including the sequence of SEQ ID NOs: 2-9, 59, or 11-19 and other polypeptides as described herein, or hEbola epitope or antigen-binding fragments thereof are used in a preferred embodiment for detecting, screening, and isolating the polypeptide of the invention or fragments thereof, or similar sequences that might encode similar enzymes from the other organisms. For example, in one specific embodiment, an antibody which immunospecifically binds hEbola epitope, or a fragment thereof, is used for various in vitro detection assays, including enzyme-linked immunosorbent assays (ELISA), radioimmunoassays, western blot, etc., for the detection of a polypeptide of the invention or, preferably, hEbola, in samples, for example, a biological material, including cells, cell culture media (e.g., bacterial cell culture media, mammalian cell culture media, insect cell culture media, yeast cell

culture media, etc.), blood, plasma, serum, tissues, sputum, naseopharyngeal aspirates, etc.

[0173] Antibodies specific for a polypeptide of the invention or any epitope of hEbola are optionally generated by any suitable method known in the art. Polyclonal antibodies to an antigen of interest, for example, the hEbola virus from Deposit Accession No. 200706291, or including a nucleotide sequence of SEQ ID NOs: 1 or 10, are optionally produced by various procedures well known in the art. For example, an antigen is optionally administered to various host animals including, but not limited to, rabbits, mice, rats, etc., to induce the production of antisera containing polyclonal antibodies specific for the antigen. Various adjuvants are optionally used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete) adjuvant, mineral gels such as aluminum hydroxide, surface active substances such as lysollecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful adjuvants for humans such as BCG (*Bacille Calmette-Guerin*) and *Corynebacterium parvum*. Such adjuvants are also well known in the art.

[0174] Monoclonal antibodies are optionally prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. In one example, monoclonal antibodies are produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual* (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas*, pp. 563-681 (Elsevier, N.Y., 1981) (both of which are incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

[0175] Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art. In a non-limiting example, mice are immunized with an antigen of interest or a cell expressing such an antigen. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells. Hybridomas are selected and cloned by limiting dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding the antigen. Ascites fluid, which generally contains high levels of antibodies, is optionally generated by inoculating mice intraperitoneally with positive hybridoma clones.

[0176] Antibody fragments which recognize specific epitopes are optionally generated by known techniques. For example, Fab and F(ab')₂ fragments are illustratively produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). F(ab')₂ fragments preferably contain the complete light chain, and the variable region, the CH1 region and the hinge region of the heavy chain.

[0177] The antibodies of the invention or fragments thereof are optionally produced by any method known in the art for

the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

[0178] The nucleotide sequence encoding an antibody is obtained from any information available to those skilled in the art (i.e., from Genbank, the literature, or by routine cloning and sequence analysis). If a clone containing a nucleic acid encoding a particular antibody or an epitope-binding fragment thereof is not available, but the sequence of the antibody molecule or epitope-binding fragment thereof is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+RNA, isolated from any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR are optionally then cloned into replicable cloning vectors using any method known in the art.

[0179] Once the nucleotide sequence of the antibody is determined, the nucleotide sequence of the antibody is optionally manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., supra; and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence by, for example, introducing amino acid substitutions, deletions, and/or insertions into the epitope-binding domain regions of the antibodies or any portion of antibodies which may enhance or reduce biological activities of the antibodies.

[0180] Recombinant expression of an antibody requires construction of an expression vector containing a nucleotide sequence that encodes the antibody. Once a nucleotide sequence encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof has been obtained, the vector for the production of the antibody molecule is optionally produced by recombinant DNA technology using techniques known in the art as discussed in the previous sections. Methods which are known to those skilled in the art are optionally used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The nucleotide sequence encoding the heavy-chain variable region, light-chain variable region, both the heavy-chain and light-chain variable regions, an epitope-binding fragment of the heavy- and/or light-chain variable region, or one or more complementarity determining regions (CDRs) of an antibody are optionally cloned into such a vector for expression. Thus, prepared expression vector is optionally then introduced into appropriate host cells for the expression of the antibody. Accordingly, the invention includes host cells containing a polynucleotide encoding an antibody specific for the polypeptides of the invention or fragments thereof.

[0181] The host cell is optionally co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector

encoding a light chain derived polypeptide. The two vectors illustratively contain identical selectable markers which enable equal expression of heavy and light chain polypeptides or different selectable markers to ensure maintenance of both plasmids. Alternatively, a single vector is optionally used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, *Nature*, 322:52, 1986; and Kohler, *Proc. Natl. Acad. Sci. USA*, 77:2 197, 1980). The coding sequences for the heavy and light chains optionally include cDNA or genomic DNA.

[0182] In another embodiment, antibodies are generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage is utilized to display antigen binding domains, such as Fab and Fv or disulfide-bond stabilized Fv, expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest is optionally selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phages used in these methods are typically filamentous phage, including fd and M13. The antigen binding domains are expressed as a recombinantly fused protein to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the immunoglobulins, or fragments thereof, of the present invention include those disclosed in Brinkman et al., *J. Immunol. Methods*, 182:41-50, 1995; Ames et al., *J. Immunol. Methods*, 184:177-186, 1995; Kettleborough et al., *Eur. J. Immunol.*, 24:952-958, 1994; Persic et al., *Gene*, 187:9-18, 1997; Burton et al., *Advances in Immunology*, 57:191-280, 1994; PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Pat. Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

[0183] As described in the above references, after phage selection, the antibody coding regions from the phage is optionally isolated and used to generate whole antibodies, including human antibodies, or any other desired fragments, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')₂ fragments are optionally employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., *BioTechniques*, 12(6):864-869, 1992; and Sawai et al., *AJR* 1, 34:26-34, 1995; and Better et al., *Science*, 240:1041-1043, 1988 (each of which is incorporated by reference in its entirety). Examples of techniques operable to produce single-chain Fvs and antibodies include those described in U.S. Pat. Nos. 4,946,778 and 5,258,498; Huston et al., *Methods in Enzymology*, 203:46-88, 1991; Shu et al., *PNAS*, 90:7995-7999, 1993; and Skerra et al., *Science*, 240:1038-1040, 1988.

[0184] Once an antibody molecule of the invention has been produced by any methods described above, or otherwise known in the art, it is then optionally purified by any method known in the art for purification of an immunoglobulin mol-

ecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A or Protein G purification, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique(s) for the purification of proteins. Further, the antibodies of the present invention or fragments thereof are optionally fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification. Illustrative examples include 6×His tag, FLAG tag, biotin, avidin, or other system.

[0185] For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it is preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a constant region derived from a human immunoglobulin. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, *Science*, 229:1202, 1985; Oi et al., *BioTechniques*, 4:214 1986; Gillies et al., *J. Immunol. Methods*, 125:191-202, 1989; U.S. Pat. Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entireties. Humanized antibodies are antibody molecules from non-human species that bind the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. See, e.g., Queen et al., U.S. Pat. No. 5,585,089; Riechmann et al., *Nature*, 332:323, 1988, which are incorporated herein by reference in their entireties. Antibodies are humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Pat. Nos. 5,225,539; 5,530,101 and 5,585,089), veneering or resurfacing (EP 592, 106; EP 519,596; Padlan, *Molecular Immunology*, 28(4/5): 489-498, 1991; Studnicka et al., *Protein Engineering*, 7(6): 805-814, 1994; Roguska et al., *Proc Natl. Acad. Sci. USA*, 91:969-973, 1994), and chain shuffling (U.S. Pat. No. 5,565, 332), all of which are hereby incorporated by reference in their entireties.

[0186] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies are made by a variety of methods known in the art illustratively including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See U.S. Pat. Nos. 4,444,887 and 4,716, 111; and PCT publications WO 98/46645; WO 98/50433; WO 98/24893; WO 98/16654; WO 96/34096; WO 96/33735; and WO 91/10741, each of which is incorporated herein by reference in its entirety.

[0187] Human antibodies are also illustratively produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, *Int. Rev. Immunol.*, 13:65-93, 1995. For a

detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Pat. Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entireties. In addition, companies such as Abgenix, Inc. (Fremont, Calif.), Medarex (NJ) and Genpharm (San Jose, Calif.) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

[0188] Completely human antibodies which recognize a selected epitope are optionally generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., *Bio/technology*, 12:899-903, 1988).

[0189] Antibodies fused or conjugated to heterologous polypeptides are optionally used in *in vitro* immunoassays and in purification methods (e.g., affinity chromatography) known in the art. See e.g., PCT publication No. WO 93/21232; EP 439,095; Naramura et al., *Immunol. Lett.*, 39:91-99, 1994; U.S. Pat. No. 5,474,981; Gillies et al., *PNAS*, 89:1428-1432, 1992; and Fell et al., *J. Immunol.*, 146:2446-2452, 1991, which are incorporated herein by reference in their entireties.

[0190] Antibodies may also be illustratively attached to solid supports, which are particularly useful for immunoassays or purification of the polypeptides of the invention or fragments, derivatives, analogs, or variants thereof, or similar molecules having the similar enzymatic activities as the polypeptide of the invention. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Pharmaceutical Compositions and Kits

[0191] The present invention encompasses pharmaceutical compositions including antiviral agents of the present invention. In a specific embodiment, the antiviral agent is preferably an antibody which immunospecifically binds and neutralizes the hEbola virus or variants thereof, or any proteins derived therefrom. In another specific embodiment, the antiviral agent is a polypeptide or nucleic acid molecule of the invention. The pharmaceutical compositions have utility as an antiviral prophylactic agent are illustratively administered to a subject where the subject has been exposed or is expected to be exposed to a virus.

[0192] Various delivery systems are known and operable to administer the pharmaceutical composition of the invention, illustratively, encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the mutant viruses, and receptor mediated endocytosis (see, e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432). Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and optionally administered together with other biologically active agents. Administration is systemic

or local. In a preferred embodiment, it is desirable to introduce the pharmaceutical compositions of the invention into the lungs by any suitable route. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

[0193] In a specific embodiment, it is desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment. This administration may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, by means of nasal spray, or by means of an implant, the implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) infected tissues.

[0194] In another embodiment, the pharmaceutical composition is delivered in a vesicle, in particular a liposome (see Langer, 1990, *Science* 249:1527-1533; Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*).

[0195] In yet another embodiment, the pharmaceutical composition is delivered in a controlled release system. In one embodiment, a pump is used (see Langer, *supra*; Sefton, 1987, *CRC Crit. Ref. Biomed. Eng.* 14:201; Buchwald et al., 1980, *Surgery* 88:507; and Saudek et al., 1989, *N. Engl. J. Med.* 321:574). In another embodiment, polymeric materials are used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, *J. Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., 1985, *Science* 228:190; Doring et al., 1989, *Ann. Neurol.* 25:351; Howard et al., 1989, *J. Neurosurg.* 71:105). In yet another embodiment, a controlled release system is placed in proximity of the composition's target, i.e., the lung, thus, requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

[0196] Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)) the contents of which are incorporated herein by reference.

[0197] The pharmaceutical compositions of the present invention illustratively include a therapeutically effective amount of a live attenuated, inactivated or killed West African hEbola virus, or recombinant or chimeric hEbola virus, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the pharmaceutical composition is administered. Such pharmaceutical carriers are illustratively sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are optionally

employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, also contains wetting or emulsifying agents, or pH buffering agents. These compositions optionally take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained release formulations and the like. The composition is optionally formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation illustratively includes standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin. The formulation should suit the mode of administration.

[0198] In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. The composition also includes an optional solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline is optionally provided so that the ingredients may be mixed prior to administration.

[0199] The pharmaceutical compositions of the invention are illustratively formulated as neutral or salt forms. Pharmaceutically acceptable salts illustratively include those formed with free amino groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with free carboxyl groups such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2 ethylamino ethanol, histidine, procaine, etc.

[0200] The amount of the pharmaceutical composition of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, *in vitro* assays are optionally employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20 to 500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose response curves derived from *in vitro* or animal model test systems.

[0201] Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

[0202] The invention also provides a pharmaceutical pack or kit including one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) is a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In a preferred embodiment, the kit contains an antiviral agent of the invention, e.g., an antibody specific for the polypeptides encoded by a nucleotide sequence of SEQ ID NOs: 1 or 10, or as shown in SEQ ID NOs: 2-9, 59, or 11-19, or any hEbola epitope, or a polypeptide or protein of the present invention, or a nucleic acid molecule of the invention, alone or in combination with adjuvants, antivirals, antibiotics, analgesic, bronchodilators, or other pharmaceutically acceptable excipients.

[0203] The present invention further encompasses kits including a container containing a pharmaceutical composition of the present invention and instructions for use.

Detection Assays

[0204] The present invention provides a method for detecting an antibody, which immunospecifically binds to the hEbola virus, in a biological sample, including for example blood, serum, plasma, saliva, urine, feces, etc., from a patient suffering from hEbola infection, and/or hemorrhagic fever. In a specific embodiment, the method including contacting the sample with the hEbola virus, for example, of Deposit Accession No. 200706291, or having a genomic nucleic acid sequence of SEQ ID NOs: 1 or 10, directly immobilized on a substrate and detecting the virus-bound antibody directly or indirectly by a labeled heterologous anti-isotype antibody. In another specific embodiment, the sample is contacted with a host cell which is infected by the hEbola virus, for example, of Deposit Accession No. 200706291, or having a genomic nucleic acid sequence of SEQ ID NOs: 1 or 10, and the bound antibody is optionally detected by immunofluorescent assay.

[0205] An exemplary method for detecting the presence or absence of a polypeptide or nucleic acid of the invention in a biological sample involves obtaining a biological sample from various sources and contacting the sample with a compound or an agent capable of detecting an epitope or nucleic acid (e.g., mRNA, genomic DNA) of the hEbola virus such that the presence of the hEbola virus is detected in the sample. A preferred agent for detecting hEbola mRNA or genomic RNA of the invention is a labeled nucleic acid probe capable of hybridizing to mRNA or genomic RNA encoding a polypeptide of the invention. The nucleic acid probe is, for example, a nucleic acid molecule including the nucleotide sequence of SEQ ID NOs: 1 or 10, a complement thereof, or a portion thereof, such as an oligonucleotide of at least 15, 20, 25, 30, 50, 100, 250, 500, 750, 1000 or more contiguous nucleotides in length and sufficient to specifically hybridize under stringent conditions to a hEbola mRNA or genomic RNA.

[0206] As used herein, the term "stringent conditions" describes conditions for hybridization and washing under which nucleotide sequences having at least 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% identity to each other typically remain hybridized to

each other. Such hybridization conditions are described in, for example but not limited to, *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1 6.3.6; *Basic Methods in Molecular Biology*, Elsevier Science Publishing Co., Inc., N.Y. (1986), pp. 75 78, and 84 87; and *Molecular Cloning*, Cold Spring Harbor Laboratory, N.Y. (1982), pp. 387 389, and are well known to those skilled in the art. A preferred, non-limiting example of stringent hybridization conditions is hybridization in 6× sodium chloride/sodium citrate (SSC), 0.5% SDS at about 68° C. followed by one or more washes in 2×SSC, 0.5% SDS at room temperature. Another preferred, non-limiting example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C. followed by one or more washes in 0.2×SSC, 0.1% SDS at 50 to 65° C.

[0207] A nucleic acid probe, polynucleotide, oligonucleotide, or other nucleic acid is preferably purified. An “isolated” or “purified” nucleotide sequence is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the nucleotide is derived, or is substantially free of chemical precursors or other chemicals when chemically synthesized. The language “substantially free of cellular material” includes preparations of a nucleotide/oligonucleotide in which the nucleotide/oligonucleotide is separated from cellular components of the cells from which it is isolated or produced. Thus, a nucleotide/oligonucleotide that is substantially free of cellular material includes preparations of the nucleotide having less than about 30%, 20%, 10%, 5%, 2.5%, or 1%, (by dry weight) of contaminating material. When nucleotide/oligonucleotide is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the nucleotide/oligonucleotide have less than about 30%, 20%, 10%, or 5% (by dry weight) of chemical precursors or compounds other than the nucleotide/oligonucleotide of interest. In a preferred embodiment of the present invention, the nucleotide/oligonucleotide is isolated or purified.

[0208] In another preferred specific embodiment, the presence of hEbola virus is detected in the sample by a reverse transcription polymerase chain reaction (RT-PCR) using the primers that are constructed based on a partial nucleotide sequence of the genome of hEbola virus, for example, that of Deposit Accession No. 200706291, or having a genomic nucleic acid sequence of SEQ ID NOs: 1 or 10. In a non-limiting specific embodiment, preferred primers to be used in a RT-PCR method are the primers are described in detail herein.

[0209] In more preferred specific embodiment, the present invention provides a real-time quantitative PCR assay to detect the presence of hEbola virus in a biological sample by subjecting the cDNA obtained by reverse transcription of the extracted total RNA from the sample to PCR reactions using the specific primers described in detail herein, and a fluorescence dye, such as SYBR® Green I, which fluoresces when bound nonspecifically to double-stranded DNA. The fluorescence signals from these reactions are captured at the end of extension steps as PCR product is generated over a range of the thermal cycles, thereby allowing the quantitative determination of the viral load in the sample based on an amplification plot.

[0210] A preferred agent for detecting hEbola is an antibody that specifically binds a polypeptide of the invention or any hEbola epitope, preferably an antibody with a detectable label. Antibodies are illustratively polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')₂) is operable herein.

[0211] The term “labeled”, with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, optionally via a linker, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it is detectable with fluorescently labeled streptavidin. The detection method of the invention is optionally used to detect mRNA, protein (or any epitope), or genomic RNA in a sample in vitro as well as in vivo. Exemplary in vitro techniques for detection of mRNA include northern hybridizations, in situ hybridizations, RT-PCR, and RNase protection. In vitro techniques for detection of an epitope of hEbola illustratively include enzyme linked immunosorbent assays (ELISAs), western blots, immunoprecipitations and immunofluorescence. In vitro techniques for detection of genomic RNA include northern hybridizations, RT-PCT, and RNase protection. Furthermore, in vivo techniques for detection of hEbola include introducing into a subject organism a labeled antibody directed against the polypeptide. In one embodiment, the antibody is labeled with a radioactive marker whose presence and location in the subject organism is detected by standard imaging techniques, including autoradiography.

[0212] In a specific embodiment, the methods further involve obtaining a control sample from a control subject, contacting the control sample with a compound or agent capable of detecting hEbola, e.g., a polypeptide of the invention or mRNA or genomic RNA encoding a polypeptide of the invention, such that the presence of hEbola or the polypeptide or mRNA or genomic RNA encoding the polypeptide is detected in the sample, and comparing the absence of hEbola or the polypeptide or mRNA or genomic RNA encoding the polypeptide in the control sample with the presence of hEbola, or the polypeptide or mRNA or genomic DNA encoding the polypeptide in the test sample.

[0213] The invention also encompasses kits for detecting the presence of hEbola or a polypeptide or nucleic acid of the invention in a test sample. The kit illustratively includes a labeled compound or agent capable of detecting hEbola or the polypeptide or a nucleic acid molecule encoding the polypeptide in a test sample and, in certain embodiments, a means for determining the amount of the polypeptide or mRNA in the sample (e.g., an antibody which binds the polypeptide or an oligonucleotide probe which binds to DNA or mRNA encoding the polypeptide). Kits optionally include instructions for use.

