



US00RE44916E

(19) **United States**
 (12) **Reissued Patent**
Yoon et al.

(10) **Patent Number:** **US RE44,916 E**
 (45) **Date of Reissued Patent:** **May 27, 2014**

(54) **CANINE INFLUENZA VIRUS AND RELATED COMPOSITIONS AND METHODS OF USE**

(71) Applicants: **Kyoung-Jin Yoon**, Ames, IA (US);
Vickie Cooper, Ames, IA (US)

(72) Inventors: **Kyoung-Jin Yoon**, Ames, IA (US);
Vickie Cooper, Ames, IA (US)

(73) Assignee: **Iowa State University Research Foundation, Inc.**, Ames, IA (US)

(21) Appl. No.: **13/688,990**

(22) Filed: **Nov. 29, 2012**

Related U.S. Patent Documents

Reissue of:

(64) Patent No.: **7,842,295**
 Issued: **Nov. 30, 2010**
 Appl. No.: **12/210,837**
 Filed: **Sep. 15, 2008**

U.S. Applications:

(62) Division of application No. 11/539,123, filed on Oct. 5, 2006, now Pat. No. 7,468,187.

(60) Provisional application No. 60/727,808, filed on Oct. 18, 2005.

(51) **Int. Cl.**

A61K 39/12 (2006.01)
A61K 39/38 (2006.01)
A61K 39/145 (2006.01)
C12N 7/04 (2006.01)
C12N 15/00 (2006.01)
C07H 21/02 (2006.01)
A61K 38/18 (2006.01)
C07K 16/00 (2006.01)

(52) **U.S. Cl.**

USPC **424/186.1**; 424/184.1; 424/204.1;
 424/206.1; 424/210.1; 435/236; 435/320.1;
 536/23.1; 530/380; 530/396

(58) **Field of Classification Search**

None
 See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,991,179 A 11/1976 Beare et al.
 4,009,258 A 2/1977 Kilbourne
 4,029,763 A 6/1977 Kilbourne
 4,140,762 A 2/1979 Bachmayer et al.
 4,278,662 A 7/1981 Löbmann et al.
 4,318,903 A 3/1982 Löbmann et al.
 4,338,296 A 7/1982 Löbmann et al.
 4,693,893 A 9/1987 Campbell
 4,826,687 A 5/1989 Nerome et al.
 5,136,019 A 8/1992 Judd et al.
 5,162,112 A 11/1992 Oxford et al.
 5,616,327 A 4/1997 Judd et al.
 5,741,493 A 4/1998 Moste-Deshairs et al.
 5,762,939 A 6/1998 Smith et al.
 6,245,532 B1 6/2001 Smith et al.
 6,605,457 B1 8/2003 Fiers et al.
 6,740,325 B1 5/2004 Arnon et al.
 7,959,929 B2 * 6/2011 Crawford et al. 424/206.1

2003/0129197 A1 7/2003 Fiers et al.
 2003/0199074 A1 10/2003 Dowling et al.
 2005/0089533 A1 * 4/2005 Frantz et al. 424/234.1
 2007/0048819 A1 * 3/2007 Minke et al. 435/69.1
 2007/0082012 A1 * 4/2007 Shields et al. 424/209.1

FOREIGN PATENT DOCUMENTS

WO WO 00/09702 8/2000
 WO WO 01/60849 2/2001
 WO WO 2006/116082 11/2006

OTHER PUBLICATIONS

GenBank Accession # ABA39850, hemagglutinin, partial [Influenza A virus (A/canine/Texas/1/2004 (H3N8))], Sep. 28, 2005.*

GenBank Accession # DQ124196, Influenza A virus (A/canine/Texas/1/2004 (H3N8)) hemagglutinin gene, partial cds., Sep. 28, 2005.*

GenBank Accession # AAX23575, hemagglutinin precursor [Influenza A virus (A/equine/Kentucky/5/2002 (H3N8))], Mar. 12, 2005.*

GenBank Accession # AY855341, Influenza A virus, (A/equine/Kentucky/5/02 (H3N8)) hemagglutinin precursor, gene, complete cds., Mar. 12, 2005.*

Kay et al., Screening Phage-Displayed Combinatorial Peptide Libraries, 2001, Methods, vol. 24, pp. 240-246.*

Weis et al., "Structure of the Influenza virus haemagglutinin complexed with its receptor, sialic acid," *Nature* 333(2): 426-431 (1998).