[0214] For antibody-based kits, the kit illustratively includes: (1) a first antibody (e.g., attached to a solid support) which binds to a polypeptide of the invention or hEbola epitope; and, optionally, (2) a second, different antibody which binds to either the polypeptide or the first antibody and is preferably conjugated to a detectable agent.

[0215] For oligonucleotide-based kits, the kit illustratively includes: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a nucleic acid sequence

encoding a polypeptide of the invention or to a sequence within the hEbola genome; or (2) a pair of primers useful for amplifying a nucleic acid molecule containing an hEbola sequence. The kit optionally includes a buffering agent, a preservative, or a protein stabilizing agent. The kit optionally includes components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit optionally contains a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for use.

Screening Assays to Identify Antiviral Agents

[0216] The invention provides methods for the identification of a compound that inhibits the ability of hEbola virus to infect a host or a host cell. In certain embodiments, the invention provides methods for the identification of a compound that reduces the ability of hEbola virus to replicate in a host or a host cell. Any technique well known to the skilled artisan is illustratively used to screen for a compound useful to abolish or reduce the ability of hEbola virus to infect a host and/or to replicate in a host or a host cell.

[0217] In certain embodiments, the invention provides methods for the identification of a compound that inhibits the ability of hEbola virus to replicate in a mammal or a mammalian cell. More specifically, the invention provides methods for the identification of a compound that inhibits the ability of hEbola virus to infect a mammal or a mammalian cell. In certain embodiments, the invention provides methods for the identification of a compound that inhibits the ability of hEbola virus to replicate in a mammalian cell. In a specific embodiment, the mammalian cell is a human cell.

[0218] In another embodiment, a cell is contacted with a test compound and infected with the hEbola virus. In certain embodiments, a control culture is infected with the hEbola virus in the absence of a test compound. The cell is optionally contacted with a test compound before, concurrently with, or subsequent to the infection with the hEbola virus. In a specific embodiment, the cell is a mammalian cell. In an even more specific embodiment, the cell is a human cell. In certain embodiments, the cell is incubated with the test compound for at least 1 minute, at least 5 minutes, at least 15 minutes, at least 30 minutes, at least 1 hour, at least 2 hours, at least 5 hours, at least 12 hours, or at least 1 day. The titer of the virus is optionally measured at any time during the assay. In certain embodiments, a time course of viral growth in the culture is determined. If the viral growth is inhibited or reduced in the presence of the test compound, the test compound is identified as being effective in inhibiting or reducing the growth or infection of the hEbola virus. In a specific embodiment, the compound that inhibits or reduces the growth of the hEbola virus is tested for its ability to inhibit or reduce the growth rate of other viruses to test its specificity for the hEbola virus.

[0219] In one embodiment, a test compound is administered to a model animal and the model animal is infected with the hEbola virus. In certain embodiments, a control model animal is infected with the hEbola virus without the administration of a test compound. The test compound is optionally administered before, concurrently with, or subsequent to the infection with the hEbola virus. In a specific embodiment, the model animal is a mammal. In an even more specific embodiment, the model animal is, but is not limited to, a cotton rat, a mouse, or a monkey. The titer of the virus in the model animal

is optionally measured at any time during the assay. In certain embodiments, a time course of viral growth in the culture is determined. If the viral growth is inhibited or reduced in the presence of the test compound, the test compound is identified as being effective in inhibiting or reducing the growth or infection of the hEbola virus. In a specific embodiment, the compound that inhibits or reduces the growth of the hEbola in the model animal is tested for its ability to inhibit or reduce the growth rate of other viruses to test its specificity for the hEbola virus.

[0220] According to the method of the invention, a human or an animal is optionally treated for for EboBun or EboIC, other viral infection or bacterial infection by administering an effective amount of an inventive therapeutic composition. Preferably, a vaccine is administered prophylactically. An "effective amount" is an amount that will induce an immune response in a subject. Illustratively, an effective amount of the compositions of this invention ranges from nanogram/kg to milligram/kg amounts for young children and adults. Equivalent dosages for lighter or heavier body weights can readily be determined. The dose should be adjusted to suit the individual to whom the composition is administered and will vary with age, weight and metabolism of the individual. The exact amount of the composition required will vary from subject to subject, depending on the species, age, weight and general condition of the subject, the particular peptide or polypeptide used, its mode of administration and the like. An appropriate amount can be determined by one of ordinary skill in the art using only routine experimentation given the teachings herein. One skilled in the art will realize that dosages are best optimized by the practicing physician or veterinarian and methods for determining dose amounts and regimens and preparing dosage forms are described, for example, in Remington's Pharmaceutical Sciences, (Martin, E. W., ed., latest edition), Mack Publishing Co., Easton, Pa. Preferably, a single administration is operable to induce an immune response.

[0221] Methods involving conventional biological techniques are described herein. Such techniques are generally known in the art and are described in detail in methodology treatises such as *Molecular Cloning: A Laboratory Manual*, 2nd ed., vol. 1-3, ed. Sambrook et al., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989; and *Current Protocols in Molecular Biology*, ed. Ausubel et al., Greene Publishing and Wiley-Interscience, New York, 1992 (with periodic updates). Immunological methods (e.g., preparation of antigen-specific antibodies, immunoprecipitation, and immunoblotting) are described, e.g., in *Current Protocols in Immunology*, ed. Coligan et al., John Wiley & Sons, New York, 1991; and *Methods of Immunological Analysis*, ed. Masseyeff et al., John Wiley & Sons, New York, 1992.

[0222] Embodiments of inventive compositions and methods are illustrated in the following detailed examples. These examples are provided for illustrative purposes and are not considered limitations on the scope of inventive compositions and methods.

EXAMPLES

Example 1

Newly Discovered Ebola Virus Associated with Hemorrhagic Fever Outbreak in Bundibugyo, Uganda

[0223] In late November 2007 HF cases were reported in the townships of Bundibugyo and Kikyoo in Bundibugyo Dis-

trict, Western Uganda (FIG. 1A). These samples were assayed as described by Towner, JS, et al., *PLoS Pathog*, 2008 November; 4(11): e1000212, the contents of which are incorporated herein by reference for methods, results, reagents, and all other aspects of the publication. A total of 29 blood samples were initially collected from suspect cases and showed evidence of acute ebolavirus infection in eight specimens using a broadly reactive ebolavirus antigen capture assay known to cross-react with the different ebolavirus species⁷ and an IgM capture assay based on Zaire ebolavirus reagents (Table 1). These specimens were negative when initially tested with highly sensitive real-time RT-PCR assays specific for all known Zaire and Sudan ebolaviruses and marburgviruses. However, further evidence of acute ebolavirus infection was obtained using a traditionally less sensitive (relative to the real-time RT-PCR assays) but more broadly reactive filovirus L gene-specific RT-PCR assay (1 specimen) (Table 1). Sequence analysis of the PCR fragment (400 bp of the virus L gene) revealed the reason for the initial failure of the real-time RT-PCR assays, as the sequence was distinct from that of the 4 known species of ebolavirus, although distantly related to Côte d'Ivoire ebolavirus. In total, 9 of 29 specimens showed evidence of ebolavirus infection, and all tests were negative for marburgvirus (data not shown).

[0224] Approximately 70% of the virus genome was rapidly sequenced from total RNA extracted from a patient serum (#200706291) using a newly established metagenomics pyrosequencing method (454 Life Sciences) which involves successive rounds of random DNA amplification⁸. Using the newly derived draft sequence, a real-time RT-PCR assay specific for the NP gene of this virus was quickly developed and evaluated. The assay was shown to have excellent sensitivity (Table 1), finding positive all the initial six samples that tested positive by either virus antigen capture (five specimens) or virus isolation assays (four specimens). The antigen-capture, IgM, IgG and newly designed real-time PCR assays were quickly transferred to the Uganda Virus Research Institute during the course of the outbreak to facilitate rapid identification and isolation of Ebola cases in the affected area for efficient control of the outbreak. The outbreak continued through late December 2007, and resulted in 149 suspected cases and 37 deaths⁹.

[0225] Table 1. Ebolavirus diagnostic results of initial 29 specimens obtained from Bundibugyo District with numerical specimen numbers assigned. RT-PCR refers to results obtained from conventional PCR using the broadly reactive Filo A/B primers¹³. Ag, IgM, and IgG refer to results from ELISA-based assays^{10, 11} with Zaire ebolavirus reagents while virus isolation refers to culture attempts on Vero E6 cells². Q-RT-PCR refers to results obtained using the optimized Bundibugyo ebolavirus specific real-time RT-PCR assay with cycle threshold (Ct) values of positive (Pos) samples indicated in the far right column. * Specimen #200706291 is the clinical sample from which prototype isolate #811250 was obtained.

TABLE 1

Sample No.	RT-PCR	Ag	IgM	IgG	Virus Isolation	Q- RT-PCR	Ct
200706288	neg	neg	neg	neg	neg	neg	40
200706289	neg	neg	neg	neg	neg	neg	40
200706290	neg	neg	neg	neg	neg	neg	40
200706291*	Pos	Pos	neg	neg	Pos	Pos	23.64

TABLE 1-continued

Sample No.	RT-PCR	Ag	IgM	IgG	Virus Isolation	Q- RT-PCR	Ct
200706292	neg	neg	neg	neg	neg	neg	40
200706293	neg	neg	neg	neg	neg	neg	40
200706294	neg	neg	neg	neg	neg	neg	40
200706295	neg	neg	neg	neg	neg	neg	40
200706296	neg	neg	Pos	Pos	neg	neg	40
200706297	neg	neg	Pos	Pos	neg	neg	40
200706298	neg	Pos	Pos	Pos	neg	Pos	34.83
200706299	neg	neg	Pos	Pos	neg	neg	40
200706300	neg	neg	neg	neg	neg	neg	40
200706301	neg	neg	neg	neg	neg	neg	40
200706302	neg	Pos	Pos	neg	neg	Pos	35.01
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200706327	ND	Pos	neg	neg	Pos	Pos	34.41
200706328	ND	neg	neg	neg	neg	neg	40

[0226] The entire genome sequence of this virus was completed using a classic primer walking sequencing approach on RNA. The complete genome of the Eb ebolavirus was not available, so it too was derived by a similar combination of random primed pyrosequencing and primer walking approaches. Acquisition of these sequences allowed for the first time the phylogenetic analysis of the complete genomes of representatives of all known species of Ebola and Marburg viruses. The analysis revealed that the newly discovered virus differed from the four existing ebolavirus species (FIG. 1), with approximately 32% nucleotide difference from even the closest relative, EboIC (Table 2). Similar complete genome divergence (35-45%) is seen between the previously characterized ebolavirus species.

[0227] Table 2. Identity matrix based on comparisons of full-length genome sequences of Zaire ebolaviruses 1976 (Genbank accession number NC_002549) and 1995 (Genbank accession number AY354458), Sudan ebolavirus 2000 (Genbank accession number NC_006432), Cote d'Ivoire ebolavirus 1994 (SEQ ID NO: 10), Reston ebolavirus 1989 (Genbank accession number NC_004161), and Bundibugyo ebolavirus 2007 (SEQ ID NO: 1).

TABLE 2

	Zaire '95	Sudan '00	EboIC '94	EboBun '07	Reston '89
Zaire '76	.988	.577	.630	.632	.581
Zaire '95		.577	.631	.633	.581
Sudan '00			.577	.577	.609
EboIC '94				.683	.575
EboBun '07					.576

[0228] The material and information obtained from the discovery of the new unique virus EboBun and the realization that together with EboIC these viruses represent a Glade of Bundibugyo-Ivory Coast Ebola virus species is valuable,

and makes possible the development of clinical, diagnostic and research tools directed to human hEbola infection.

Material and Methods

[0229] Ebolavirus Detection and Virus Isolation.

[0230] Several diagnostic techniques were used for each sample: (i) antigen capture, IgG, and IgM assays were performed as previously described¹¹ (ii) virus isolation attempts were performed on Vero E6 cells² and monitored for 14 days; (iii) RNA was extracted and tested for Zaire¹⁶ and Sudan ebolavirus and marburgvirus⁴ using real-time quantitative RT-PCR assays designed to detect all known species of each respective virus species the primers/probe for the Sudan ebolavirus assay were EboSudBMG 1(+)-5'-GCC ATG GIT TCA GGT TTG AG-3' (SEQ ID NO: 21), EboSudBMG 1(-)-5'-GGT IAC ATT GGG CAA CAA TTC A-3' (SEQ ID NO: 22) and Ebola Sudan BMG Probe 5'FAM-AC GGT GCA CAT TCT CCT TTT CTC GGA-BHQ1 (SEQ ID NO: 23)]; (iv) the conventional RT-PCR was performed with the filo A/B primer set as previously described¹⁶ using Superscript III (Invitrogen) according to the manufacturer's instructions. The specimen 200706291 was selected as the reference sample for further sequence analysis.

[0231] Genome Sequencing.

[0232] Pyrosequencing was carried out utilizing the approach developed by 454 Life Sciences, and the method described by Cox-Foster et al.⁸ Subsequent virus whole genome primer walking was performed as previously described¹⁷ but using the primers specific for Bundibugyo ebolavirus RT-PCR amplification. In total, the entire virus genome was amplified in six overlapping RT-PCR fragments (all primers listed 5' to 3'): fragment A (predicted size 2.7 kb) was amplified using forward-GTGAGACAAAGAATCAATCCTG (SEQ ID NO: 24) with reverse-CATCAATTGCTCAGAGATCCACC (SEQ ID NO: 25); fragment B (predicted size 3.0 kb) was amplified using forward-CCAACAACACTGCATGTAAGT (SEQ ID NO: 26) with reverse-AGGTCGCGTAAATCTTCATC (SEQ ID NO: 27); fragment C (predicted size 3.5 kb) was amplified using forward-GATGGTTGAGTTACTTCCGG (SEQ ID NO: 28) with reverse-GTCTTGAGTCATCAATGCC (SEQ ID NO: 29); fragment D (predicted size 3.1 kb) was amplified using forward-CCACCAGCACCAAAGGAC (SEQ ID NO: 30) with reverse-CTATCGGCAATGTAAGTATTGG (SEQ ID NO: 31); fragment E (predicted size 3.4 kb) was amplified using forward-GCCGTTGTAGAGGACACAC (SEQ ID NO: 32) with reverse-CACATTAATTGTTCTAACATGCAAG (SEQ ID NO: 33) and fragment F (predicted size 3.5 kb) was amplified using forward-CCTAGGTTATTTA-GAAGGGACTA (SEQ ID NO: 34) with reverse-GGT AGA TGT ATT GAC AGC AAT ATC (SEQ ID NO: 35).

[0233] The exact 5' and 3' ends of Bundibugyo ebolavirus were determined by 3' RACE from virus RNA extracted from virus infected Vero E6 cell monolayers using TriPure isolation reagent. RNAs were then polyadenylated in vitro using A-Plus poly(A) polymerase tailing kit (Epicenter Biotechnologies) following the manufacturer's instructions and then purified using an RNeasy kit (Qiagen) following standard protocols. Ten microliters of in vitro polyadenylated RNA were added as template in RT-PCR reactions, using SuperScript III One-Step RT-PCR system with Platinum Taq High Fidelity (Invitrogen) following the manufacturer's protocol. Two parallel RT-PCR reactions using the oligo(dT)-containing 3'RACE-AP primer (Invitrogen) mixed with 1 of 2 viral

specific primers, Ebo-U 692(-) AAAAAAGCTATCTGCACTAT (SEQ ID NO: 36) and Ebo-V18269(+) CTCA-GAAGCAAAATTAATGG (SEQ ID NO: 37), generated ~700 nt long fragments containing the 3' ends of either genomic and antigenomic RNAs. The resulting RT-PCR products were analyzed by agarose electrophoresis, and DNA bands of the correct sizes were purified using QIAquick Gel Extraction Kit (Qiagen) and sequenced using standard protocols (ABI).

[0234] The nucleotide sequence of the Côte d'Ivoire ebolavirus (EboIC) isolate RNA was initially determined using the exact same pyrosequencing strategy as that used for Bundibugyo ebolavirus described above. This method generated sequence for approximately 70% of the entire genome. This draft sequence was then used to design a whole genome primer walking strategy for filling any gaps and confirming the initial sequence. The following Côte d'Ivoire ebolavirus-specific primers were used to generate RT-PCR fragments, designated A-F, as follows: Fragment A (predicted size 3.0 kb) was amplified using forward-GTGTGCGAATAACTATGAGGAAG (SEQ ID NO: 38) and reverse-GTCTGTGCAATGTTGATGAAGG (SEQ ID NO: 39); Fragment B (predicted size 3.2 kb) was amplified using forward-CATGAAAACCACACTCAACAAC (SEQ ID NO: 40) and reverse-GTTGCCTTAATCTTCATCAAGTTC (SEQ ID NO: 41); Fragment C (predicted size 3.0 kb) was amplified using forward-GGCTATAATGAATTCCTCCAG (SEQ ID NO: 42) and reverse-CAAGTGTATTTGTGGTCCTAGC (SEQ ID NO: 43); fragment D (predicted size 3.5 kb) was amplified using forward-GCTGGAATAGGAATCACAGG (SEQ ID NO: 44) and reverse-CGGTAGTCTACAGTTCTTTAG (SEQ ID NO: 45); fragment E (predicted size 4.0 kb) was amplified using forward-GACAAAGAGATTAGATTAGCTATAG (SEQ ID NO: 46) and reverse-GTAATGAGAAGGTGTCATTTGG (SEQ ID NO: 47); fragment F (predicted size 2.9 kb) was amplified using forward-CACGACTTAGTTGGACAATTGG (SEQ ID NO: 48) and reverse-CAGACACTAATTAGATCTGGAAG (SEQ ID NO: 49); fragment G (predicted size 1.3 kb) was amplified using forward-CGGACACACAAAAAGAAWRAA (SEQ ID NO: 50) and reverse-CGTTCTTGACCTTAGCAGTTC (SEQ ID NO: 51); and fragment H (predicted size 2.5 kb) was amplified using forward-GCACTATAAGCTCGATGAAGTC (SEQ ID NO: 52) and reverse-TGGACACACAAAAARGARRAA (SEQ ID NO: 53). A gap in the sequence contig was located between fragments C and D and this was resolved using the following primers to generate a predicted fragment of 1.5 kb: forward-CTGAGAGGATCCAGAAGAAAG (SEQ ID NO: 54) and reverse-GTGTAAGCGTTGATATACCTCC (SEQ ID NO: 55). The terminal ~20 nucleotides of the sequence were not experimentally determined but were inferred by comparing with the other known Ebola genome sequences.

[0235] Bundibugyo ebolavirus Real-Time RT-PCR Assay.

[0236] The primers and probe used in the Bundibugyo ebolavirus specific Q-RT-PCR assay were as follows: EboU965 (+): 5'-GAGAAAAGGCTGTCTGGAGAA-3' (SEQ ID NO: 56), EboU1039(-): 5'-TCGGGTATTGAATCAGACCTTGTT-3' (SEQ ID NO: 57) and EboU989 Prb: 5'Fam-TTCAACGACAAATCCAAGTGCACGCA-3'BHQ1 (SEQ ID NO 58). Q-RT-PCR reactions were set up using SuperScript III One-Step Q-RT-PCR (Invitrogen) according to the manufacturer's instructions and run for 40 cycles with a 58° C. annealing temperature.

[0237] Phylogenetic Analysis.

[0238] Modeltest 3.7¹⁸ was used to examine 56 models of nucleotide substitution to determine the model most appropriate for the data. The General Time Reversible model incorporating invariant sites and a gamma distribution (GTR+I+G) was selected using the Akaike Information Criterion (AIC). Nucleotide frequencies were A=0.3278, C=0.2101, G=0.1832, T=0.2789, the proportion of invariant sites=0.1412, and the gamma shape parameter=1.0593. A maximum likelihood analysis was subsequently performed in PAUP*4.0b10¹⁹ using the GTR+I+G model parameters. Bootstrap support values were used to assess topological support and were calculated based on 1,000 pseudoreplicates²⁰.

[0239] In addition, a Bayesian phylogenetic analysis was conducted in MrBayes 3.2²¹ using the GTR+I+G model of nucleotide substitution. Two simultaneous analyses, each with four Markov chains, were run for 5,000,000 generations sampling every 100 generations. Prior to termination of the run, the AWTY module was used to assess Markov Chain Monte Carlo convergence to ensure that the length of the analysis was sufficient²². Trees generated before the stabilization of the likelihood scores were discarded (burn in =40), and the remaining trees were used to construct a consensus tree. Nodal support was assessed by posterior probability values (>95=statistical support).

Example 2

Immunization against EboBun

[0240] To determine the capability of immunogens to elicit an immune response in non-human primates (NHP), 12 cynomolgus macaques, of which 10 are immunized with VSVΔG/EboBunGP either orally (OR; n=4), intranasally (IN; n=4) or intramuscularly (IM; n=2) in accordance with all animal control and safety guidelines and essentially as described by Qiu, X, et al., PLoS ONE. 2009; 4(5): e5547. The remaining 2 control animals are vaccinated intramuscularly with VSVΔG/MARVGP. VSVΔG/MARVGP does not provide heterologous protection against EboBun, therefore these NHPs succumb to EboBun infection. Animals are acclimatized for 14 days prior to infection. Animals are fed and monitored twice daily (pre- and post-infection) and fed commercial monkey chow, treats and fruit. Husbandry enrichment consists of commercial toys and visual stimulation.

[0241] The recombinant VSVΔG/EboBun vaccines are synthesized expressing the EboBun glycoprotein (GP) (SEQ ID NO: 9), soluble glycoprotein (sGP) (SEQ ID NO: 4), or nucleoprotein (NP) (SEQ ID NO: 3). Control VSVΔG/MARVGP vaccines represent the analogous proteins from Lake victoria marburgvirus (MARV) (strain Musoke). The following results for GP are similar for sGP and NP. Vaccines are generated using VSV (Indiana serotype) as described previously. Garbutt, M, et al., J Virol, 2004; 78(10):5458-5465; Schnell, M J, et al., PNAS USA, 1996; 93(21):11359-11365. EboBun challenge virus is passaged in Vero E6 cells prior to challenge, as described previously Jones, S M, et al., Nat Med. 2005; 11(7):786-790; Jahrling, P B, et al., J Infect Dis, 1999; 179 (Suppl 1):S224-34. An EboBun immunogen peptide pool consisting of 15mers with 11 amino acid overlaps (Sigma-Genosys) spanning the entire sequence of the EboBun immunogens and strain Mayinga 1976 GP are used.

[0242] Twelve filovirus naïve cynomolgus monkeys randomized into four groups receive 2 ml of 1×10^7 PFU/ml of vaccine in Dulbecco's modified Eagle's medium (DMEM).

Animals in the three experimental groups are vaccinated with either: 1) 2 ml orally (OR) (n=4); 2) 1 ml dripped into each nostril, intranasally (IN) (n=4); or 3) 1 ml each into two sites intramuscularly (IM) (n=2). The two controls are injected intramuscularly with 2 ml of 1×10^7 PFU/ml of VSVΔG/MARVGP. All animals are challenged intramuscularly 28 days later with 1,000 PFU of EboBun.

[0243] Routine examination is conducted on 0, 2, 4, 6, 10, 14 and 21 days post-vaccination, then 0, 3, 6, 10, 14, 19, 26 days, 6 and 9 months after the EboBun challenge. For the examinations animals are anaesthetized by intramuscular injection with 10 mg/kg of ketaset (Ayerst). Examinations include haematological analysis, monitoring temperature (rectal), respiration rate, lymph nodes, weight, hydration, discharges and mucous membranes. Also, swabs (throat, oral, nasal, rectal, vaginal) and blood samples are collected (4 ml from femoral vein, 1 ml in EDTA vacutainer tube; 3 ml in serum separator vacutainer tube). Cynomolgus monkey PBMCs are isolated using BD CPT sodium citrate Vacutainers (Becton Dickinson) as per manufacturer's protocol.

[0244] All VSVΔG/EboBunGP immunized animals are protected from high dose challenge. These animals show no evidence of clinical illness after vaccination or EboBun challenge. Both control animals demonstrate typical symptoms associated with EboBun HF including fever, macular rashes, lethargy, and unresponsiveness. Continued infection requires euthanization. Hematology analyses at each examination date demonstrate increases in the platelet-crit in the OR and IN groups post-challenge, however, no significant changes are observed in any NHPs post-immunization or in the VSVΔG/EboBunGP immunized NHPs post-challenge.

[0245] EboBun antibody production from humoral antibody response to vaccination and challenge is examined by a virus like particle (VLP) based ELISA assay. Generation of EboBun VLPs is performed by the protocol for ZEBOV as described by Wahl-Jensen, V., et al., J Virol, 2005; 79(4): 2413-2419. ELISA is performed by the protocol described by Qiu, X, et al., PLoS ONE. 2009; 4(5): e5547.

[0246] The VSVΔG/MARVGP immunized animals do not develop a detectable antibody response to EboBun. In contrast, potent antibody responses are detected in all VSVΔG/EboBunGP immunized animals independent of immunization route. Between days 14 and 21 post-vaccination, all VSVΔG/EboBunGP immunized NHPs develop high levels of IgA, IgM, and IgG against EboBunGP. After challenge the IgM titres do not exceed the post-vaccination levels, however, IgG and IgA antibody titres are increased peaking 14 days post-challenge then slowly decreasing before maintaining a relatively high antibody titre up to 9 months.

[0247] The level of neutralization antibodies is detected by a EboBun-GFP flow cytometric neutralization assay in serum collected at days 0 and 21 post-vaccination. Samples are assayed in duplicate for their ability to neutralize an infection with EboBun-GFP in VeroE6 cells. Serially diluted serum samples are incubated with an equal volume of EboBun-GFP in DMEM, at 37° C., 5% CO₂ for 1 hr followed by addition of 150 µl per well of a confluent 12 well plate of VeroE6 cells (MOI=0.0005). After 2 hours at 37° C., 5% CO₂, 1 ml of DMEM, 2% fetal bovine serym (FBS), 100 U/ml penicillin, 100 µg/ml streptomycin is added per well and incubated for 5 days. Cells are harvested by removing the culture supernatant, washing with 1 ml PBS, 0.04% EDTA, then adding 800 µl of PBS 0.04% EDTA for 5 minutes at 37° C. before adding 8 ml PBS, 4% paraformaldehyde (PFA) and overnight incu-

bation. The cells are acquired (10,000 events) and analyzed with CellQuest Pro v3.3 on a Becton Dickinson FACSCalibur flow cytometer.

[0248] The OR and IN routes produce EboBunGP-specific neutralizing antibodies with the OR route producing the highest titres post-vaccination. The IM immunization produces detectable levels of neutralizing antibody. In comparison, 3/4 NHPs in the OR group demonstrate a 50% reduction in EboBun-GFP positive cells at a titre of 1:40. Similarly, the IN route results in a reduction of EboBun-GFP positive cells at the 1:40 dilution.

[0249] EboBunGP-specific effector cellular immune responses are determined using IL-2 and IFN- γ ELISPOT assays as described by Qin, X, et al., PLoS ONE. 2009; 4(5): e5547 to determine the number of IL-2 and IFN- γ secreting lymphocytes. Prior to challenge on days 10 to 14 post-vaccination there is a detectable EboBun immunogen-specific IFN- γ response in all immunized animals. The IM route is the most potent, inducing approximately 2-fold more IFN- γ secreting cells than OR ($p < 0.001$) or IN ($p = 0.043$) routes. A strong post-challenge secondary IFN- γ response is induced in all VSV Δ G/EboBun immunized animals with the IM route producing the most IFN- γ cells at day 6. By day 10 the OR group demonstrates a stronger response. The IFN- γ in the IN group rises steadily, peaking at day 26 post-challenge with 4.3 and 2 fold more EboBun specific IFN- γ secreting cells than the IM ($p = 0.003$) and OR ($p = 0.075$) group, respectively. All three routes produce strong EboBun-specific IFN- γ responses.

[0250] Post-vaccination, the IM group also has more EboBunGP-specific IL-2 secreting cells than either of the mucosally immunized groups. Post-challenge, the IM route continues to dominate early after challenge peaking on day 10. This difference shows a trend when compared to the IN group ($p = 0.067$) and is significant when compared to the OR group ($p < 0.001$). Additionally, the IN group has more IL-2 producing cells than the OR group ($p = 0.090$) on day 10 post-challenge. By day 26 post-challenge all three routes continue to produce a EboBunGP-specific IL-2 response, however, the IN group response is strongest. At day 26 post-challenge the IN group has the most potent IFN- γ and IL-2 responses, as well as the highest IgA and IgG antibody titre, indicating this immunization route, followed by a EboBun challenge, results in the development of potent and sustained effector responses.

[0251] Absolute lymphocyte numbers for CD3⁺, CD4⁺, and CD8⁺ (CD3⁺CD4⁻) T cell populations are determined by flow cytometry. No decrease is observed in the lymphocyte populations for any of the VSV Δ G/EboBunGP vaccinated NHPs. In contrast, control animals who are not protected from EboBun show lymphocyte numbers decreased by 28-57%.

[0252] Macrophage numbers are slightly increased in control animals. However, the number of CD14⁺ cells is greater in the VSV Δ G/EboBunGP vaccinated groups with the IM route showing the most significant increases.

[0253] In order to determine the long term immune response after challenge, EboBunGP-specific CD4⁺ and CD8⁺ memory T-lymphocytes are examined for their ability to proliferate (CFSE⁻) or produce IFN- γ in response to EboBunGP peptides at 6 months post-vaccination. EboBunGP-specific memory responses are observed as a result of vaccination followed by a ZEBOV challenge. These responses persist for at least 6 months. The memory popula-

tions in OR and IN inoculation routes demonstrate the greatest potential for proliferation and IFN- γ production post-challenge.

[0254] Any patents or publications mentioned in this specification are incorporated herein by reference to the same extent as if each individual publication is specifically and individually indicated to be incorporated by reference.

[0255] The compositions and methods described herein are presently representative of preferred embodiments, exemplary, and not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art. Such changes and other uses can be made without departing from the scope of the invention as set forth in the claims. All numerical ranges are inclusive of the whole integers and decimals between the endpoints, and inclusive of the endpoints.

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<210> SEQ ID NO 2
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<223> OTHER INFORMATION: Bundibugyo ebolavirus L viral protein

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<400> SEQUENCE: 2

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Ser Ser Tyr Ser Leu Asn Pro Gln Leu Lys Asn Cys Arg Leu Pro Lys
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Asp Val Pro Ile Val Thr Leu Pro Ile Asp Tyr Leu Thr Pro Leu Leu
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Leu Arg Thr Leu Ser Gly Glu Gly Leu Cys Pro Val Glu Pro Lys Cys
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Ser Gln Phe Leu Asp Glu Ile Val Ser Tyr Val Leu Gln Asp Ala Arg
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Phe Leu Arg Tyr Tyr Phe Arg His Val Gly Val His Asp Asp Asn Val
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Gly Lys Asn Phe Glu Pro Lys Ile Lys Ala Leu Ile Tyr Asp Asn Glu
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Phe Leu Gln Gln Leu Phe Tyr Trp Tyr Asp Leu Ala Ile Leu Thr Arg
 145 150 155 160

Arg Gly Arg Leu Asn Arg Gly Asn Asn Arg Ser Thr Trp Phe Ala Asn
 165 170 175

Asp Asp Leu Ile Asp Ile Leu Gly Tyr Gly Asp Tyr Ile Phe Trp Lys
 180 185 190

Ile Pro Leu Ser Leu Leu Ser Leu Asn Thr Glu Gly Ile Pro His Ala
 195 200 205

Ala Lys Asp Trp Tyr His Ala Ser Ile Phe Lys Glu Ala Val Gln Gly
 210 215 220

His Thr His Ile Val Ser Val Ser Thr Ala Asp Val Leu Ile Met Cys
 225 230 235 240

Lys Asp Ile Ile Thr Cys Arg Phe Asn Thr Thr Leu Ile Ala Ala Leu
 245 250 255

Ala Asn Leu Glu Asp Ser Ile Cys Ser Asp Tyr Pro Gln Pro Glu Thr
 260 265 270

Ile Ser Asn Leu Tyr Lys Ala Gly Asp Tyr Leu Ile Ser Ile Leu Gly
 275 280 285

Ser Glu Gly Tyr Lys Val Ile Lys Phe Leu Glu Pro Leu Cys Leu Ala
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Lys Ile Gln Leu Cys Ser Asn Tyr Thr Glu Arg Lys Gly Arg Phe Leu
 305 310 315 320

Thr Gln Met His Leu Ala Val Asn His Thr Leu Glu Glu Leu Ile Glu
 325 330 335

Gly Arg Gly Leu Lys Ser Gln Gln Asp Trp Lys Met Arg Glu Phe His
 340 345 350

Arg Ile Leu Val Asn Leu Lys Ser Thr Pro Gln Gln Leu Cys Glu Leu
 355 360 365

Phe Ser Val Gln Lys His Trp Gly His Pro Val Leu His Ser Glu Lys
 370 375 380

Ala Ile Gln Lys Val Lys Lys His Ala Thr Val Ile Lys Ala Leu Arg
 385 390 395 400

Pro Val Ile Ile Phe Glu Thr Tyr Cys Val Phe Lys Tyr Ser Ile Ala
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Lys His Tyr Phe Asp Ser Gln Gly Ser Trp Tyr Ser Val Ile Ser Asp
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Lys His Leu Thr Pro Gly Leu His Ser Tyr Ile Lys Arg Asn Gln Phe
 435 440 445

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Phe	Ile	Lys	Asp	Arg	Ala	Thr	Ala	Val	Glu	Lys	Thr	Cys	Trp	Asp	Ala
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Val	Phe	Glu	Pro	Asn	Val	Leu	Gly	Tyr	Ser	Pro	Pro	Asn	Lys	Phe	Ser
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Thr	Lys	Arg	Val	Pro	Glu	Gln	Phe	Leu	Glu	Gln	Glu	Asn	Phe	Ser	Ile
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Asp	Ser	Val	Leu	Thr	Tyr	Ala	Gln	Arg	Leu	Asp	Tyr	Leu	Leu	Pro	Gln
	530					535				540					
Tyr	Arg	Asn	Phe	Ser	Phe	Ser	Leu	Lys	Glu	Lys	Glu	Leu	Asn	Val	Gly
545					550					555					560
Arg	Ala	Phe	Gly	Lys	Leu	Pro	Tyr	Pro	Thr	Arg	Asn	Val	Gln	Thr	Leu
				565					570					575	
Cys	Glu	Ala	Leu	Leu	Ala	Asp	Gly	Leu	Ala	Lys	Ala	Phe	Pro	Ser	Asn
			580					585					590		
Met	Met	Val	Val	Thr	Glu	Arg	Glu	Gln	Lys	Glu	Ser	Leu	Leu	His	Gln
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Ala	Ser	Trp	His	His	Thr	Ser	Asp	Asp	Phe	Gly	Glu	Asn	Ala	Thr	Val
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Arg	Gly	Ser	Ser	Phe	Val	Thr	Asp	Leu	Glu	Lys	Tyr	Asn	Leu	Ala	Phe
625					630					635					640
Arg	Tyr	Glu	Phe	Thr	Ala	Pro	Phe	Ile	Glu	Tyr	Cys	Asn	Arg	Cys	Tyr
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Gly	Val	Lys	Asn	Leu	Phe	Asn	Trp	Met	His	Tyr	Thr	Ile	Pro	Gln	Cys
			660					665					670		
Tyr	Ile	His	Val	Ser	Asp	Tyr	Tyr	Asn	Pro	Pro	His	Gly	Val	Ser	Leu
		675					680					685			
Glu	Asn	Arg	Glu	Asp	Pro	Pro	Glu	Gly	Pro	Ser	Ser	Tyr	Arg	Gly	His
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Leu	Gly	Gly	Ile	Glu	Gly	Leu	Gln	Gln	Lys	Leu	Trp	Thr	Ser	Ile	Ser
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Cys	Ala	Gln	Ile	Ser	Leu	Val	Glu	Ile	Lys	Thr	Gly	Phe	Lys	Leu	Arg
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Ser	Ala	Val	Met	Gly	Asp	Asn	Gln	Cys	Ile	Thr	Val	Leu	Ser	Val	Phe
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Pro	Leu	Glu	Thr	Asp	Ser	Asn	Glu	Gln	Glu	His	Ser	Ser	Glu	Asp	Asn
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Ala	Ala	Arg	Val	Ala	Ala	Ser	Leu	Ala	Lys	Val	Thr	Ser	Ala	Cys	Gly
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Ile	Phe	Leu	Lys	Pro	Asp	Glu	Thr	Phe	Val	His	Ser	Gly	Phe	Ile	Tyr
785					790					795					800
Phe	Gly	Lys	Lys	Gln	Tyr	Leu	Asn	Gly	Val	Gln	Leu	Pro	Gln	Ser	Leu
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Lys	Thr	Ala	Thr	Arg	Ile	Ala	Pro	Leu	Ser	Asp	Ala	Ile	Phe	Asp	Asp
			820					825					830		
Leu	Gln	Gly	Thr	Leu	Ala	Ser	Ile	Gly	Thr	Ala	Phe	Glu	Arg	Ser	Ile
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Ser	Glu	Thr	Arg	His	Val	Tyr	Pro	Cys	Arg	Val	Val	Ala	Ala	Phe	His