Anderson et al., "Canine Influenza Virus Agglutination of Avian and Mammalian Red Blood Cells," *Proceedings of the American Association of Veterinary Laboratory Diagnosticians 49th Annual Conference*, p. 44 (2006).

Anderson et al., "Development of a Hemagglutination Inhibition Assay for Diagnosis of Canine Influenza Virus Infection," *Proceedings of the American Association of Veterinary Laboratory Diagnosticians 49th Annual Conference*, p. 45 (2006).

Crawford et al.: "Influenza A virus (A/canine/Texas/1/2004 (H3N9))" Database accession No. DQ124159 (2005).

Crawford et al., "Transmission of Equine Influenza Virus to Dogs," *Science*, 310: pp. 482-485 (2005).

Daly, "Equine Influenza in dogs: Too late to bolt the stable door?," *The Veterinary Journal* 171 pp. 7-8 (2006).

Dubovi et al., "Isolation of Equine Influenza Virus from Racing Greyhounds with Fatal Hemorrhagic Pneumonia," In: *Proceedings of the 47th Annual Meeting of American Association of Veterinary Laboratory Diagnosticians*, Greensboro, NC, p. 158 (2005).

Ito, T. et al.: "Evolutionary analysis of the influenza A virus M gene with comparison of the M1 and M2 proteins," *Journal of Virology*, vol. 65, No. 10, 1991, pp. 5491-5498, ISSN: 0022-538X, 06173, the whole document (1991).

(Continued)

Primary Examiner — Benjamin P Blumel

(74) Attorney, Agent, or Firm — Barnes & Thornburg LLP

(57) **ABSTRACT**

The present invention provides an isolated canine influenza virus of subtype H3N8 comprising an HA having SEQ ID NO: 4 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4, with the proviso that the amino acids at positions 94 and 233 are identical to SEQ ID NO: 4; a composition comprising attenuated or inactivated virus; isolated or purified HA, NM, NP, M1, NS1, PA, PB1, and PB2 proteins and fragments thereof and compositions comprising same or nucleic acids, optionally as part of a vector, encoding same; and a method of inducing an immune response to canine influenza virus in an animal comprising administering to the animal an aforementioned composition.

15 Claims, 14 Drawing Sheets

(56)

References Cited

OTHER PUBLICATIONS

Joly, "Canine Influenza Virus" *The Veterinary Record*, p. 527 (2005).
 Keawcharoen et al., "Avian Influenza H5N1 in Tigers and Leopards," *Emerg. Infect. Dis.*, 10: pp. 2189-2191 (2004).

Lindstrom et al.: "Phylogenetic analyses of the matrix and non-structural genes of equine influenza viruses," *Archives of Virology*, New York, vol. 143, No. 8, 1998, pp. 1585-1598, NY, US, ISSN: 0304-8608, the whole document (1998).

Macken et al., "The value of a database in surveillance and vaccine selection," In: *Options for the Control of Influenza IV*, Osterhaus et al., eds. Elsevier Science, Amsterdam, pp. 103-106 (2001).

Peek, Simon F. et al.: "Acute respiratory distress syndrome and fatal interstitial pneumonia associated with equine influenza in a neonatal foal," *Journal of Veterinary Internal Medicine*, Lippincott, Philadelphia, U.S., vol. 18, No. 1, pp. 132-134 (2004).

Peek et al.: Database accession No. Q30BG0 (2005).

Peek et al.: Database accession No. Q30BG2 (2005).

Peek et al.: Database accession No. Q30BG4 (2005).

Peek et al.: Database accession No. Q30BG5 (2005).

Peek et al.: Database accession No. Q30BG6 (2005).

Peek et al.: Database accession No. Q30BF7 (2005).