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850					855					860					
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865					870					875					880
Lys	Gly	Thr	Asp	Leu	Gly	Gln	Leu	Ser	Leu	Ser	Lys	Pro	Leu	Asp	Phe
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Gly	Thr	Ile	Thr	Leu	Ala	Leu	Ala	Val	Pro	Gln	Val	Leu	Gly	Gly	Leu
			900					905					910		
Ser	Phe	Leu	Asn	Pro	Glu	Lys	Cys	Phe	Tyr	Arg	Asn	Leu	Gly	Asp	Pro
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Val	Thr	Ser	Gly	Leu	Phe	Gln	Leu	Arg	Thr	Tyr	Leu	Gln	Met	Ile	Asn
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Met	Asp	Asp	Leu	Phe	Leu	Pro	Leu	Ile	Ala	Lys	Asn	Pro	Gly	Asn	Cys
945					950					955					960
Ser	Ala	Ile	Asp	Phe	Val	Leu	Asn	Pro	Ser	Gly	Leu	Asn	Val	Pro	Gly
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			980					985						990	
Thr	Leu	Ser	Ala	Lys	Asn	Lys	Leu	Ile	Asn	Thr	Leu	Phe	His	Ser	Ser
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	1010					1015					1020				
Thr	Pro	Val	Met	Ser	Arg	Phe	Ala	Ala	Asp	Ile	Phe	Ser	Arg	Thr	
	1025					1030					1035				
Pro	Ser	Gly	Lys	Arg	Leu	Gln	Ile	Leu	Gly	Tyr	Leu	Glu	Gly	Thr	
	1040					1045					1050				
Arg	Thr	Leu	Leu	Ala	Ser	Lys	Val	Ile	Asn	Asn	Asn	Ala	Glu	Thr	
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Pro	Ile	Leu	Asp	Arg	Leu	Arg	Lys	Ile	Thr	Leu	Gln	Arg	Trp	Ser	
	1070					1075					1080				
Leu	Trp	Phe	Ser	Tyr	Leu	Asp	His	Cys	Asp	Gln	Val	Leu	Ala	Asp	
	1085					1090					1095				
Ala	Leu	Ile	Lys	Val	Ser	Cys	Thr	Val	Asp	Leu	Ala	Gln	Ile	Leu	
	1100					1105					1110				
Arg	Glu	Tyr	Thr	Trp	Ala	His	Ile	Leu	Glu	Gly	Arg	Gln	Leu	Ile	
	1115					1120					1125				
Gly	Ala	Thr	Leu	Pro	Cys	Met	Leu	Glu	Gln	Phe	Asn	Val	Phe	Trp	
	1130					1135					1140				
Leu	Lys	Ser	Tyr	Glu	Gln	Cys	Pro	Lys	Cys	Ala	Lys	Ser	Arg	Asn	
	1145					1150					1155				
Pro	Lys	Gly	Glu	Pro	Phe	Val	Ser	Ile	Ala	Ile	Lys	Lys	Gln	Val	
	1160					1165					1170				
Val	Ser	Ala	Trp	Pro	Asn	Gln	Ser	Arg	Leu	Asn	Trp	Thr	Ile	Gly	
	1175					1180					1185				
Asp	Gly	Val	Pro	Tyr	Ile	Gly	Ser	Arg	Thr	Glu	Asp	Lys	Ile	Gly	
	1190					1195					1200				
Gln	Pro	Ala	Ile	Lys	Pro	Lys	Cys	Pro	Ser	Ala	Ala	Leu	Arg	Glu	
	1205					1210					1215				
Ala	Ile	Glu	Leu	Thr	Ser	Arg	Leu	Thr	Trp	Val	Thr	Gln	Gly	Gly	
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Ala	Asn	Ser	Asp	Leu	Leu	Val	Lys	Pro	Phe	Val	Glu	Ala	Arg	Val	
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Asn	Leu	Ser	Val	Gln	Glu	Ile	Leu	Gln	Met	Thr	Pro	Ser	His	Tyr
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Ser	Phe	Met	Ala	Asn	Arg	Met	Ser	Asn	Ser	Ala	Thr	Arg	Leu	Val
1280						1285					1290			
Val	Ser	Thr	Asn	Thr	Leu	Gly	Glu	Phe	Ser	Gly	Gly	Gly	Gln	Ser
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Ala	Arg	Asp	Ser	Asn	Ile	Ile	Phe	Gln	Asn	Val	Ile	Asn	Phe	Ser
1310						1315					1320			
Val	Ala	Leu	Phe	Asp	Leu	Arg	Phe	Arg	Asn	Thr	Glu	Thr	Ser	Ser
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Arg	Glu	Val	Pro	Ala	Gln	Tyr	Leu	Thr	Tyr	Thr	Ser	Thr	Leu	Ser
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Tyr	Pro	Lys	Val	Gly	Leu	Leu	Tyr	Ser	Phe	Gly	Ala	Ile	Val	Ser
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Ser	His	Phe	Met	Tyr	Tyr	Leu	Thr	Thr	Gln	Ile	His	Asn	Leu	Pro
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Val	Ile	Ser	Arg	Leu	Met	Ser	Ile	Asp	Pro	His	Phe	Ser	Ile	Tyr
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Lys	Trp	Ile	Val	Glu	Tyr	Lys	Thr	Ala	Ile	Pro	Leu	Trp	Val	Ile
1565						1570					1575			
Tyr	Pro	Leu	Glu	Gly	Gln	Asn	Pro	Asp	Pro	Ile	Asn	Ser	Phe	Leu
1580						1585					1590			
His	Leu	Ile	Ile	Ala	Leu	Leu	Gln	Asn	Glu	Ser	Pro	Gln	Asn	Asn
1595						1600					1605			
Ile	Gln	Phe	Gln	Glu	Asp	Arg	Asn	Asn	Gln	Gln	Leu	Ser	Asp	Asn
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Leu Val 1625	Tyr Met Cys Lys Ser 1630	Thr Ala Ser Asn Phe 1635	Phe His Ala
Ser Leu 1640	Ala Tyr Trp Arg Ser 1645	Arg His Lys Gly Arg 1650	Pro Lys Asn
Arg Ser 1655	Thr Glu Glu Gln Thr 1660	Val Lys Pro Ile Pro 1665	Tyr Asp Asn
Phe His 1670	Ser Val Lys Cys Ala 1675	Ser Asn Pro Pro Ser 1680	Ile Pro Lys
Ser Lys 1685	Ser Gly Thr Gln Gly 1690	Ser Ser Ala Phe Phe 1695	Glu Lys Leu
Glu Tyr 1700	Asp Lys Glu Arg Glu 1705	Leu Pro Thr Ala Ser 1710	Thr Pro Ala
Glu Gln 1715	Ser Lys Thr Tyr Ile 1720	Lys Ala Leu Ser Ser 1725	Arg Ile Tyr
His Gly 1730	Lys Thr Pro Ser Asn 1735	Ala Ala Lys Asp Asp 1740	Ser Thr Thr
Ser Lys 1745	Gly Cys Asp Ser Lys 1750	Glu Glu Asn Ala Val 1755	Gln Ala Ser
His Arg 1760	Ile Val Leu Pro Phe 1765	Phe Thr Leu Ser Gln 1770	Asn Asp Tyr
Arg Thr 1775	Pro Ser Ala Lys Lys 1780	Ser Glu Tyr Ile Thr 1785	Glu Ile Thr
Lys Leu 1790	Ile Arg Gln Leu Lys 1795	Ala Ile Pro Asp Thr 1800	Thr Val Tyr
Cys Arg 1805	Phe Thr Gly Val Val 1810	Ser Ser Met His Tyr 1815	Lys Leu Asp
Glu Val 1820	Leu Trp Glu Phe Asp 1825	Ser Phe Lys Thr Ala 1830	Val Thr Leu
Ala Glu 1835	Gly Glu Gly Ser Gly 1840	Ala Leu Leu Leu Leu 1845	Gln Lys Tyr
Lys Val 1850	Arg Thr Ile Phe Phe 1855	Asn Thr Leu Ala Thr 1860	Glu His Ser
Ile Glu 1865	Ala Glu Ile Val Ser 1870	Gly Thr Thr Thr Pro 1875	Arg Met Leu
Leu Pro 1880	Val Met Ala Lys Leu 1885	His Asp Asp Gln Ile 1890	Asn Val Ile
Leu Asn 1895	Asn Ser Ala Ser Gln 1900	Val Thr Asp Ile Thr 1905	Asn Pro Ala
Trp Phe 1910	Thr Asp Gln Lys Ser 1915	Arg Ile Pro Thr Gln 1920	Val Glu Ile
Met Thr 1925	Met Asp Ala Glu Thr 1930	Thr Glu Asn Ile Asn 1935	Arg Ser Lys
Leu Tyr 1940	Glu Ala Ile Gln Gln 1945	Leu Ile Val Ser His 1950	Ile Asp Thr
Arg Val 1955	Leu Lys Ile Val Ile 1960	Ile Lys Val Phe Leu 1965	Ser Asp Ile
Glu Gly 1970	Leu Leu Trp Leu Asn 1975	Asp His Leu Ala Pro 1980	Leu Phe Gly
Ser Gly 1985	Tyr Leu Ile Lys Pro 1990	Ile Thr Ser Ser Pro 1995	Lys Ser Ser
Glu Trp	Tyr Leu Cys Leu Ser	Asn Phe Leu Ser Ala	Ser Arg Arg

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2000	2005	2010
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Ala Leu Arg Leu Gln Val 2030	Gln Arg Ser Ser Tyr Trp 2035	Leu Ser His 2040
Leu Val Gln Tyr Ala Asp 2045	Ile Asn Leu His Leu Ser 2050	Tyr Val Asn 2055
Leu Gly Phe Pro Ser Leu 2060	Glu Lys Val Leu Tyr His 2065	Arg Tyr Asn 2070
Leu Val Asp Ser Arg Lys 2075	Gly Pro Leu Val Ser Ile 2080	Leu Tyr His 2085
Leu Thr His Leu Gln Ala 2090	Glu Ile Arg Glu Leu Val 2095	Cys Asp Tyr 2100
Asn Gln Gln Arg Gln Ser 2105	Arg Thr Gln Thr Tyr His 2110	Phe Ile Lys 2115
Thr Thr Lys Gly Arg Ile 2120	Thr Lys Leu Val Asn Asp 2125	Tyr Leu Lys 2130
Phe Tyr Leu Val Val Gln 2135	Ala Leu Lys His Asn Cys 2140	Leu Trp Gln 2145
Glu Glu Leu Arg Thr Leu 2150	Pro Asp Leu Ile Asn Val 2155	Cys Asn Arg 2160
Phe Tyr His Ile Arg Asp 2165	Cys Ser Cys Glu Asp Arg 2170	Phe Leu Ile 2175
Gln Thr Leu Tyr Leu Thr 2180	Arg Met Gln Asp Ser Glu 2185	Ala Lys Leu 2190
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<210> SEQ ID NO 3
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<400> SEQUENCE: 3

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Leu Glu Glu Val Cys Gln Leu Ile Ile Gln Ala Phe Glu Ala Gly Val 50 55 60
Asp Phe Gln Asp Ser Ala Asp Ser Phe Leu Leu Met Leu Cys Leu His 65 70 75 80
His Ala Tyr Gln Gly Asp Tyr Lys Gln Phe Leu Glu Ser Asn Ala Val 85 90 95
Lys Tyr Leu Glu Gly His Gly Phe Arg Phe Glu Met Lys Lys Lys Glu 100 105 110

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Gly	Val	Lys	Arg	Leu	Glu	Glu	Leu	Leu	Pro	Ala	Ala	Ser	Ser	Gly	Lys
		115					120					125			
Asn	Ile	Lys	Arg	Thr	Leu	Ala	Ala	Met	Pro	Glu	Glu	Glu	Thr	Thr	Glu
		130				135					140				
Ala	Asn	Ala	Gly	Gln	Phe	Leu	Ser	Phe	Ala	Ser	Leu	Phe	Leu	Pro	Lys
145					150					155					160
Leu	Val	Val	Gly	Glu	Lys	Ala	Cys	Leu	Glu	Lys	Val	Gln	Arg	Gln	Ile
				165					170					175	
Gln	Val	His	Ala	Glu	Gln	Gly	Leu	Ile	Gln	Tyr	Pro	Thr	Ser	Trp	Gln
			180					185					190		
Ser	Val	Gly	His	Met	Met	Val	Ile	Phe	Arg	Leu	Met	Arg	Thr	Asn	Phe
		195					200					205			
Leu	Ile	Lys	Phe	Leu	Leu	Ile	His	Gln	Gly	Met	His	Met	Val	Ala	Gly
	210					215					220				
His	Asp	Ala	Asn	Asp	Ala	Val	Ile	Ala	Asn	Ser	Val	Ala	Gln	Ala	Arg
225					230					235					240
Phe	Ser	Gly	Leu	Leu	Ile	Val	Lys	Thr	Val	Leu	Asp	His	Ile	Leu	Gln
			245						250					255	
Lys	Thr	Glu	His	Gly	Val	Arg	Leu	His	Pro	Leu	Ala	Arg	Thr	Ala	Lys
			260					265					270		
Val	Lys	Asn	Glu	Val	Ser	Ser	Phe	Lys	Ala	Ala	Leu	Ala	Ser	Leu	Ala
		275					280					285			
Gln	His	Gly	Glu	Tyr	Ala	Pro	Phe	Ala	Arg	Leu	Leu	Asn	Leu	Ser	Gly
	290					295					300				
Val	Asn	Asn	Leu	Glu	His	Gly	Leu	Phe	Pro	Gln	Leu	Ser	Ala	Ile	Ala
305					310					315					320
Leu	Gly	Val	Ala	Thr	Ala	His	Gly	Ser	Thr	Leu	Ala	Gly	Val	Asn	Val
				325					330					335	
Gly	Glu	Gln	Tyr	Gln	Gln	Leu	Arg	Glu	Ala	Ala	Thr	Glu	Ala	Glu	Lys
			340					345					350		
Gln	Leu	Gln	Lys	Tyr	Ala	Glu	Ser	Arg	Glu	Leu	Asp	His	Leu	Gly	Leu
		355					360					365			
Asp	Asp	Gln	Glu	Lys	Lys	Ile	Leu	Lys	Asp	Phe	His	Gln	Lys	Lys	Asn
	370					375					380				
Glu	Ile	Ser	Phe	Gln	Gln	Thr	Thr	Ala	Met	Val	Thr	Leu	Arg	Lys	Glu
385					390					395					400
Arg	Leu	Ala	Lys	Leu	Thr	Glu	Ala	Ile	Thr	Ser	Thr	Ser	Ile	Leu	Lys
				405					410					415	
Thr	Gly	Arg	Arg	Tyr	Asp	Asp	Asp	Asn	Asp	Ile	Pro	Phe	Pro	Gly	Pro
			420					425					430		
Ile	Asn	Asp	Asn	Glu	Asn	Ser	Gly	Gln	Asn	Asp	Asp	Asp	Pro	Thr	Asp
		435					440					445			
Ser	Gln	Asp	Thr	Thr	Ile	Pro	Asp	Val	Ile	Ile	Asp	Pro	Asn	Asp	Gly
		450				455					460				
Gly	Tyr	Asn	Asn	Tyr	Ser	Asp	Tyr	Ala	Asn	Asp	Ala	Ala	Ser	Ala	Pro
465					470					475					480
Asp	Asp	Leu	Val	Leu	Phe	Asp	Leu	Glu	Asp	Glu	Asp	Asp	Ala	Asp	Asn
				485					490					495	
Pro	Ala	Gln	Asn	Thr	Pro	Glu	Lys	Asn	Asp	Arg	Pro	Ala	Thr	Thr	Lys
			500					505					510		
Leu	Arg	Asn	Gly	Gln	Asp	Gln	Asp	Gly	Asn	Gln	Gly	Glu	Thr	Ala	Ser

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515	520	525
Pro Arg Val Ala Pro Asn Gln Tyr Arg Asp Lys Pro Met Pro Gln Val 530 535 540		
Gln Asp Arg Ser Glu Asn His Asp Gln Thr Leu Gln Thr Gln Ser Arg 545 550 555 560		
Val Leu Thr Pro Ile Ser Glu Glu Ala Asp Pro Ser Asp His Asn Asp 565 570 575		
Gly Asp Asn Glu Ser Ile Pro Pro Leu Glu Ser Asp Asp Glu Gly Ser 580 585 590		
Thr Asp Thr Thr Ala Ala Glu Thr Lys Pro Ala Thr Ala Pro Pro Ala 595 600 605		
Pro Val Tyr Arg Ser Ile Ser Val Asp Asp Ser Val Pro Ser Glu Asn 610 615 620		
Ile Pro Ala Gln Ser Asn Gln Thr Asn Asn Glu Asp Asn Val Arg Asn 625 630 635 640		
Asn Ala Gln Ser Glu Gln Ser Ile Ala Glu Met Tyr Gln His Ile Leu 645 650 655		
Lys Thr Gln Gly Pro Phe Asp Ala Ile Leu Tyr Tyr His Met Met Lys 660 665 670		
Glu Glu Pro Ile Ile Phe Ser Thr Ser Asp Gly Lys Glu Tyr Thr Tyr 675 680 685		
Pro Asp Ser Leu Glu Asp Glu Tyr Pro Pro Trp Leu Ser Glu Lys Glu 690 695 700		
Ala Met Asn Glu Asp Asn Arg Phe Ile Thr Met Asp Gly Gln Gln Phe 705 710 715 720		
Tyr Trp Pro Val Met Asn His Arg Asn Lys Phe Met Ala Ile Leu Gln 725 730 735		

His His Arg

<210> SEQ ID NO 4
 <211> LENGTH: 373
 <212> TYPE: PRT
 <213> ORGANISM: Bundibugyo ebolavirus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <223> OTHER INFORMATION: Bundibugyo ebolavirus SGP viral protein

<400> SEQUENCE: 4

Met Val Thr Ser Gly Ile Leu Gln Leu Pro Arg Glu Arg Phe Arg Lys 1 5 10 15
Thr Ser Phe Phe Val Trp Val Ile Ile Leu Phe His Lys Val Phe Pro 20 25 30
Ile Pro Leu Gly Val Val His Asn Asn Thr Leu Gln Val Ser Asp Ile 35 40 45
Asp Lys Leu Val Cys Arg Asp Lys Leu Ser Ser Thr Ser Gln Leu Lys 50 55 60
Ser Val Gly Leu Asn Leu Glu Gly Asn Gly Val Ala Thr Asp Val Pro 65 70 75 80
Thr Ala Thr Lys Arg Trp Gly Phe Arg Ala Gly Val Pro Pro Lys Val 85 90 95
Val Asn Tyr Glu Ala Gly Glu Trp Ala Glu Asn Cys Tyr Asn Leu Asp 100 105 110
Ile Lys Lys Ala Asp Gly Ser Glu Cys Leu Pro Glu Ala Pro Glu Gly

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115					120					125					
Val	Arg	Gly	Phe	Pro	Arg	Cys	Arg	Tyr	Val	His	Lys	Val	Ser	Gly	Thr
	130					135					140				
Gly	Pro	Cys	Pro	Glu	Gly	Tyr	Ala	Phe	His	Lys	Glu	Gly	Ala	Phe	Phe
145					150					155					160
Leu	Tyr	Asp	Arg	Leu	Ala	Ser	Thr	Ile	Ile	Tyr	Arg	Ser	Thr	Thr	Phe
				165					170						175
Ser	Glu	Gly	Val	Val	Ala	Phe	Leu	Ile	Leu	Pro	Glu	Thr	Lys	Lys	Asp
			180						185					190	
Phe	Phe	Gln	Ser	Pro	Pro	Leu	His	Glu	Pro	Ala	Asn	Met	Thr	Thr	Asp
		195					200					205			
Pro	Ser	Ser	Tyr	Tyr	His	Thr	Val	Thr	Leu	Asn	Tyr	Val	Ala	Asp	Asn
	210					215					220				
Phe	Gly	Thr	Asn	Met	Thr	Asn	Phe	Leu	Phe	Gln	Val	Asp	His	Leu	Thr
225					230					235					240
Tyr	Val	Gln	Leu	Glu	Pro	Arg	Phe	Thr	Pro	Gln	Phe	Leu	Val	Gln	Leu
				245					250					255	
Asn	Glu	Thr	Ile	Tyr	Thr	Asn	Gly	Arg	Arg	Ser	Asn	Thr	Thr	Gly	Thr
			260					265						270	
Leu	Ile	Trp	Lys	Val	Asn	Pro	Thr	Val	Asp	Thr	Gly	Val	Gly	Glu	Trp
	275						280					285			
Ala	Phe	Trp	Glu	Asn	Lys	Lys	Thr	Ser	Gln	Lys	Pro	Phe	Gln	Val	Lys
	290					295					300				
Ser	Cys	Leu	Ser	Tyr	Leu	Tyr	Gln	Glu	Pro	Arg	Ile	Gln	Ala	Ala	Thr
305					310					315					320
Arg	Arg	Arg	Arg	Ser	Leu	Pro	Pro	Ala	Ser	Pro	Thr	Thr	Lys	Pro	Pro
				325					330					335	
Arg	Thr	Thr	Lys	Thr	Trp	Phe	Gln	Arg	Ile	Pro	Leu	Gln	Trp	Phe	Lys
			340					345						350	
Cys	Glu	Thr	Ser	Arg	Gly	Lys	Thr	Gln	Cys	Arg	Pro	His	Pro	Gln	Thr
		355					360					365			
Gln	Ser	Pro	Gln	Leu											
	370														