Peek et al.: Database accession No. Q30BF8 (2005).

Peek et al.: Database accession No. Q30BF9 (2005).

Quinlivan et al., "Attenuation of equine influenza viruses through truncations of the N protein," Database accession No. Q5BUA9 (2005).

Quinlivan et al., "Attenuation of equine influenza viruses through truncations of the N protein," Database accession No. Q5BUA7 (2005).

Quinlivan et al.; "Attenuation of equine influenza viruses through truncations of the N protein," Database accession No. Q5BUB2 (2005).

Quinlivan et al.: "Attenuation of equine influenza viruses through truncations of the N protein," Database accession No. Q5BUB3 (2005).

Smith et al., "Canine Influenza Virus" *The Veterinary Record*, p. 599 (2005).

Yoon et al., "Influenza Virus Infection in Racing Greyhounds," *Emerg. Infect. Dis.*, 11(12): pp. 1974-1976 (2005).

Yoon et al.: "Influenza virus A (A/canine/Iowa/13628/2005 (H3N8))," Database accession No. Q2XXL0 (2005).

Enserink, "Epidemiology. Horse Flu Virus Jumps to Dogs," *Science*, 309: 2147 (2005).

Wood et al., "The standardization of inactivated equine influenza vaccines by single-radial immunodiffusion," *Jrnl. Biol. Standardization*, 11: 133-136 (1983).

International Search Report issued in PCT/IB2006/002741 (2007).

* cited by examiner

NM

AGTTTAAATGAATCCAAATCAAAAGATAATAGCAATTGGATTTGCATCATTGGG
GATATTAATCATTAAATGTCATTCTCCATGTAGTCAGCATTATAGTAACAGTACTG
GTCCTCAATAACAATAGAACAGATCTGAACTGCAAAGGGACGATCATAAGAGAA
TACAATGAAACAGTAAGAGTAGAAAACTTACTCAATGGTATAATACCAGTACA
ATTAAGTACATAGAGAGACCTTCAAATGAATACTACATGAATAACACTGAACCA
CTTTGTGAGGCCCAAGGCTTTGCACCATTTTCCAAAGATAATGGAATACGAATTG
GGTCGAGAGGCCCATGTTTTGTGATAAGAGAACCCTTTGTATCATGTTCCGCCCTC
AGAATGTAGAACCTTTTCTCACACAGGGCTCATTACTCAATGACAAACATTC
AACGGCACAATAAAGGATCGAAGCCCGTATAGGACTTTGATGAGTGTCAAATA
GGGCAATCACCCAATGTATATCAAGCTAGGTTTGAATCGGTGGCATGGTCAGCA
ACAGCATGCCATGATGGAAAAAATGGATGACAGTTGGAGTCACAGGGCCCGAC
AATCAAGCAATTGCAGTAGTGAACATATGGAGGTGTTCCGGTTGATACTATTAATT
CATGGGCAGGGGATATTTAAGAACCCAAGAATCATCATGCACCTGCAATAAAG
GAGACTGTTATTGGGTAATGACTGATGGACCGGCAAATAGGCAAGCTAAATATA
GGATATTCAAAGCAAAAGATGGAAGAGTAATTGGACAAACTGATATAAGTTTCA
ATGGGGGACACATAGAGGAGTGTTCTTGTTACCCCAATGAAGGGAAGGTGGAAT
GCATATGCAGGGACAATTGGACTGGAACAAATAGACCAATTCTGGTAATATCTTC
TGATCTATCGTACACAGTTGGATATTGTGTGCTGGCATTCACACGACTCCTA
GGGGAGAGGATAGTCAATTCACAGGCTCATGTACAAGTCCTTTGGGAAATAAAG
GATACGGTGTAAGGGCTTCGGGTTTCGACAAGGAACTGACGTATGGGCCGGAA
GGACAATTAGTAGGACTTCAAGATCAGGATTCGAAATAATAAAAAATCAGGAATG
GTTGGACACAGAACAGTAAGGACCAATCAGGAGGCAAGTGATTATCGATGACC
CAAATTGGTCAGGATATAGCGGTTCTTTACATTGCCGGTTGAACTGACAAAAAA
GGGATGTTTGGTCCCTGTTTCTGGGTTGAAATGATTAGAGGTAAACCTGAAGAA
ACAACAATATGGACCTCTAGCAGCTCCATTGTGATGTGTGGAGTAGATCATAAAA
TTGCCAGTTGGTCATGGCACGATGGAGCTATTCTTCCCTTTGACATCGATAAGAT
GTAATTTACGAAAAAACTCCTTGTTTCTACTA (SEQ ID NO: 1)

FIG. 1

NM - Amino

MNPNQKHAI GFASLGILII NVILHVVSII VTVLVLN NNR TDLNCKGTII REYNETVRVEK
LTQWYNTSTIKYIERPSNEY YMNNTEPLCEA QGFAPFSKDNGIRIGSRGHVFVIREPFV
SCSPSECR TFFLTQGSLLNDKHSNGTIKDRSPYRTLMSVKIGQSPNVYQARFESVAWS
ATACHDGKKWMTVGV TGPDNQAI AVVNYGGVPVDTINSWAGDILRTQESSCTCIKG
DCYWVMTDGPANRQAKYRIFKAKDGRVIGQTDISFNGGHIEECSCYPNEGKVEICR
DNWTGTNRPII.VISSDI.SYTVGYLCAGIPTDTPRGEDSQFTGSCTSPLGNKGYGVKGF
GFRQGTDVWAGRTISRTSRSGFEIIRNGWTQNSKDQIRRQVIIDDPNWSGYSGSFTL
PVELTKKGCLVPCFWVEMIRGKPEETTIWTSSSSIVMCGVDHKIASWSWIIDGAILPF
DIDKM (SEQ ID NO: 2)

FIG. 2

HA:

AGCAAAAGCAGGGGATATTTCTGTCAATCATGAAGACAACCAATTATTTTAATACT
ACTGACCCATTGGGCCTACAGTCAAAACCCAATCAGTGGCAATAACACAGCCAC
ACTGTGTCTGGGACACCATGACGTAGCAAATGGAACATTGGTAAAAACAATGAG
TGATGATCAAATTGAGGTGACAAATGCTACAGAATTAGTTCAGAGCATTTCATG
GGGAAAATATGCAACAAATCATATAGAATTCTAGATGGAAGAAATTGCACATTA
ATAGATGCAATGCTAGGAGACCCCCACTGTGACGCCCTTCAGTATGAGAGTTGG
GACCTCTTTATAGAAAGAAGCAGCGCTTTCAGCAATTGCTACCCATATGACATCC
CTGACTATGCATCGCTCCGATCCATTGTAGCATCCTCAGGAACAGTTGAATTCAC
AGCAGAGGGATTACATGGACAGGTGTAACCTCAAAACGGAAGAAGTGGAGCCTG
CaaAAGGGGATCAGCCGATAGTTTCTTTAGCCGACTGAATTGGCTAACAAAATCT
GGAAGCTTTACCCACATTGAATGTGACAATGCCTAACAAATAAAAATTTTCGACA
AGCTATACATCTGGGGGATTTCATCACCCGAGCTCAAATCAAGAGCAGACAAAAT
TGTACATCCAAGAATCAGGACGAGTAACAGTCTCAACAAAAAGAGTCAACAAA
CAATAATCCCTAACATCGAATCTAGACCGTTGGTCAGAGGTCAATCAGGCAGGA
TAAGCATATACTGGACCAATTGTAACCTGGAGATATCCTAATGATAAACAGTA
ATGGCAACTTAGTTGCACCGCGGGGATATTTTAAATTGAACACAGGGAAAAGCT
CTGTAAATGAGATCCGATGTACCCATAGACATTTGTGTGTCTGAATGTATTACACC
AAATGGAAGCATCTCCAACGACAAGCCATTCCAAAATGTGAACAAAAGTTACATA
TGGAAAATGCCCCAAGTATATCAGGCAAAACACTTTAAAGCTGGCCACTGGGAT
GAGGAATGTACCAGAAAAGCAAAACCAGAGGAATCTTTGGAGCAATAGCGGGATT
CATCGAAAACGGCTGGGAAGGAATGGTTGATGGGTGGTATGGGTTCCGATATCA
AAACTCTGAAGGAACAGGGCAAGCTGCAGATCTAAAGAGCACTCAAGCAGCCAT
TGACCAGATTAATGGAAAGTTAAACAGAGTGATTGAAAGAACCAATGAGAAATT
CCATCAAAATAGAGAAGGAATTCTCAGAAGTAGAAGGAAGAATTCAGGACTTGGG
GAAATATGTAGAAGACACCAAAATAGACCTATGGTCCTACAATGCAGAATTGCT
GGTGGCTCTAGAAAATCAACATACAATTGACTTAACAGATGCAGAAATGAATAA
ATTATTTGAGAAGACTAGACGCCAGTTAAGAGAAAACGCAGAAGACATGGGAGG
TGGATGTTTCAAGATTTACCACAAATGTGATAATGCATGCATTGAATCAATAAGA
ACTGGGACATATGACCATTACATATACAGAGATGAAGCATTAAACAACCGATTT
CAGATCAAAGGTGTAGAGTTGAAATCAGGCTACAAAGATTGGATACTGTGGATT
TCATTCCGCATATCATGCTTCTTAATTGCGTTGTTCTATTGGGTTTCATTATGTGG
GCTTGCCAAAAAGGCAACATCAGATGCAACATTTGCATTTGAGTAACTGATAGT
TAAAAACACCCCTTGTTTCTACT (SEQ ID NO:3)