<210> SEQ ID NO 5
 <211> LENGTH: 251
 <212> TYPE: PRT
 <213> ORGANISM: Bundibugyo ebolavirus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <223> OTHER INFORMATION: Bundibugyo ebolavirus VP24 viral protein

<400> SEQUENCE: 5

Met	Ala	Lys	Ala	Thr	Gly	Arg	Tyr	Asn	Leu	Val	Ser	Pro	Lys	Lys	Asp
1				5					10					15	
Leu	Glu	Arg	Gly	Leu	Val	Leu	Ser	Asp	Leu	Cys	Thr	Phe	Leu	Val	Asp
			20					25					30		
Gln	Thr	Ile	Gln	Gly	Trp	Arg	Val	Thr	Trp	Val	Gly	Ile	Glu	Phe	Asp
		35				40						45			
Ile	Ala	Gln	Lys	Gly	Met	Ala	Leu	Leu	His	Arg	Leu	Lys	Thr	Ala	Asp
	50					55					60				
Phe	Ala	Pro	Ala	Trp	Ser	Met	Thr	Arg	Asn	Leu	Phe	Pro	His	Leu	Phe
65					70					75					80

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Gln Asn Ser Asn Ser Thr Ile Glu Ser Pro Leu Trp Ala Leu Arg Val
85 90 95

Ile Leu Ala Ala Gly Ile Gln Asp Gln Leu Ile Asp Gln Ser Leu Val
100 105 110

Glu Pro Leu Ala Gly Ala Leu Ser Leu Val Ser Asp Trp Leu Leu Thr
115 120 125

Thr Asn Thr Asn His Phe Gln Met Arg Thr Gln His Ala Lys Glu Gln
130 135 140

Leu Ser Leu Lys Met Leu Ser Leu Val Arg Ser Asn Ile Leu Lys Phe
145 150 155 160

Ile Ser Gln Leu Asp Ala Leu His Val Val Asn Tyr Asn Gly Leu Leu
165 170 175

Ser Ser Ile Glu Ile Gly Thr Arg Asn His Thr Ile Ile Ile Thr Arg
180 185 190

Thr Asn Met Gly Phe Leu Val Glu Leu Gln Glu Pro Asp Lys Ser Ala
195 200 205

Met Asn Gln Lys Lys Pro Gly Pro Val Lys Phe Ser Leu Leu His Glu
210 215 220

Ser Thr Phe Lys Ala Leu Ile Lys Lys Pro Ala Thr Lys Met Gln Ala
225 230 235 240

Leu Ile Leu Glu Phe Asn Ser Ser Leu Ala Ile
245 250

<210> SEQ ID NO 6
<211> LENGTH: 289
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Bundibugyo ebolavirus VP30 viral protein

<400> SEQUENCE: 6

Met Asp Ser Phe His Glu Arg Gly Arg Ser Arg Thr Ile Arg Gln Ser
1 5 10 15

Ala Arg Asp Gly Pro Ser His Gln Val Arg Thr Arg Ser Ser Ser Arg
20 25 30

Asp Ser His Arg Ser Glu Tyr His Thr Pro Arg Ser Ser Ser Gln Val
35 40 45

Arg Val Pro Thr Val Phe His Arg Lys Arg Thr Asp Ser Leu Thr Val
50 55 60

Pro Pro Ala Pro Lys Asp Ile Cys Pro Thr Leu Arg Lys Gly Phe Leu
65 70 75 80

Cys Asp Ser Asn Phe Cys Lys Lys Asp His Gln Leu Glu Ser Leu Thr
85 90 95

Asp Arg Glu Leu Leu Leu Ile Ala Arg Lys Thr Cys Gly Ser Leu
100 105 110

Glu Gln Gln Leu Asn Ile Thr Ala Pro Lys Asp Thr Arg Leu Ala Asn
115 120 125

Pro Ile Ala Asp Asp Phe Gln Gln Lys Asp Gly Pro Lys Ile Thr Leu
130 135 140

Leu Thr Leu Leu Glu Thr Ala Glu Tyr Trp Ser Lys Gln Asp Ile Lys
145 150 155 160

Gly Ile Asp Asp Ser Arg Leu Arg Ala Leu Leu Thr Leu Cys Ala Val
165 170 175

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Leu Arg Asn Ile Met Tyr Asp His Leu Pro Gly Phe Gly Thr Ala Phe
 225 230 235 240
 His Gln Leu Val Gln Val Ile Cys Lys Leu Gly Lys Asp Asn Ser Ser
 245 250 255
 Leu Asp Val Ile His Ala Glu Phe Gln Ala Ser Leu Ala Glu Gly Asp
 260 265 270
 Ser Pro Gln Cys Ala Leu Ile Gln Ile Thr Lys Arg Ile Pro Ile Phe
 275 280 285
 Gln Asp Ala Ala Pro Pro Val Ile His Ile Arg Ser Arg Gly Asp Ile
 290 295 300
 Pro Lys Ala Cys Gln Lys Ser Leu Arg Pro Val Pro Pro Ser Pro Lys
 305 310 315 320
 Ile Asp Arg Gly Trp Val Cys Ile Phe Gln Leu Gln Asp Gly Lys Thr
 325 330 335
 Leu Gly Leu Lys Ile
 340

<210> SEQ ID NO 8
 <211> LENGTH: 326
 <212> TYPE: PRT
 <213> ORGANISM: Bundibugyo ebolavirus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <223> OTHER INFORMATION: Bundibugyo ebolavirus VP40 viral protein

<400> SEQUENCE: 8

Met Arg Arg Ala Ile Leu Pro Thr Ala Pro Pro Glu Tyr Ile Glu Ala
 1 5 10 15
 Val Tyr Pro Met Arg Thr Val Ser Thr Ser Ile Asn Ser Thr Ala Ser
 20 25 30
 Gly Pro Asn Phe Pro Ala Pro Asp Val Met Met Ser Asp Thr Pro Ser
 35 40 45
 Asn Ser Leu Arg Pro Ile Ala Asp Asp Asn Ile Asp His Pro Ser His
 50 55 60
 Thr Pro Thr Ser Val Ser Ser Ala Phe Ile Leu Glu Ala Met Val Asn
 65 70 75 80
 Val Ile Ser Gly Pro Lys Val Leu Met Lys Gln Ile Pro Ile Trp Leu
 85 90 95
 Pro Leu Gly Val Ala Asp Gln Lys Thr Tyr Ser Phe Asp Ser Thr Thr
 100 105 110
 Ala Ala Ile Met Leu Ala Ser Tyr Thr Ile Thr His Phe Gly Lys Thr
 115 120 125
 Ser Asn Pro Leu Val Arg Ile Asn Arg Leu Gly Pro Gly Ile Pro Asp
 130 135 140
 His Pro Leu Arg Leu Leu Arg Ile Gly Asn Gln Ala Phe Leu Gln Glu
 145 150 155 160
 Phe Val Leu Pro Pro Val Gln Leu Pro Gln Tyr Phe Thr Phe Asp Leu
 165 170 175
 Thr Ala Leu Lys Leu Ile Thr Gln Pro Leu Pro Ala Ala Thr Trp Thr
 180 185 190
 Asp Asp Thr Pro Thr Gly Pro Thr Gly Ile Leu Arg Pro Gly Ile Ser
 195 200 205
 Phe His Pro Lys Leu Arg Pro Ile Leu Leu Pro Gly Lys Thr Gly Lys

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210		215		220
Arg Gly Ser Ser Ser	Asp Leu Thr Ser Pro	Asp Lys Ile Gln Ala Ile		
225	230	235		240
Met Asn Phe Leu Gln	Asp Leu Lys Leu Val	Pro Ile Asp Pro Ala Lys		
	245	250		255
Asn Ile Met Gly Ile	Glu Val Pro Glu Leu	Leu Val His Arg Leu Thr		
	260	265		270
Gly Lys Lys Ile Thr	Thr Lys Asn Gly Gln	Pro Ile Ile Pro Ile Leu		
	275	280		285
Leu Pro Lys Tyr Ile	Gly Met Asp Pro Ile	Ser Gln Gly Asp Leu Thr		
	290	295		300
Met Val Ile Thr Gln	Asp Cys Asp Thr Cys	His Ser Pro Ala Ser Leu		
305	310	315		320
Pro Pro Val Ser Glu	Lys			
	325			

<210> SEQ ID NO 9
 <211> LENGTH: 676
 <212> TYPE: PRT
 <213> ORGANISM: Bundibugyo ebolavirus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <223> OTHER INFORMATION: Bundibugyo ebolavirus GP viral protein

<400> SEQUENCE: 9

Met Val Thr Ser Gly	Ile Leu Gln Leu Pro	Arg Glu Arg Phe Arg Lys
1	5	10
Thr Ser Phe Phe Val	Trp Val Ile Ile Leu	Phe His Lys Val Phe Pro
	20	25
Ile Pro Leu Gly Val	Val His Asn Asn Thr	Leu Gln Val Ser Asp Ile
	35	40
Asp Lys Leu Val Cys	Arg Asp Lys Leu Ser	Ser Thr Ser Gln Leu Lys
	50	55
Ser Val Gly Leu Asn	Leu Glu Gly Asn Gly	Val Ala Thr Asp Val Pro
65	70	75
Thr Ala Thr Lys Arg	Trp Gly Phe Arg Ala	Gly Val Pro Pro Lys Val
	85	90
Val Asn Tyr Glu Ala	Gly Glu Trp Ala Glu	Asn Cys Tyr Asn Leu Asp
	100	105
Ile Lys Lys Ala Asp	Gly Ser Glu Cys Leu	Pro Glu Ala Pro Glu Gly
	115	120
Val Arg Gly Phe Pro	Arg Cys Arg Tyr Val	His Lys Val Ser Gly Thr
	130	135
Gly Pro Cys Pro Glu	Gly Tyr Ala Phe His	Lys Glu Gly Ala Phe Phe
145	150	155
Leu Tyr Asp Arg Leu	Ala Ser Thr Ile Ile	Tyr Arg Ser Thr Thr Phe
	165	170
Ser Glu Gly Val Val	Ala Phe Leu Ile Leu	Pro Glu Thr Lys Lys Asp
	180	185
Phe Phe Gln Ser Pro	Pro Leu His Glu Pro	Ala Asn Met Thr Thr Asp
	195	200
Pro Ser Ser Tyr Tyr	His Thr Val Thr Leu	Asn Tyr Val Ala Asp Asn
	210	215
		220

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Phe	Gly	Thr	Asn	Met	Thr	Asn	Phe	Leu	Phe	Gln	Val	Asp	His	Leu	Thr
225					230					235					240
Tyr	Val	Gln	Leu	Glu	Pro	Arg	Phe	Thr	Pro	Gln	Phe	Leu	Val	Gln	Leu
				245					250					255	
Asn	Glu	Thr	Ile	Tyr	Thr	Asn	Gly	Arg	Arg	Ser	Asn	Thr	Thr	Gly	Thr
			260					265						270	
Leu	Ile	Trp	Lys	Val	Asn	Pro	Thr	Val	Asp	Thr	Gly	Val	Gly	Glu	Trp
		275					280					285			
Ala	Phe	Trp	Glu	Asn	Lys	Lys	Asn	Phe	Thr	Lys	Thr	Leu	Ser	Ser	Glu
	290					295						300			
Glu	Leu	Ser	Val	Ile	Phe	Val	Pro	Arg	Ala	Gln	Asp	Pro	Gly	Ser	Asn
305					310					315					320
Gln	Lys	Thr	Lys	Val	Thr	Pro	Thr	Ser	Phe	Ala	Asn	Asn	Gln	Thr	Ser
				325					330						335
Lys	Asn	His	Glu	Asp	Leu	Val	Pro	Glu	Asp	Pro	Ala	Ser	Val	Val	Gln
			340						345					350	
Val	Arg	Asp	Leu	Gln	Arg	Glu	Asn	Thr	Val	Pro	Thr	Pro	Pro	Pro	Asp
		355					360						365		
Thr	Val	Pro	Thr	Thr	Leu	Ile	Pro	Asp	Thr	Met	Glu	Glu	Gln	Thr	Thr
		370				375						380			
Ser	His	Tyr	Glu	Pro	Pro	Asn	Ile	Ser	Arg	Asn	His	Gln	Glu	Arg	Asn
385						390				395					400
Asn	Thr	Ala	His	Pro	Glu	Thr	Leu	Ala	Asn	Asn	Pro	Pro	Asp	Asn	Thr
				405					410					415	
Thr	Pro	Ser	Thr	Pro	Pro	Gln	Asp	Gly	Glu	Arg	Thr	Ser	Ser	His	Thr
			420					425						430	
Thr	Pro	Ser	Pro	Arg	Pro	Val	Pro	Thr	Ser	Thr	Ile	His	Pro	Thr	Thr
		435					440						445		
Arg	Glu	Thr	His	Ile	Pro	Thr	Thr	Met	Thr	Thr	Ser	His	Asp	Thr	Asp
	450					455							460		
Ser	Asn	Arg	Pro	Asn	Pro	Ile	Asp	Ile	Ser	Glu	Ser	Thr	Glu	Pro	Gly
465					470					475					480
Pro	Leu	Thr	Asn	Thr	Thr	Arg	Gly	Ala	Ala	Asn	Leu	Leu	Thr	Gly	Ser
				485					490					495	
Arg	Arg	Thr	Arg	Arg	Glu	Ile	Thr	Leu	Arg	Thr	Gln	Ala	Lys	Cys	Asn
			500					505						510	
Pro	Asn	Leu	His	Tyr	Trp	Thr	Thr	Gln	Asp	Glu	Gly	Ala	Ala	Ile	Gly
		515					520						525		
Leu	Ala	Trp	Ile	Pro	Tyr	Phe	Gly	Pro	Ala	Ala	Glu	Gly	Ile	Tyr	Thr
	530					535						540			
Glu	Gly	Ile	Met	His	Asn	Gln	Asn	Gly	Leu	Ile	Cys	Gly	Leu	Arg	Gln
545					550					555					560
Leu	Ala	Asn	Glu	Thr	Thr	Gln	Ala	Leu	Gln	Leu	Phe	Leu	Arg	Ala	Thr
				565					570					575	
Thr	Glu	Leu	Arg	Thr	Phe	Ser	Ile	Leu	Asn	Arg	Lys	Ala	Ile	Asp	Phe
			580					585						590	
Leu	Leu	Gln	Arg	Trp	Gly	Gly	Thr	Cys	His	Ile	Leu	Gly	Pro	Asp	Cys
		595					600						605		
Cys	Ile	Glu	Pro	His	Asp	Trp	Thr	Lys	Asn	Ile	Thr	Asp	Lys	Ile	Asp
	610					615						620			
Gln	Ile	Ile	His	Asp	Phe	Ile	Asp	Lys	Pro	Leu	Pro	Asp	Gln	Thr	Asp

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625	630	635	640
Asn Asp Asn Trp Trp Thr Gly Trp Arg Gln Trp Val Pro Ala Gly Ile			
	645	650	655
Gly Ile Thr Gly Val Ile Ile Ala Val Ile Ala Leu Leu Cys Ile Cys			
	660	665	670
Lys Phe Leu Leu			
	675		
<210> SEQ ID NO 10			
<211> LENGTH: 18935			
<212> TYPE: DNA			
<213> ORGANISM: Cote d'Ivoire ebolavirus			
<400> SEQUENCE: 10			
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agattaataa ttttctctc attgacactt acattaagat taagattctc attgatctgt			120
tacttactct gaggataata attggtgttc agaagtacc cttccccag tgggggcaaa			180
gacagtccaa aagactcaac ttgtcctatt caactaatct gttttgtctc agtagttcac			240
atattgatca taccaggag ttggacctaa ttccaaagct tagagtggga cctagtgtat			300
cctcggggct gtaatataat cagccattta acacataaca agccctactg ttttctgtt			360
ttgccgtgca tttagaataa gagacaactt aaacctccga ttccggcaaca caggaataa			420
tctcaccaga cccggcagtg tcttcaggct tcatagcccc aagatggaga gtcgggcca			480
caaagcatgg atgacgcaca ccgcatcagg ttccgaaaca gattaccata agattttaac			540
agcaggattg tcagtccaac aaggcattgt gagacaacgg gtcattcaag tccaccaggt			600
tacaaaccta gaagaaatat gccaatgtat cattcaagcc tttgaagctg gtgttgattt			660
tcaagagagt gcagacagtt tcttctgtat gctatgttta catcatgctt atcagggtga			720
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tgaggtcagg aaaaaggaag gagtcaagcg actcgaagaa ttgcttcctg ctgcatccag			840
tggaagagc atcaggagaa cactggctgc aatgcctgaa gaggagacaa cagaagcaaa			900
tgccggacag ttcctctctt ttgctagctt atttcttct aagctagttg tccgagaaaa			960
agcctgtcta gaaaaggtgc agcggcaaat tcaagttcat tctgagcagg gattgatcca			1020
atccccaca gcctggcagt cagttggaca catgatggtc atttcagac tgatgagaac			1080
aaatcttcta attaagttcc tccttataca tcaagggatg catatggtag caggacacga			1140
tgctaacgat gctgtcatcg caaactctgt agctcaagca cgtttttcag gattattgat			1200
cgttaaaaca gtgctagatc acatccttca gaaaacagag cacggagtgc gtcttcatcc			1260
tttggcaaga actgctaagg tcaagaacga agtaaatcc ttttaaggctg cccttagctc			1320
gctagacaaa catggagagt atgctcctt ttgctgcttg ctgaatctt ctggagtcaa			1380
caatctcgag cacggactgt ttcctcagct ttctgcaatt gccctaggtg tcgcaacggc			1440
acacggcagt accctggcag gagtaaatgt gggggaacag taccagcaac tacgagaagc			1500
agccactgag gcagaaaaac aattgcagaa atacgctgaa tctcgcgagc ttgaccatct			1560
aggtctcgat gatcaagaga agaagatctt gaaagacttc catcagaaga aaaatgaaat			1620
cagcttccag cagacaacag ccatggctac actacggaag gaaaggctag ccaagctcac			1680
tgaggcaatc acctccacat cccttctcaa gacaggaaaa cagtatgatg atgacaacga			1740