FIG. 3

HA - Amino

MKTTIILLTHWAYSQNPISGNNTATLCLGHHAVANGTLVKTMSDDQIEVTNATEL
VQSISMGKICNKSYRILDGRNCTLIDAMLGDPHCDALQYESWDLFIERSSAFSNCYPY
DIPDYASLRISIVASSGIVEFTAEGF1WTGVTQNGRSGACKRGSADSFRLNWLTKS
GSSYPTLNVTMPNNKNFDKLYIWGIHPSSNQEQTCLYIQESGRVTVSTKRSQQTIIP
NIESRPLVRGQSGRISYWTIVKPGDILMINSNGNLVAPRGYFKLNTGKSSVMRSDVPI
DICVSECITPNGSISNDKPFQNVNKVTYGKCPKYIRQNTLKLATGMRNVPEKQTRGIF
GAIAGFIENGWEGMVDGWYGFYQNSEGTGQAADLKSTQAAIDQINGKLN RVIER
NEKFHQIEKEFSEVEGRIQDLEKYVEDTKIDLWSYNAELLVALENQHTIDLDAEMN
K1FEKTRRQ1RENAEDMGGGCFKIYHKCDNACIESIRTGTYDHYIYRDEALNNRFQI
KGVELKSGYKDWILWISFAISCFLICVLLGFIMWACQKGNIRCNICI (SEQ ID NO: 4)