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aaaaactgta tccaatctat aatttctgac agcaacaatt catcaacgga tccaatcagt 15900
agtggggaaa cacgatcatt caccactcac ttcttgacat atcctaagat tggactacta 15960
tatagttttg gtgactcat cagttattat ctaggcaaca ccattattag aacccccaaa 16020
ttgactctta acaacttcat atattaccta gctactcaa tacataatth acctcatcgc 16080
tcgttgagaa tccttaaacc tactttgaaa cacgctagtg ttatctcgag attaataagt 16140
attgactctc acttctcaat ttatattgga ggaactgctg gtgatcgagg actttccgat 16200
gcggaagat tgtttcttag aactgccatt actgtcttcc ttcaattcgt tagaaagtgg 16260
atagttgaac gcaagacagc tattccactg tgggtcatct acctctaga aggtcaaagt 16320
cctagtccga tcaacagttt tctacaccac gtcactcgcg ttgtgcaaca tgagtctctc 16380
cacgatcatg tttgtgctgc agaagcccac agtcgagtgg agacattga taatttagtt 16440
tatatgtgta aaagcacagc aagtaacttc tttcatgctt cattagcata ctggagaagt 16500
cgatctaaaa atcaagacaa aagagagatg acaagatat tatctttgac gcaaacggaa 16560
aagaaaaatt cattcggtca tacagcacat ccagaaagca ctgctgttct tggttccctc 16620
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aattttaagt ctgctataac acttgccgaa ggtgaagggt cgggtgcatt actcttatta 17100
caaaaatata aagtagaaac cttgtttttt aatacactag ccacagaaca cagcattgaa 17160
gcagaaatta tttctggaat aactacacca agaatgcttc tccctattat gtctaggttc 17220
catggtggac aaataaaagt cactttaaac aattctgcaa gccagattac cgatattact 17280
aatccaaagt ggttggcaga ccaaaaatct aggatcccta agcaagtaga gattataacc 17340
atggatgctg aaacaacaga aacatthaat cgggtcaaat tgtacgaagc agtccaacag 17400
ctgattgtct cacatattga tccgaatgca ctcaaagttg tggttcttaa agttttctta 17460
agtgacattg atggaatcct atggctgaat gataacctta cccctttggt tgggctgggt 17520
tacttgatca agccgatcac ctctagccca aatctagtg agtggtaacct atgtctctca 17580
aacctcttt caactcaag acgattacct catcagagtc ataactcttg catgcatggt 17640
attcaaacag cactccagct acaaatcag aggagctcat attggcttag ccaoctgtc 17700

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cagtatgcca atcataatTT gcatttagat tatattaatc tcggtttccc ttcattggag 17760
aggggtttat accatagata caatttagtc gattctcaga aaggcccttt gacttccatt 17820
gtccaacatc tagcgcacct gcagaccgag attagggagt tggtaatga ctataatcaa 17880
caaagacaaa gtcgaaccca aacatatcat ttcattaaaa caataaaagg tcgtattaca 17940
aaattggtaa atgattacct taagtctttt ctaataatac aagccttaaa gcacaattgc 18000
acatggcaag aggaactaag agctcttcca gatctaatta gtgtctgcac tcgattctat 18060
catactcgaa actggtcatg tgaaaaccgg ttcctagtac agactttata cttatcacgc 18120
atgcaggatt cggaaatcaa actaatagat agattgaccg gccttcttag tctatgtcca 18180
aatgggtttt ttcgtaagg actcttgacg taaaaactcc acatagtat acaatggtac 18240
caggacacta tatgtaaatt gaccctaaga aagagtaatt cgacacacag agttctcaag 18300
tgaaacccct catctcagat tatctgtggt tgcaattcta atatccgatt gttaccccg 18360
gagtataact ccagattaat ataagaaaat accttttgtc ctgcaaatTT atcttaaatt 18420
caagtacata cgctccaaat cgtataaaat attaagaaaa agttaatctg cttgctttaa 18480
ttataacttt aatattcgac aaatagttaa cggctctatc actcaaaaat ttcattaaca 18540
aaagaagtac tctgagtata ttcacatc atatgtgatt aacatataag caacgcatga 18600
tgcgccttcc tcttacttat tgtgtgtgca cgcagtcggt gtactacctc gaaaattcca 18660
aacaataaat cgtgtctatc ccgcatTTag tgtctttaa ttaagatctc aaatccaaaa 18720
aactgggttt atggtgatgt aaatcaataa taccgaaatt gcttgatatt aaaataaagc 18780
ttaaggatt tttccttaaa cgggtgatgt aggtatatag gaaagctcga tcacgatgtc 18840
ccttactcag aaaaagaaaa acggaagccc tattggccat ttaatcgtac aaaaaaatat 18900
ctttacaaa ttgttttctc ttttttgtgt gtcca 18935

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<210> SEQ ID NO 11
<211> LENGTH: 739
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Cote d'Ivoire ebolavirus NP protein

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<400> SEQUENCE: 11

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Met Glu Ser Arg Ala His Lys Ala Trp Met Thr His Thr Ala Ser Gly
 1             5             10             15
Phe Glu Thr Asp Tyr His Lys Ile Leu Thr Ala Gly Leu Ser Val Gln
 20             25             30
Gln Gly Ile Val Arg Gln Arg Val Ile Gln Val His Gln Val Thr Asn
 35             40             45
Leu Glu Glu Ile Cys Gln Leu Ile Ile Gln Ala Phe Glu Ala Gly Val
 50             55             60
Asp Phe Gln Glu Ser Ala Asp Ser Phe Leu Leu Met Leu Cys Leu His
 65             70             75             80
His Ala Tyr Gln Gly Asp Tyr Lys Gln Phe Leu Glu Ser Asn Ala Val
 85             90             95
Lys Tyr Leu Glu Gly His Gly Phe Arg Phe Glu Val Arg Lys Lys Glu
100            105            110
Gly Val Lys Arg Leu Glu Glu Leu Leu Pro Ala Ala Ser Ser Gly Lys

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115					120					125					
Ser	Ile	Arg	Arg	Thr	Leu	Ala	Ala	Met	Pro	Glu	Glu	Glu	Thr	Thr	Glu
130					135					140					
Ala	Asn	Ala	Gly	Gln	Phe	Leu	Ser	Phe	Ala	Ser	Leu	Phe	Leu	Pro	Lys
145					150					155					160
Leu	Val	Val	Gly	Glu	Lys	Ala	Cys	Leu	Glu	Lys	Val	Gln	Arg	Gln	Ile
				165					170					175	
Gln	Val	His	Ser	Glu	Gln	Gly	Leu	Ile	Gln	Tyr	Pro	Thr	Ala	Trp	Gln
			180					185						190	
Ser	Val	Gly	His	Met	Met	Val	Ile	Phe	Arg	Leu	Met	Arg	Thr	Asn	Phe
		195					200					205			
Leu	Ile	Lys	Phe	Leu	Leu	Ile	His	Gln	Gly	Met	His	Met	Val	Ala	Gly
	210					215					220				
His	Asp	Ala	Asn	Asp	Ala	Val	Ile	Ala	Asn	Ser	Val	Ala	Gln	Ala	Arg
225					230					235					240
Phe	Ser	Gly	Leu	Leu	Ile	Val	Lys	Thr	Val	Leu	Asp	His	Ile	Leu	Gln
				245					250					255	
Lys	Thr	Glu	His	Gly	Val	Arg	Leu	His	Pro	Leu	Ala	Arg	Thr	Ala	Lys
			260					265						270	
Val	Lys	Asn	Glu	Val	Asn	Ser	Phe	Lys	Ala	Ala	Leu	Ser	Ser	Leu	Ala
		275					280					285			
Gln	His	Gly	Glu	Tyr	Ala	Pro	Phe	Ala	Arg	Leu	Leu	Asn	Leu	Ser	Gly
	290					295					300				
Val	Asn	Asn	Leu	Glu	His	Gly	Leu	Phe	Pro	Gln	Leu	Ser	Ala	Ile	Ala
305					310					315					320
Leu	Gly	Val	Ala	Thr	Ala	His	Gly	Ser	Thr	Leu	Ala	Gly	Val	Asn	Val
				325					330					335	
Gly	Glu	Gln	Tyr	Gln	Gln	Leu	Arg	Glu	Ala	Ala	Thr	Glu	Ala	Glu	Lys
			340					345						350	
Gln	Leu	Gln	Lys	Tyr	Ala	Glu	Ser	Arg	Glu	Leu	Asp	His	Leu	Gly	Leu
		355					360					365			
Asp	Asp	Gln	Glu	Lys	Lys	Ile	Leu	Lys	Asp	Phe	His	Gln	Lys	Lys	Asn
	370					375					380				
Glu	Ile	Ser	Phe	Gln	Gln	Thr	Thr	Ala	Met	Val	Thr	Leu	Arg	Lys	Glu
385					390					395					400
Arg	Leu	Ala	Lys	Leu	Thr	Glu	Ala	Ile	Thr	Ser	Thr	Ser	Leu	Leu	Lys
				405					410					415	
Thr	Gly	Lys	Gln	Tyr	Asp	Asp	Asp	Asn	Asp	Ile	Pro	Phe	Pro	Gly	Pro
			420					425						430	
Ile	Asn	Asp	Asn	Glu	Asn	Ser	Glu	Gln	Gln	Asp	Asp	Asp	Pro	Thr	Asp
		435					440					445			
Ser	Gln	Asp	Thr	Thr	Ile	Pro	Asp	Ile	Ile	Val	Asp	Pro	Asp	Asp	Gly
		450				455					460				
Arg	Tyr	Asn	Asn	Tyr	Gly	Asp	Tyr	Pro	Ser	Glu	Thr	Ala	Asn	Ala	Pro
465					470					475					480
Glu	Asp	Leu	Val	Leu	Phe	Asp	Leu	Glu	Asp	Gly	Asp	Glu	Asp	Asp	His
				485					490					495	
Arg	Pro	Ser	Ser	Ser	Ser	Glu	Asn	Asn	Asn	Lys	His	Ser	Leu	Thr	Gly
			500					505						510	
Thr	Asp	Ser	Asn	Lys	Thr	Ser	Asn	Trp	Asn	Arg	Asn	Pro	Thr	Asn	Met
		515					520					525			

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Pro Lys Lys Asp Ser Thr Gln Asn Asn Asp Asn Pro Ala Gln Arg Ala
 530 535 540
 Gln Glu Tyr Ala Arg Asp Asn Ile Gln Asp Thr Pro Thr Pro His Arg
 545 550 555 560
 Ala Leu Thr Pro Ile Ser Glu Glu Thr Gly Ser Asn Gly His Asn Glu
 565 570 575
 Asp Asp Ile Asp Ser Ile Pro Pro Leu Glu Ser Asp Glu Glu Asn Asn
 580 585 590
 Thr Glu Thr Thr Ile Thr Thr Thr Lys Asn Thr Thr Ala Pro Pro Ala
 595 600 605
 Pro Val Tyr Arg Ser Asn Ser Glu Lys Glu Pro Leu Pro Gln Glu Lys
 610 615 620
 Ser Gln Lys Gln Pro Asn Gln Val Ser Gly Ser Glu Asn Thr Asp Asn
 625 630 635 640
 Lys Pro His Ser Glu Gln Ser Val Glu Glu Met Tyr Arg His Ile Leu
 645 650 655
 Gln Thr Gln Gly Pro Phe Asp Ala Ile Leu Tyr Tyr Tyr Met Met Thr
 660 665 670
 Glu Glu Pro Ile Val Phe Ser Thr Ser Asp Gly Lys Glu Tyr Val Tyr
 675 680 685
 Pro Asp Ser Leu Glu Gly Glu His Pro Pro Trp Leu Ser Glu Lys Glu
 690 695 700
 Ala Leu Asn Glu Asp Asn Arg Phe Ile Thr Met Asp Asp Gln Gln Phe
 705 710 715 720
 Tyr Trp Pro Val Met Asn His Arg Asn Lys Phe Met Ala Ile Leu Gln
 725 730 735
 His His Lys

<210> SEQ ID NO 12
 <211> LENGTH: 341
 <212> TYPE: PRT
 <213> ORGANISM: Bundibugyo ebolavirus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <223> OTHER INFORMATION: Cote d'Ivoire ebolavirus VP35 NP protein

<400> SEQUENCE: 12

Met Ile Ser Thr Arg Ala Ala Ala Ile Asn Asp Pro Ser Leu Pro Ile
 1 5 10 15
 Arg Asn Gln Cys Thr Arg Gly Pro Glu Leu Ser Gly Trp Ile Ser Glu
 20 25 30
 Gln Leu Met Thr Gly Lys Ile Pro Val His Glu Ile Phe Asn Asp Thr
 35 40 45
 Glu Pro His Ile Ser Ser Gly Ser Asp Cys Leu Pro Arg Pro Lys Asn
 50 55 60
 Thr Ala Pro Arg Thr Arg Asn Thr Gln Thr Gln Thr Asp Pro Val Cys
 65 70 75 80
 Asn His Asn Phe Glu Asp Val Thr Gln Ala Leu Thr Ser Leu Thr Asn
 85 90 95
 Val Ile Gln Lys Gln Ala Leu Asn Leu Glu Ser Leu Glu Gln Arg Ile
 100 105 110
 Ile Asp Leu Glu Asn Gly Leu Lys Pro Met Tyr Asp Met Ala Lys Val
 115 120 125

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Ile Ser Ala Leu Asn Arg Ser Cys Ala Glu Met Val Ala Lys Tyr Asp
 130                               135                               140

Leu Leu Val Met Thr Thr Gly Arg Ala Thr Ala Thr Ala Ala Thr
 145                               150                               155                               160

Glu Ala Tyr Trp Glu Glu His Gly Gln Pro Pro Pro Gly Pro Ser Leu
 165                               170                               175

Tyr Glu Glu Ser Ala Ile Arg Gly Lys Ile Asn Lys Gln Glu Asp Lys
 180                               185                               190

Val Pro Lys Glu Val Gln Glu Ala Phe Arg Asn Leu Asp Ser Thr Ser
 195                               200                               205

Ser Leu Thr Glu Glu Asn Phe Gly Lys Pro Asp Ile Ser Ala Lys Asp
 210                               215                               220

Leu Arg Asp Ile Met Tyr Asp His Leu Pro Gly Phe Gly Thr Ala Phe
 225                               230                               235                               240

His Gln Leu Val Gln Val Ile Cys Lys Leu Gly Lys Asp Asn Ser Ala
 245                               250                               255

Leu Asp Ile Ile His Ala Glu Phe Gln Ala Ser Leu Ala Glu Gly Asp
 260                               265                               270

Ser Pro Gln Cys Ala Leu Ile Gln Ile Thr Lys Arg Ile Pro Ile Phe
 275                               280                               285

Gln Asp Ala Thr Pro Pro Thr Ile His Ile Arg Ser Arg Gly Asp Ile
 290                               295                               300

Pro Arg Ala Cys Gln Lys Ser Leu Arg Pro Val Pro Pro Ser Pro Lys
 305                               310                               315                               320

Ile Asp Arg Gly Trp Val Cys Ile Phe Gln Leu Gln Asp Gly Lys Thr
 325                               330                               335

Leu Gly Leu Lys Ile
 340

<210> SEQ ID NO 13
<211> LENGTH: 326
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Cote d'Ivoire ebolavirus VP40 NP protein

<400> SEQUENCE: 13

Met Arg Arg Ile Ile Leu Pro Thr Ala Pro Pro Glu Tyr Met Glu Ala
 1                               5                               10                               15

Val Tyr Pro Met Arg Thr Met Asn Ser Gly Ala Asp Asn Thr Ala Ser
 20                               25                               30

Gly Pro Asn Tyr Thr Thr Thr Gly Val Met Thr Asn Asp Thr Pro Ser
 35                               40                               45

Asn Ser Leu Arg Pro Val Ala Asp Asp Asn Ile Asp His Pro Ser His
 50                               55                               60

Thr Pro Asn Ser Val Ala Ser Ala Phe Ile Leu Glu Ala Met Val Asn
 65                               70                               75                               80

Val Ile Ser Gly Pro Lys Val Leu Met Lys Gln Ile Pro Ile Trp Leu
 85                               90                               95

Pro Leu Gly Val Ser Asp Gln Lys Thr Tyr Ser Phe Asp Ser Thr Thr
 100                              105                              110

Ala Ala Ile Met Leu Ala Ser Tyr Thr Ile Thr His Phe Gly Lys Thr

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530	535	540
Glu Gly Ile Met	Glu Asn Gln Asn Gly Leu	Ile Cys Gly Leu Arg Gln
545	550	555 560
Leu Ala Asn Glu Thr Thr Gln Ala Leu Gln Leu Phe Leu Arg Ala Thr		
	565	570 575
Thr Glu Leu Arg Thr Phe Ser Ile Leu Asn Arg Lys Ala Ile Asp Phe		
	580	585 590
Leu Leu Gln Arg Trp Gly Gly Thr Cys His Ile Leu Gly Pro Asp Cys		
	595	600 605
Cys Ile Glu Pro Gln Asp Trp Thr Lys Asn Ile Thr Asp Lys Ile Asp		
	610	615 620
Gln Ile Ile His Asp Phe Val Asp Asn Asn Leu Pro Asn Gln Asn Asp		
	625	630 635 640
Gly Ser Asn Trp Trp Thr Gly Trp Lys Gln Trp Val Pro Ala Gly Ile		
	645	650 655
Gly Ile Thr Gly Val Ile Ile Ala Ile Ile Ala Leu Leu Cys Ile Cys		
	660	665 670
Lys Phe Met Leu		
	675	

<210> SEQ ID NO 15
 <211> LENGTH: 365
 <212> TYPE: PRT
 <213> ORGANISM: Bundibugyo ebolavirus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <223> OTHER INFORMATION: Cote d'Ivoire ebolavirus SGP NP protein

<400> SEQUENCE: 15

Met Gly Ala Ser Gly Ile Leu Gln Leu Pro Arg Glu Arg Phe Arg Lys		
1	5	10 15
Thr Ser Phe Phe Val Trp Val Ile Ile Leu Phe His Lys Val Phe Ser		
	20	25 30
Ile Pro Leu Gly Val Val His Asn Asn Thr Leu Gln Val Ser Asp Ile		
	35	40 45
Asp Lys Phe Val Cys Arg Asp Lys Leu Ser Ser Thr Ser Gln Leu Lys		
	50	55 60
Ser Val Gly Leu Asn Leu Glu Gly Asn Gly Val Ala Thr Asp Val Pro		
	65	70 75 80
Thr Ala Thr Lys Arg Trp Gly Phe Arg Ala Gly Val Pro Pro Lys Val		
	85	90 95
Val Asn Cys Glu Ala Gly Glu Trp Ala Glu Asn Cys Tyr Asn Leu Ala		
	100	105 110
Ile Lys Lys Val Asp Gly Ser Glu Cys Leu Pro Glu Ala Pro Glu Gly		
	115	120 125
Val Arg Asp Phe Pro Arg Cys Arg Tyr Val His Lys Val Ser Gly Thr		
	130	135 140
Gly Pro Cys Pro Gly Gly Leu Ala Phe His Lys Glu Gly Ala Phe Phe		
	145	150 155 160
Leu Tyr Asp Arg Leu Ala Ser Thr Ile Ile Tyr Arg Gly Thr Thr Phe		
	165	170 175
Ala Glu Gly Val Ile Ala Phe Leu Ile Leu Pro Lys Ala Arg Lys Asp		
	180	185 190