FIG. 4

NP

CAGGGAGCAAAAGCAGGGTAGATAATCACTCACTGAGTGACATCAAAGTCATGG
CGTCTCAAGGCACCAAACGATCCTATGAACAGATGGAAACTGATGGGGAACGCC
AGAATGCAACTGAAATCAGAGCATCTGTCCGAAGGATGGTGGGAGGAATCGGAC
GGTTTTATGTCCAGATGTGTACTGAGCTTAAACTAAACGACCATGAAGGGCGGCT
GATTCAGAACAGCATAACAATAGAAAGGATGGTACTTTCAGCATTTCGACGAAAG
AAGAAACAAGTATCTCGAGGAGCATCCCAGTGCTGGGAAAAGACCCTAAGAAAAC
GGGAGGCCCGATATACAGAAGAAAAGATGGGAAATGGATGAGGGAACATCATCC
TCCATGATAAAGAAGAAATCATGAGAATCTGGCGTCAGGCCAACAATGGTGAAG
ACGCTACTGCTGGTCTTACTCATATGATGATCTGGCACTCCAATCTCAATGACAC
CACATACCAAAGAACAAGGGCTCTTGTTCGGACTGGGATGGATCCCAGAATGTG
CTCTCTGATGCAAGGCTCAACCCTCCACGGAGATCTGGAGCCGCTGGTGTGCA
GTAAAAGGTGTTGGAACAATGGTAATGGAACATCATCAGGATGATCAAACGCCGA
ATAAATGATCGGAATTTCTGGAGAGGTGAAAATGGTCGAAGAACCAGAATTGCT
TATGAAAGAATGTGCAATATCCTCAAAGGGAAATTTTCAGACAGCAGCACAAACGG
GCTATGATGGACCAGGTGAGGGAAGGCCGCAATCCTGGAAACGCTGAGATTGAG
GATCTCATTTTTCTTGGCACGATCAGCACTTATTTTGAGAGGATCAGTAGCCCAT
AATCATGCCTACCTGCCTGTGTTTATGGCCTTGCAAGTAACCAAGTGGGTATGACTTT
GAGAAGGAAGGATACTCTCTGGTTGGAATTGATCCTTTCAAACACTCCAGAACA
GTCAAATTTTCAGTCTAATCAGACCAAAAAGAAAACCCAGCACACAAAAGCCAGT
TGGTGTGGATGGCATGCCATTCTGCAGCATTGAGGATCTGAGAGTTTTAAATTT
CATTAGAGGAACCAAAGTAATCCCAAGAGGACAGTTAACAACCAGAGGAGTTCA
AATTGCTTCAAATGAAAACATGGAGACAATAAATTTCTAGCACACTTGAAGTGA
AAGCAAATATTGGGCAATAAGGACCAGAAGCGGAGGAAAACACCAGTCAACAGA
GAGCATTTGCAGGACAGATAAGTGTGCAACCTACTTTCTCAGTACAGAGAAATCT
TCCCTTTGAGAGAGCAACCATTATGGCTGCATTCACTGGTAACACTGAAGGGAGG
ACTTCCGACATGAGAACGGAAATCATAAGGATGATGGAAAATGCCAAATCAGAA
GATGTGTCTTTCCAGGGGCGGGGAGTCTTCGAGCTCTCGGACGAAAAGGCAACG
AACCCGATCGTGGCTTTCCCTTTGACATGAGCAAIGAAGGGTCTTATTTCTCTGGAG
ACAATGCTGAGGAGTTTGACAGTTAAAGAAAAATACCCTTGTCTTCTACTAATACG
AGACGATAT (SEQ ID NO: 5)

FIG. 5

NP - Amino

MASQGTKRSYEQMETDGERQNATEIRASVGRMVGGIGRFYVQMCTELKLNDHEGR
LIQNSITIERMVLSAFDERRNKYLEEHPSAGKDPKKTGGPIYRRKD GKWMRELILHD
KEEIMRIWRQANNGEDATAGLTHMMIWHSNLNDTTYQRTRALVRTGMDPRMCSL
MQGSTLPRRSGAAGA AVKGVGTMMELJRMIKRGINDRNFWRGENGRRTRIAYER
MCNILKGKFQTAAQRAMMDQVREGRNPGNAEIEDLIFLARSALILRGSVAHKSLPA
CVYGLAVTSGYDFEKEGYSLVGIDPFKLLQNSQIFSLIRPKENPAHKSQLVWMACHS
AAFEDLRVLNFIRGTKVIPRGQLTTRGVQIASNENMETINSSTLELRSKYWAIRTRSG
GNTSQRAFAGQISVQPTFSVQRNLPFERATIMAAFTGNTEGRTSDMRTEIIRMMEN
AKSEDVSFQGRGVFEL.SDEKATNPVPSFDMSNEGSYFFGDNAEEFDS (SEQ ID NO:
6)