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Phe Phe Gln Ser Pro Pro Leu His Glu Pro Ala Asn Met Thr Thr Asp
   195                               200                               205

Pro Ser Ser Tyr Tyr His Thr Thr Thr Ile Asn Tyr Val Val Asp Asn
   210                               215                               220

Phe Gly Thr Asn Thr Thr Glu Phe Leu Phe Gln Val Asp His Leu Thr
  225                               230                               235                               240

Tyr Val Gln Leu Glu Ala Arg Phe Thr Pro Gln Phe Leu Val Leu Leu
   245                               250                               255

Asn Glu Thr Ile Tyr Ser Asp Asn Arg Arg Ser Asn Thr Thr Gly Lys
   260                               265                               270

Leu Ile Trp Lys Ile Asn Pro Thr Val Asp Thr Ser Met Gly Glu Trp
   275                               280                               285

Ala Phe Trp Glu Asn Lys Lys Thr Ser Gln Lys Pro Phe Gln Val Lys
   290                               295                               300

Ser Cys Leu Ser Tyr Leu Tyr Gln Lys Pro Arg Thr Arg Ser Leu Thr
  305                               310                               315                               320

Arg Gln Arg Arg Ser Leu Leu Pro Ser Pro Pro Thr Thr Thr Gln Pro
   325                               330                               335

Lys Thr Thr Lys Asn Trp Phe Gln Arg Ile Pro Leu Gln Trp Phe Arg
   340                               345                               350

Cys Lys Thr Ser Arg Glu Arg Thr Gln Cys Gln Pro Gln
   355                               360                               365

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<210> SEQ ID NO 16
<211> LENGTH: 302
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Cote d'Ivoire ebolavirus SSGP NP protein

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<400> SEQUENCE: 16

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Met Gly Ala Ser Gly Ile Leu Gln Leu Pro Arg Glu Arg Phe Arg Lys
  1                               5                               10                               15

Thr Ser Phe Phe Val Trp Val Ile Ile Leu Phe His Lys Val Phe Ser
   20                               25                               30

Ile Pro Leu Gly Val Val His Asn Asn Thr Leu Gln Val Ser Asp Ile
   35                               40                               45

Asp Lys Phe Val Cys Arg Asp Lys Leu Ser Ser Thr Ser Gln Leu Lys
   50                               55                               60

Ser Val Gly Leu Asn Leu Glu Gly Asn Gly Val Ala Thr Asp Val Pro
   65                               70                               75                               80

Thr Ala Thr Lys Arg Trp Gly Phe Arg Ala Gly Val Pro Pro Lys Val
   85                               90                               95

Val Asn Cys Glu Ala Gly Glu Trp Ala Glu Asn Cys Tyr Asn Leu Ala
  100                               105                               110

Ile Lys Lys Val Asp Gly Ser Glu Cys Leu Pro Glu Ala Pro Glu Gly
  115                               120                               125

Val Arg Asp Phe Pro Arg Cys Arg Tyr Val His Lys Val Ser Gly Thr
  130                               135                               140

Gly Pro Cys Pro Gly Gly Leu Ala Phe His Lys Glu Gly Ala Phe Phe
  145                               150                               155                               160

Leu Tyr Asp Arg Leu Ala Ser Thr Ile Ile Tyr Arg Gly Thr Thr Phe
  165                               170                               175

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Ala Glu Gly Val Ile Ala Phe Leu Ile Leu Pro Lys Ala Arg Lys Asp
180 185 190

Phe Phe Gln Ser Pro Pro Leu His Glu Pro Ala Asn Met Thr Thr Asp
195 200 205

Pro Ser Ser Tyr Tyr His Thr Thr Thr Ile Asn Tyr Val Val Asp Asn
210 215 220

Phe Gly Thr Asn Thr Thr Glu Phe Leu Phe Gln Val Asp His Leu Thr
225 230 235 240

Tyr Val Gln Leu Glu Ala Arg Phe Thr Pro Gln Phe Leu Val Leu Leu
245 250 255

Asn Glu Thr Ile Tyr Ser Asp Asn Arg Arg Ser Asn Thr Thr Gly Lys
260 265 270

Leu Ile Trp Lys Ile Asn Pro Thr Val Asp Thr Ser Met Gly Glu Trp
275 280 285

Ala Phe Trp Glu Asn Lys Lys Leu His Lys Asn Pro Phe Lys
290 295 300

<210> SEQ ID NO 17
<211> LENGTH: 289
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Cote d'Ivoire ebolavirus VP30 NP protein

<400> SEQUENCE: 17

Met Glu Val Val His Glu Arg Gly Arg Ser Arg Ile Ser Arg Gln Asn
1 5 10 15

Thr Arg Asp Gly Pro Ser His Leu Val Arg Ala Arg Ser Ser Ser Arg
20 25 30

Ala Ser Tyr Arg Ser Glu Tyr His Thr Pro Arg Ser Ala Ser Gln Ile
35 40 45

Arg Val Pro Thr Val Phe His Arg Lys Lys Thr Asp Leu Leu Thr Val
50 55 60

Pro Pro Ala Pro Lys Asp Val Cys Pro Thr Leu Lys Lys Gly Phe Leu
65 70 75 80

Cys Asp Ser Asn Phe Cys Lys Lys Asp His Gln Leu Glu Ser Leu Thr
85 90 95

Asp Arg Glu Leu Leu Leu Leu Ile Ala Arg Lys Thr Cys Gly Ser Thr
100 105 110

Glu Gln Gln Leu Ser Ile Val Ala Pro Lys Asp Ser Arg Leu Ala Asn
115 120 125

Pro Ile Ala Glu Asp Phe Gln Gln Lys Asp Gly Pro Lys Val Thr Leu
130 135 140

Ser Met Leu Ile Glu Thr Ala Glu Tyr Trp Ser Lys Gln Asp Ile Lys
145 150 155 160

Asn Ile Asp Asp Ser Arg Leu Arg Ala Leu Leu Thr Leu Cys Ala Val
165 170 175

Met Thr Arg Lys Phe Ser Lys Ser Gln Leu Ser Leu Leu Cys Glu Ser
180 185 190

His Leu Arg Arg Glu Gly Leu Gly Gln Asp Gln Ser Glu Ser Val Leu
195 200 205

Glu Val Tyr Gln Arg Leu His Ser Asp Lys Gly Gly Asn Phe Glu Ala

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210	215	220
Ala Leu Trp Gln Gln Trp Asp Arg Gln Ser Leu Ile Met Phe Ile Thr 225 230 235 240		
Ala Phe Leu Asn Ile Ala Leu Gln Leu Pro Cys Glu Ser Ser Ser Val 245 250 255		
Val Ile Ser Gly Leu Arg Met Leu Ile Pro Gln Ser Glu Ala Thr Glu 260 265 270		
Val Val Thr Pro Ser Glu Thr Cys Thr Trp Ser Glu Gly Gly Ser Ser 275 280 285		

His

<210> SEQ ID NO 18
<211> LENGTH: 251
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Cote d'Ivoire ebolavirus VP24 NP protein

<400> SEQUENCE: 18

Met Ala Lys Ala Thr Gly Arg Tyr Asn Leu Ile Ser Pro Lys Lys Asp 1 5 10 15		
Leu Glu Lys Gly Leu Val Leu Asn Asp Leu Cys Thr Leu Ser Val Ala 20 25 30		
Gln Thr Val Gln Gly Trp Lys Val Thr Trp Ala Gly Ile Glu Phe Asp 35 40 45		
Val Thr Gln Lys Gly Met Ala Leu Leu His Arg Leu Lys Thr Ser Asp 50 55 60		
Phe Ala Pro Ala Trp Ser Met Thr Arg Asn Leu Phe Pro His Leu Phe 65 70 75 80		
Gln Asn Pro Asn Ser Thr Ile Glu Ser Pro Leu Trp Ala Leu Arg Val 85 90 95		
Ile Leu Ala Ala Gly Ile Gln Asp Gln Leu Ile Asp Gln Ser Leu Ile 100 105 110		
Glu Pro Leu Ala Gly Ala Leu Gly Leu Ile Ala Asp Trp Leu Leu Thr 115 120 125		
Thr Gly Thr Asn His Phe Gln Met Arg Thr Gln Gln Ala Lys Glu Gln 130 135 140		
Leu Ser Leu Lys Met Leu Ser Leu Val Arg Ser Asn Ile Leu Lys Phe 145 150 155 160		
Ile Asn Gln Leu Asp Ala Leu His Val Val Asn Tyr Asn Gly Leu Leu 165 170 175		
Ser Ser Ile Glu Ile Gly Thr Lys Ser His Thr Ile Ile Ile Thr Arg 180 185 190		
Thr Asn Met Gly Phe Leu Val Glu Leu Gln Glu Pro Asp Lys Ser Ala 195 200 205		
Met Asn Thr Arg Lys Pro Gly Pro Val Lys Phe Ser Leu Leu His Glu 210 215 220		
Ser Thr Leu Lys Thr Leu Ala Lys Lys Pro Ala Thr Gln Met Gln Ala 225 230 235 240		
Leu Ile Leu Glu Phe Asn Ser Ser Leu Ala Ile 245 250		

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<210> SEQ ID NO 19
<211> LENGTH: 2210
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: Cote d'Ivoire ebolavirus L NP protein

<400> SEQUENCE: 19

Met Ala Thr Gln His Thr Gln Tyr Pro Asp Ala Arg Leu Ser Ser Pro
1          5          10          15

Ile Val Leu Asp Gln Cys Asp Leu Val Thr Arg Ala Cys Gly Leu Tyr
20         25         30

Ser Ala Tyr Ser Leu Asn Pro Gln Leu Lys Asn Cys Arg Leu Pro Lys
35         40         45

His Ile Tyr Arg Leu Lys Tyr Asp Thr Thr Val Thr Glu Phe Leu Ser
50         55         60

Asp Val Pro Val Ala Thr Leu Pro Ala Asp Phe Leu Val Pro Thr Phe
65         70         75         80

Leu Arg Thr Leu Ser Gly Asn Gly Ser Cys Pro Ile Asp Pro Lys Cys
85         90         95

Ser Gln Phe Leu Glu Glu Ile Val Asn Tyr Thr Leu Gln Asp Ile Arg
100        105        110

Phe Leu Asn Tyr Tyr Leu Asn Arg Ala Gly Val His Asn Asp His Val
115        120        125

Asp Arg Asp Phe Gly Gln Lys Ile Arg Asn Leu Ile Cys Asp Asn Glu
130        135        140

Val Leu His Gln Met Phe His Trp Tyr Asp Leu Ala Ile Leu Ala Arg
145        150        155        160

Arg Gly Arg Leu Asn Arg Gly Asn Asn Arg Ser Thr Trp Phe Ala Ser
165        170        175

Asp Asn Leu Val Asp Ile Leu Gly Tyr Gly Asp Tyr Ile Phe Trp Lys
180        185        190

Ile Pro Leu Ser Leu Leu Pro Val Asp Thr Gln Gly Leu Pro His Ala
195        200        205

Ala Lys Asp Trp Tyr His Glu Ser Val Phe Lys Glu Ala Ile Gln Gly
210        215        220

His Thr His Ile Val Ser Ile Ser Thr Ala Asp Val Leu Ile Met Cys
225        230        235        240

Lys Asp Ile Ile Thr Cys Arg Phe Asn Thr Leu Leu Ile Ala Ala Val
245        250        255

Ala Asn Leu Glu Asp Ser Val His Ser Asp Tyr Pro Leu Pro Glu Thr
260        265        270

Val Ser Asp Leu Tyr Lys Ala Gly Asp Tyr Leu Ile Ser Leu Leu Gly
275        280        285

Ser Glu Gly Tyr Lys Val Ile Lys Phe Leu Glu Pro Leu Cys Leu Ala
290        295        300

Lys Ile Gln Leu Cys Ser Asn Tyr Thr Glu Arg Lys Gly Arg Phe Leu
305        310        315        320

Thr Gln Met His Leu Ala Val Asn His Thr Leu Glu Glu Leu Thr Gly
325        330        335

Ser Arg Glu Leu Arg Pro Gln Gln Ile Arg Lys Val Arg Glu Phe His
340        345        350

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Gln Met Leu Ile Asn Leu Lys Ala Thr Pro Gln Gln Leu Cys Glu Leu
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 Phe Ser Val Gln Lys His Trp Gly His Pro Val Leu His Ser Glu Lys
 370 375 380
 Ala Ile Gln Lys Val Lys Lys His Ala Thr Val Ile Lys Ala Leu Arg
 385 390 395 400
 Pro Ile Ile Ile Phe Glu Thr Tyr Cys Val Phe Lys Tyr Ser Ile Ala
 405 410 415
 Lys His Tyr Phe Asp Ser Gln Gly Thr Trp Tyr Ser Val Thr Ser Asp
 420 425 430
 Arg Cys Leu Thr Pro Gly Leu Ser Ser Tyr Ile Lys Arg Asn Gln Phe
 435 440 445
 Pro Pro Leu Pro Met Ile Lys Glu Leu Leu Trp Glu Phe Tyr His Leu
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 Asp His Pro Pro Leu Phe Ser Thr Lys Val Ile Ser Asp Leu Ser Ile
 465 470 475 480
 Phe Ile Lys Asp Arg Ala Thr Ala Val Glu Lys Thr Cys Trp Asp Ala
 485 490 495
 Val Phe Glu Pro Asn Val Leu Gly Tyr Asn Pro Pro Asn Lys Phe Ala
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 Thr Lys Arg Val Pro Glu Gln Phe Leu Glu Gln Glu Asn Phe Ser Ile
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 Glu Ser Val Leu His Tyr Ala Gln Arg Leu Glu Tyr Leu Leu Pro Glu
 530 535 540
 Tyr Arg Asn Phe Ser Phe Ser Leu Lys Glu Lys Glu Leu Asn Ile Gly
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 Arg Ala Phe Gly Lys Leu Pro Tyr Pro Thr Arg Asn Val Gln Thr Leu
 565 570 575
 Cys Glu Ala Leu Leu Ala Asp Gly Leu Ala Lys Ala Phe Pro Ser Asn
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 Met Met Val Val Thr Glu Arg Glu Gln Lys Glu Ser Leu Leu His Gln
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 Ala Ser Trp His His Thr Ser Asp Asp Phe Gly Glu Asn Ala Thr Val
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 Arg Gly Ser Ser Phe Val Thr Asp Leu Glu Lys Tyr Asn Leu Ala Phe
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 Arg Tyr Glu Phe Thr Ala Pro Phe Ile Glu Tyr Cys Asn Arg Cys Tyr
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 Gly Val Arg Asn Leu Phe Asn Trp Met His Tyr Thr Ile Pro Gln Cys
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 Tyr Ile His Val Ser Asp Tyr Tyr Asn Pro Pro His Gly Val Ser Leu
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 Glu Asn Arg Glu Asn Pro Pro Glu Gly Pro Ser Ser Tyr Arg Gly His
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 Leu Gly Gly Ile Glu Gly Leu Gln Gln Lys Leu Trp Thr Ser Ile Ser
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 Cys Ala Gln Ile Ser Leu Val Glu Ile Lys Thr Gly Phe Lys Leu Arg
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 Ser Ala Val Met Gly Asp Asn Gln Cys Ile Thr Val Leu Ser Val Phe
 740 745 750
 Pro Leu Glu Thr Glu Ser Ser Glu Gln Glu Leu Ser Ser Glu Asp Asn

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Ser	Ala	Ile	Asp	Phe	Val	Leu	Asn	Pro	Ser	Gly	Leu	Asn	Val	Pro	Gly
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			980					985						990	
Thr	Leu	Ser	Ala	Lys	Asn	Lys	Leu	Ile	Asn	Thr	Leu	Phe	His	Ser	Ser
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Ala	Asp	Leu	Glu	Asp	Glu	Met	Val	Cys	Lys	Trp	Leu	Leu	Ser	Ser	
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Thr	Pro	Val	Met	Ser	Arg	Phe	Ala	Ala	Asp	Ile	Phe	Ser	Arg	Thr	
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Pro	Ile	Leu	Asp	Arg	Leu	Arg	Lys	Ile	Thr	Leu	Gln	Arg	Trp	Ser	
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Leu	Trp	Phe	Ser	Tyr	Leu	Asp	His	Cys	Asp	Gln	Val	Leu	Ala	Asp	
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Ala	Leu	Thr	Gln	Ile	Thr	Cys	Thr	Val	Asp	Leu	Ala	Gln	Ile	Leu	
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Leu	Lys	Pro	Tyr	Glu	His	Cys	Pro	Lys	Cys	Ala	Lys	Ser	Ala	Asn	
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Pro Lys Gly Glu Pro Phe Val Ser Ile Ala Ile Lys Lys His Val	1160	1165	1170
Val Ser Ala Trp Pro Asp Gln Ser Arg Leu Ser Trp Thr Ile Gly	1175	1180	1185
Asp Gly Ile Pro Tyr Ile Gly Ser Arg Thr Glu Asp Lys Ile Gly	1190	1195	1200
Gln Pro Ala Ile Lys Pro Lys Cys Pro Ser Ala Ala Leu Arg Glu	1205	1210	1215
Ala Ile Glu Leu Thr Ser Arg Leu Thr Trp Val Thr Gln Gly Gly	1220	1225	1230
Ala Asn Ser Asp Leu Leu Val Lys Pro Phe Ile Glu Ala Arg Val	1235	1240	1245
Asn Leu Ser Val Gln Glu Ile Leu Gln Met Thr Pro Ser His Tyr	1250	1255	1260
Ser Gly Asn Ile Val His Arg Tyr Asn Asp Gln Tyr Ser Pro His	1265	1270	1275
Ser Phe Met Ala Asn Arg Met Ser Asn Ser Ala Thr Arg Leu Val	1280	1285	1290
Val Ser Thr Asn Thr Leu Gly Glu Phe Ser Gly Gly Gln Ser	1295	1300	1305
Ala Arg Asp Ser Asn Ile Ile Phe Gln Asn Val Ile Asn Phe Ala	1310	1315	1320
Val Ala Leu Phe Asp Leu Arg Phe Arg Asn Val Ala Thr Ser Ser	1325	1330	1335
Ile Gln His His Arg Ala His Leu His Leu Ser Lys Cys Cys Thr	1340	1345	1350
Arg Glu Val Pro Ala Gln Tyr Leu Val Tyr Thr Ser Thr Leu Pro	1355	1360	1365
Leu Asp Leu Thr Arg Tyr Arg Asp Asn Glu Leu Ile Tyr Asp Asp	1370	1375	1380
Asn Pro Leu Arg Gly Gly Leu Asn Cys Asn Leu Ser Phe Asp Asn	1385	1390	1395
Pro Leu Phe Lys Gly Gln Arg Leu Asn Ile Ile Glu Glu Asp Leu	1400	1405	1410
Ile Arg Leu Pro Tyr Leu Ser Gly Trp Glu Leu Ala Lys Thr Val	1415	1420	1425
Ile Gln Ser Ile Ile Ser Asp Ser Asn Asn Ser Ser Thr Asp Pro	1430	1435	1440
Ile Ser Ser Gly Glu Thr Arg Ser Phe Thr Thr His Phe Leu Thr	1445	1450	1455
Tyr Pro Lys Ile Gly Leu Leu Tyr Ser Phe Gly Ala Leu Ile Ser	1460	1465	1470
Tyr Tyr Leu Gly Asn Thr Ile Ile Arg Thr Lys Lys Leu Thr Leu	1475	1480	1485
Asn Asn Phe Ile Tyr Tyr Leu Ala Thr Gln Ile His Asn Leu Pro	1490	1495	1500
His Arg Ser Leu Arg Ile Leu Lys Pro Thr Leu Lys His Ala Ser	1505	1510	1515
Val Ile Ser Arg Leu Ile Ser Ile Asp Ser His Phe Ser Ile Tyr	1520	1525	1530

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Ile	Gly	Gly	Thr	Ala	Gly	Asp	Arg	Gly	Leu	Ser	Asp	Ala	Ala	Arg
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1550						1555					1560			
Lys	Trp	Ile	Val	Glu	Arg	Lys	Thr	Ala	Ile	Pro	Leu	Trp	Val	Ile
1565						1570					1575			
Tyr	Pro	Leu	Glu	Gly	Gln	Ser	Pro	Ser	Pro	Ile	Asn	Ser	Phe	Leu
1580						1585					1590			
His	His	Val	Ile	Ala	Leu	Leu	Gln	His	Glu	Ser	Ser	His	Asp	His
1595						1600					1605			
Val	Cys	Ala	Ala	Glu	Ala	His	Ser	Arg	Val	Glu	Thr	Phe	Asp	Asn
1610						1615					1620			
Leu	Val	Tyr	Met	Cys	Lys	Ser	Thr	Ala	Ser	Asn	Phe	Phe	His	Ala
1625						1630					1635			
Ser	Leu	Ala	Tyr	Trp	Arg	Ser	Arg	Ser	Lys	Asn	Gln	Asp	Lys	Arg
1640						1645					1650			
Glu	Met	Thr	Lys	Ile	Leu	Ser	Leu	Thr	Gln	Thr	Glu	Lys	Lys	Asn
1655						1660					1665			
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1670						1675					1680			
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1685						1690					1695			
Thr	Tyr	Asp	Arg	Lys	Asn	Lys	Val	Leu	Lys	Ala	Ser	Arg	Pro	Gly
1700						1705					1710			
Lys	Tyr	Ser	Gln	Asn	Thr	Thr	Lys	Ala	Pro	Pro	Asn	Gln	Thr	Ser
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Lys	Val	Glu	Thr	Leu	Phe	Phe	Asn	Thr	Leu	Ala	Thr	Glu	His	Ser
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1880						1885					1890			
Leu	Asn	Asn	Ser	Ala	Ser	Gln	Ile	Thr	Asp	Ile	Thr	Asn	Pro	Ser
1895						1900					1905			
Trp	Leu	Ala	Asp	Gln	Lys	Ser	Arg	Ile	Pro	Lys	Gln	Val	Glu	Ile

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1910	1915	1920
Ile Thr Met Asp Ala Glu Thr	Thr Thr Glu Asn Ile Asn	Arg Ser Lys
1925	1930	1935
Leu Tyr Glu Ala Val Gln Gln	Leu Ile Val Ser His	Ile Asp Pro
1940	1945	1950
Asn Ala Leu Lys Val Val Val	Leu Lys Val Phe Leu	Ser Asp Ile
1955	1960	1965
Asp Gly Ile Leu Trp Leu Asn	Asp Asn Leu Thr Pro	Leu Phe Gly
1970	1975	1980
Leu Gly Tyr Leu Ile Lys Pro	Ile Thr Ser Ser Pro	Lys Ser Ser
1985	1990	1995
Glu Trp Tyr Leu Cys Leu Ser	Asn Leu Leu Ser Thr	Ser Arg Arg
2000	2005	2010
Leu Pro His Gln Ser His Thr	Thr Cys Met His Val	Ile Gln Thr
2015	2020	2025
Ala Leu Gln Leu Gln Ile Gln	Arg Ser Ser Tyr Trp	Leu Ser His
2030	2035	2040
Leu Val Gln Tyr Ala Asn His	Asn Leu His Leu Asp	Tyr Ile Asn
2045	2050	2055
Leu Gly Phe Pro Ser Leu Glu	Arg Val Leu Tyr His	Arg Tyr Asn
2060	2065	2070
Leu Val Asp Ser Gln Lys Gly	Pro Leu Thr Ser Ile	Val Gln His
2075	2080	2085
Leu Ala His Leu Gln Thr Glu	Ile Arg Glu Leu Val	Asn Asp Tyr
2090	2095	2100
Asn Gln Gln Arg Gln Ser Arg	Thr Gln Thr Tyr His	Phe Ile Lys
2105	2110	2115
Thr Ile Lys Gly Arg Ile Thr	Lys Leu Val Asn Asp	Tyr Leu Lys
2120	2125	2130
Phe Phe Leu Ile Ile Gln Ala	Leu Lys His Asn Cys	Thr Trp Gln
2135	2140	2145
Glu Glu Leu Arg Ala Leu Pro	Asp Leu Ile Ser Val	Cys Thr Arg
2150	2155	2160
Phe Tyr His Thr Arg Asn Cys	Ser Cys Glu Asn Arg	Phe Leu Val
2165	2170	2175
Gln Thr Leu Tyr Leu Ser Arg	Met Gln Asp Ser Glu	Ile Lys Leu
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Ile Asp Arg Leu Thr Gly Leu	Leu Ser Leu Cys Pro	Asn Gly Phe
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Phe Arg		
2210		

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gccttactat tgattcagaa ataccaagtt aagaccttat tttcaacac gctagctact 17160
gagtcagta tagagtcaga aatagatca ggaatgacta ctctaggat gcttctacct 17220
gttatgtcaa aattccataa tgaccaaatt gagattatc ttaacaactc agcaagccaa 17280
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ctgagtttat ttccggatgg tctctacagg tttgattgaa ttaccgtgca tagtatcctg 18240
atacttgcaa aggttggtta ttaacataca gattataaaa aactcataaa ttgctctcat 18300
acatcatatt gatctaactc caataacaa ctatttaaat aacgaaagga gtcctatat 18360

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tatatactat atttagcctc tctccctgcg tgataatcaa aaaattcaca atgcagcatg 18420
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attaagcttt aacgaaaggt ctgggctcat attgttattg atataataat gttgtatcaa 18540
tatcctgtca gatggaatag tgttttggtt gataacacaa cttcttaaaa caaaattgat 18600
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gaaatacctt ctttacaata tagcagacta gataataatc ttcgtgttaa tgataattaa 18840
gacattgacc acgctcatca gaaggctcgc cagaataaac gttgcaaaaa ggattcctgg 18900
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<210> SEQ ID NO 21
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Sudan ebola BMG
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)..(8)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)..(8)
<223> OTHER INFORMATION: n is a, c, g, or t

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<400> SEQUENCE: 21

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gccatggntt caggtttgag 20

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<210> SEQ ID NO 22
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Sudan ebola BMG
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: I
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: n is a, c, g, or t

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<400> SEQUENCE: 22

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ggtnacattg ggcaacaatt ca 22

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<210> SEQ ID NO 23
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR probe for Sudan ebola BMG
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Fluorescein (FAM)
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: Black hole quencher dye (BHQ1)

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<400> SEQUENCE: 23
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<210> SEQ ID NO 24
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Ebola Bundibugyo
fragment A

<400> SEQUENCE: 24
gtgagacaaa gaatcattcc tg 22

<210> SEQ ID NO 25
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Ebola Bundibugyo
fragment A

<400> SEQUENCE: 25
catcaattgc tcagagatcc acc 23

<210> SEQ ID NO 26
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Ebola Bundibugyo
fragment B

<400> SEQUENCE: 26
ccaacaacac tgcagtgaag t 21

<210> SEQ ID NO 27
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Ebola Bundibugyo
fragment B

<400> SEQUENCE: 27
aggtcgctt aatcttcac 20

<210> SEQ ID NO 28
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Ebola Bundibugyo
fragment C

<400> SEQUENCE: 28
gatggttgag ttactttccg g 21

<210> SEQ ID NO 29
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Ebola Bundibugyo

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fragment C

<400> SEQUENCE: 29

gtcttgagtc atcaatgccc 20

<210> SEQ ID NO 30
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Ebola Bundibugyo
fragment D

<400> SEQUENCE: 30

ccaccagcac caaaggac 18

<210> SEQ ID NO 31
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Ebola Bundibugyo
fragment D

<400> SEQUENCE: 31

ctatcggcaa tgtaactatt gg 22

<210> SEQ ID NO 32
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Ebola Bundibugyo
fragment E

<400> SEQUENCE: 32

gccggtgtag aggacacac 19

<210> SEQ ID NO 33
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Ebola Bundibugyo
fragment E

<400> SEQUENCE: 33

cacattaat tgttctaaca tgcaag 26

<210> SEQ ID NO 34
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Ebola Bundibugyo
fragment F

<400> SEQUENCE: 34

cctaggttat ttagaaggga cta 23

<210> SEQ ID NO 35
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Ebola Bundibugyo fragment F

<400> SEQUENCE: 35

ggtagatgta ttgacagcaa tatc 24

<210> SEQ ID NO 36
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR primer for Ebola Uganda 692(-)

<400> SEQUENCE: 36

acaaaaagct atctgcacta t 21

<210> SEQ ID NO 37
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR primer for Ebola Uganda 18269(+)

<400> SEQUENCE: 37

ctcagaagca aaattaatgg 20

<210> SEQ ID NO 38
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus fragment A

<400> SEQUENCE: 38

gtgtgcgaat aactatgagg aag 23

<210> SEQ ID NO 39
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus fragment A

<400> SEQUENCE: 39

gtctgtgcaa tgttgatgaa gg 22

<210> SEQ ID NO 40
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus fragment B

<400> SEQUENCE: 40

catgaaaacc aactcaaca ac 22

<210> SEQ ID NO 41
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment B

<400> SEQUENCE: 41

gttgccttaa tcttcatcaa gtcc 24

<210> SEQ ID NO 42

<211> LENGTH: 22

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus
fragment C

<400> SEQUENCE: 42

ggctataatg aatttctctcc ag 22

<210> SEQ ID NO 43

<211> LENGTH: 22

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: PCR reverse primer for ebola cote d'Ivoire virus
fragment C

<400> SEQUENCE: 43

caagtgatt tgtgtccta gc 22

<210> SEQ ID NO 44

<211> LENGTH: 20

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment C

<400> SEQUENCE: 44

gctggaatag gaatcacagg 20

<210> SEQ ID NO 45

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment D

<400> SEQUENCE: 45

cggtagtcta cagttcttta g 21

<210> SEQ ID NO 46

<211> LENGTH: 25

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus
fragment E

<400> SEQUENCE: 46

gacaaagaga ttagattagc tatag 25

<210> SEQ ID NO 47

<211> LENGTH: 22

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment E

<400> SEQUENCE: 47

gtaatgagaa ggtgtcattt gg 22

<210> SEQ ID NO 48
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus
fragment F

<400> SEQUENCE: 48

cacgacttag ttggacaatt gg 22

<210> SEQ ID NO 49
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment F

<400> SEQUENCE: 49

cagacactaa ttagatctgg aag 23

<210> SEQ ID NO 50
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus
fragment G

<400> SEQUENCE: 50

cggacacaca aaaagaawra a 21

<210> SEQ ID NO 51
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment G

<400> SEQUENCE: 51

cgttcttgac cttagcagtt c 21

<210> SEQ ID NO 52
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus
fragment H

<400> SEQUENCE: 52

gcactataag ctcgatgaag tc 22

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<210> SEQ ID NO 53
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola virus
fragment H

<400> SEQUENCE: 53

tggacacaca aaaargaraa 20

<210> SEQ ID NO 54
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for Cote d'Ivoire ebola virus
gap between fragments C and D

<400> SEQUENCE: 54

ctgagaggat ccagaagaaa g 21

<210> SEQ ID NO 55
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR reverse primer for Cote d'Ivoire ebola
virus gap between fragments C and D

<400> SEQUENCE: 55

gtgtaagcgt tgatatacct cc 22

<210> SEQ ID NO 56
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for ebola uganda virus
EboU965(+)

<400> SEQUENCE: 56

gagaaaaggc ctgtctggag aa 22

<210> SEQ ID NO 57
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR forward primer for ebola uganda virus
EboU1039(-)

<400> SEQUENCE: 57

tcgggtattg aatcagacct tgtt 24

<210> SEQ ID NO 58
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR probe for ebola uganda virus EboU989

<400> SEQUENCE: 58

ttcaacgaca aatccaagtg cacgca 26

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<210> SEQ ID NO 59
<211> LENGTH: 302
<212> TYPE: PRT
<213> ORGANISM: Bundibugyo ebolavirus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<223> OTHER INFORMATION: SSGP viral protein

<400> SEQUENCE: 59

Met Val Thr Ser Gly Ile Leu Gln Leu Pro Arg Glu Arg Phe Arg Lys
1           5           10           15

Thr Ser Phe Phe Val Trp Val Ile Ile Leu Phe His Lys Val Phe Pro
           20           25           30

Ile Pro Leu Gly Val Val His Asn Asn Thr Leu Gln Val Ser Asp Ile
           35           40           45

Asp Lys Leu Val Cys Arg Asp Lys Leu Ser Ser Thr Ser Gln Leu Lys
           50           55           60

Ser Val Gly Leu Asn Leu Glu Gly Asn Gly Val Ala Thr Asp Val Pro
65           70           75           80

Thr Ala Thr Lys Arg Trp Gly Phe Arg Ala Gly Val Pro Pro Lys Val
           85           90           95

Val Asn Tyr Glu Ala Gly Glu Trp Ala Glu Asn Cys Tyr Asn Leu Asp
           100          105          110

Ile Lys Lys Ala Asp Gly Ser Glu Cys Leu Pro Glu Ala Pro Glu Gly
           115          120          125

Val Arg Gly Phe Pro Arg Cys Arg Tyr Val His Lys Val Ser Gly Thr
           130          135          140

Gly Pro Cys Pro Glu Gly Tyr Ala Phe His Lys Glu Gly Ala Phe Phe
145          150          155          160

Leu Tyr Asp Arg Leu Ala Ser Thr Ile Ile Tyr Arg Ser Thr Thr Phe
           165          170          175

Ser Glu Gly Val Val Ala Phe Leu Ile Leu Pro Glu Thr Lys Lys Asp
           180          185          190

Phe Phe Gln Ser Pro Pro Leu His Glu Pro Ala Asn Met Thr Thr Asp
           195          200          205

Pro Ser Ser Tyr Tyr His Thr Val Thr Leu Asn Tyr Val Ala Asp Asn
210          215          220

Phe Gly Thr Asn Met Thr Asn Phe Leu Phe Gln Val Asp His Leu Thr
225          230          235          240

Tyr Val Gln Leu Glu Pro Arg Phe Thr Pro Gln Phe Leu Val Gln Leu
           245          250          255

Asn Glu Thr Ile Tyr Thr Asn Gly Arg Arg Ser Asn Thr Thr Gly Thr
           260          265          270

Leu Ile Trp Lys Val Asn Pro Thr Val Asp Thr Gly Val Gly Glu Trp
           275          280          285

Ala Phe Trp Glu Asn Lys Lys Leu His Lys Asn Pro Phe Lys
290          295          300

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1. An isolated hEbola virus comprising a nucleic acid molecule comprising a nucleotide sequence of:

- a) a nucleotide sequence set forth in SEQ ID NOS: 1 or 10;
- b) a nucleotide sequence hybridizing under stringent conditions to SEQ ID NOS: 1 or 10; or
- c) a nucleotide sequence of at least 70%-99% identity to the SEQ ID NOS: 1 or 10, with the proviso that said nucleotide sequence is not SEQ ID NO: 20.

2. An isolated hEbola virus having Centers for Disease Control Deposit Accession No. 200706291.

3. The hEbola virus of claim 1 which is killed.

4. The hEbola virus of claim 1 which is an attenuated hEbola virus.

5. The virus of claim 4 wherein at least one property of the attenuated hEbola virus is reduced from among infectivity, replication ability, protein synthesis ability, assembling ability or cytopathic effect.

6. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS: 1 or 10 or a complement thereof, or a fragment thereof wherein said fragment comprises a nucleotide sequence of between 4 and 4900 contiguous nucleotides of the nucleotide sequence of SEQ ID NOS: 1 or 10, or a complement thereof; with the proviso that said nucleotide sequence is not comprised by the nucleotide sequence set forth in SEQ ID NO: 20; or between 5500 and 6600 contiguous nucleotides of the nucleotide sequence of SEQ ID NOS: 1 or 10, or a complement thereof.

7. The isolated nucleic acid molecule of claim 6 comprising a nucleotide sequence of between 4 and 4900 contiguous nucleotides of the nucleotide sequence of SEQ ID NOS: 1 or 10, or a complement thereof; with the proviso that said nucleotide sequence is not comprised by the nucleotide sequence set forth in SEQ ID NO: 20; or between 5500 and 6600 contiguous nucleotides of the nucleotide sequence of SEQ ID NOS: 1 or 10, or a complement thereof.

8. The isolated nucleic acid molecule of claim 7 comprising a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 2-9, 59, or SEQ ID NO: 11-19 or a complement thereof.

9. An isolated RNA or DNA nucleic acid molecule which hybridizes under stringent conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS: 1 or 10 or a complement thereof.

10. An isolated polypeptide encoded by the nucleic acid molecule of claim 7.

11. The polypeptide of claim 10 comprising the amino acid of:

- a) an amino acid sequence set forth in any of SEQ ID NOS: 2-19, or 59; or
- b) an amino acid sequence that has 70%-99% homology to the amino acid sequence of (a).

12. The polypeptide of claim 10 wherein the amino acid sequence has

- 5 to 250 contiguous amino acid residues of the amino acid sequence of SEQ ID NOS: 5 or 18 (VP24);
- 5 to 280 contiguous residues of the amino acid sequence of SEQ ID NOS: 6 or 17 (VP30);
- 5 to 320 contiguous residues of the amino acid sequence of SEQ ID NOS: 8 or 13 (VP40);
- 5 to 340 contiguous residues of the amino acid sequence of SEQ ID NOS: 7 or 12 (VP35);
- 5 to 370 contiguous residues of the amino acid sequence of SEQ ID NOS: 4 or 15 (SGP);
- 5 to 370 contiguous residues of the amino acid sequence of SEQ ID NOS: 59 or 16 (SSGP);
- 5 to 670 contiguous residues of the amino acid sequence of SEQ ID NOS: 9 or 14 (GP);
- 5 to 730 contiguous residues of the amino acid sequence of SEQ ID NOS: 3 or 11 (NP); or
- 5 to 2200 contiguous residues of the amino acid sequence of SEQ ID NOS: 2 or 19 (L).

13. (canceled)

14. (canceled)

15. (canceled)

16. (canceled)

17. (canceled)

18. (canceled)

19. (canceled)

20. The hEbola virus of claims 3 or 4, or a protein extract therefrom, and a pharmaceutically acceptable carrier.

21. (canceled)

22. The nucleic acid molecule of claims 6 or 9, and a pharmaceutically acceptable carrier.

23. (canceled)

24. (canceled)

25. (canceled)

26. (canceled)

27. (canceled)

28. (canceled)

29. (canceled)

30. (canceled)

* * * * *