FIG. 6

MI

TATTCGTCTCAGGGAGCAAAAGCAGGTAGATATTTAAAGATGAGTCTTCTAACCG
AGGTCGAAACGTACGTTCTCTCTATCGTACCATCAGGCCCCCTCAAAGCCGAGAT
CGCGCAGAGACTTGAAGATGTCTTTGCGGGAAAGAACACCGATCTTGAGGCACT
CATGGAATGGCTAAAGACAAGACCAATCCTGTACCTCTGACTAAAGGGATTTTA
GGATTTGTATTACGCTCACCGTGCCCACTGAGCGAGGACTGCAGCGTAGACGCT
TTGTCCAAAATGCCCTTAGTGGAACCGGAGATCCAAAACAACATGGACAGAGCAG
TAAAACTGTACAGGAAGCTTAAAGAGAAATAACATTCCATGAGGCAAAAGAGG
TGGCACTCAGCTATTCCACTGGTGCACTAGCCAGCTGCATGGGACTCATATACAA
CAGAATGGGAACGTGTACAACCGAAGTGGCATTGGCCTGGTATGCGCCACATGT
GAACAGATTGCTGATTCCCAGCATCGATCTCACAGGCAGATGGTGACAACAACC
AACCCATTAATCAGACATGAAAACAGAATGGTATTAGCCAGTACCACGGCTAAA
GCCATGGAACAGATGGCAGGATCGAGTGAGCAGGCAGCAGAGGCCATGGAGGT
TGCTAGTAGGGCTAGGCAGATGGTACAGGCAATGAGAACCATTGGGACCCACCC
TAGCTCCAGTGCCGGTTTGAAAGATGATCTCCTTGAAAATTTACAGGCCTACCAG
AAACGGATGGGAGTGCAAATGCAGCGATTCAAGTGATCCTCTCGTTATTGCAGC
AAGTATCATTGGAATCTTGCACTTGATATTGTGGATTCTTGATCGTCTTTTCTTCA
AATTCATTTATCGICGCCTTAAATACGGGTGAAAAGAGGGCCTTCTACGGAAGG
AGTACC'TGAGTCTATGAGGGAAGAAATATCGGCAGGAACAGCAGAA'TGCTGTGGA
TGTTGACGATGGTCATTTTGTCACATAGAGCTGGAGTAAAAAACTACCTTGTTT
CTACTAATACGAGACGATAT (SEQ ID NO: 7)

FIG. 7

MI - Amino

MSLLTEVETYVLSIVPSGPLKAEIAQRLEDVFAGKNTDLEALMEWLKTRPILSPLTKG
ILGFVFTLTVPSEGLQRRRFVQNALSGNGDPNNMDRAVKLYRKLKREITFHEAKEV
ALSYSTGALASCMGLIYNRMGTVTTEVAFGLVCATCEQIADSQHRSHRQMVTNTNP
LIRHENRMVLASTTAKAMEQ MAGSSEQAAEAMEVASRARQMVQAMRTIGT'HPSS
AGLKDDLLENLQAYQKRMGVQMQRFK (SEQ ID NO: 8)

FIG. 8

NSI

GGAGCAAAAGCAGGGTGACAAAAACATAATGGATTCCAACACTGTGTCAAGCTT
TCAGGTAGACTGTTTTCTTTGGCATGTCCGCAAACGATTCCGAGACCAAGAAGCTG
GGTGATGCCCCATTCCTTGACCGGCTTCGCCGAGACCAGAAGTCCCTAAGGGGA
AGAGGTAGCACTCTTGGTCTGGACATCGAAACAGCCACTCATGCAGGAAAAGCAG
ATAGTGGAGCAGATTCTGGAAAAGGAATCAGATGAGGCACTTAAAATGACCATT
GCCTCTGTTCTGCTTCACGCTACTTAACTGACATGACTCTTGATGAGATGTCAAG
AGACTGGTTCATGCTCATGCCCAAGCAAAAAGTAACAGGCTCCCTATGTATAAG
AATGGACCAAGCAATCATGGATAAGAACATCATACTTAAAGCAAACCTTTAGTGT
GATTTTCGAAAGGCTGGAAACACTAATACTACTTAGAGCCTTCACCGAAGAAGG
AGCAGTCGTTGGCGAAATTTACCATTACCTTCTCTTCCAGGACATACTAATGAG
GATGTCAAAAATGCAATTGGGGTCCTCATCGGAGGACTTAAATGGAATGATAAT
ACGGTTAGAATCTCTGAAACTCTACAGAGATTTCGCTTGGAGAAGCAGTCATGAA
AATGGGAGACCTTCATTCCCTTCAAAGCAGAAACGAAAAATGGAGAGAACAATT
AAGCCAGAAATTTGAAGAAATAAGATGGTTGATTGAAGAAGTGCACATAGATT
GAAAAATACAGAAAAATAGTTTTGAACAAATAACATTTATGCAAGCCTTACAAC
ATTGCTTGAAGTAGAACAAGAGATAAGAACTTTCTCGTTTCAGCTTATTTAATGA
T (SEQ ID NO: 9)

FIG. 9

NSI - Amino

MDSNTVSSIQVDCTLWIIVRKRFADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIET
ATHAGKQIVEQILEKESDEALKMTIASVPASRYLTDMTLDEMSRDWFMLMPKQKV
GSLCIRMDQAIMDKNIILKANFSVIFERLETILLRAFTEEGAVVGEISPLPSLPHTNE
DVKNAIGVLIGGLKWNDNTVRISETLQRFQAWRSSHENGSRPSFSPKQKRKMERTIKPEI
(SEQ ID NO: 10)

FIG. 10

PA

TAAATGGAAGACTTTGTGCGACAGTGCTTCAATCCAATGATCGTCGAGCTTGCGG
AAAAGGCAATGAAAGAATATGGAGAGAACCCGAAAATCGAAACAAACAAATTT
GCAGCAATATGCACTCACTTGGAAAGTCTGCTTCATGTACTCGGATTTCCACTTTAT
AAATGAACTGGGTGAGTCAGTGGTCATAGAGTCTGGTGACCCAAATGCTCTTTTG
AAACACAGATTTGAAATCATTGAGGGGAGAGATCGAACAATGGCATGGACAGTA
GTAAACAGCATCTGCAACACCACAAGAGCTGAAAAACCTAAATTTCTTCCAGATT
TATACGACTATAAGGAGAACAGATTTGTTGAAATTGGTGTGACAAGGAGAGAAG
TTCACATATACTACCTGGAGAAAGCCAACAAAATAAAGTCTGAGAAAACACATA
TCCACATTTTCTCATTTACAGGAGAAGAAATGGCTACAAAAGCGGACTATACTCT
TGATGAAGAGAGTAGAGCCAGGATCAAGACCAGACTATTCCTATAAGACAAGA
AATGGCCAGTAGAGGCCTCTGGGATTCCTTTCGTCAGTCCGAGAGAGGCGAAGA
GACAATTGAAGAAAGATTTGAAATCACAGGAACGATGCGCAAGCTTGCCAATTA
CAGTCTCCCACCGAAGCTTCTCCAGCCTTGAAAATTTTAGAGTCTATATAGATGGA
TTCGAACCGAACGGCTGCATTGAGAGTAAGCTTTCTCAAATGTCCAAAGAAGTA
AATGCCAAAATCGAACCATTTTCAAAGACAACACCCCGACCACTCAAATGCCA
GGTGGTCCACCCTGCCATCAGCGATCCAAATTTCTTGCtAATGGATGCTCTGAAACT
GAGCATTGAGGACCCAAGTCACGAGGGAGAGGGGATACCACTATATGATGCAAT
CAAATGCATGAAAACCTTTCTTTGGATGGAAAGAGCCCAGTATTGTAAACCACAT
AAAAAGGGTATAAACCCGAAGTATCTCCAAACTTGGAAGCAAGTATTAGAAGAA
ATACAAGACCTTGAGAACGAAGAAAGGACCCCAAGACCAAGAATATGAAAAA
AACAAGCCAATTGAAATGGGCACTAGGTGAAAATATGGCACCAAGAGAAAGTGG
ATTTTGAGGATTGTAAAGACATCAATGATTTAAACAATATGACAGTGATGAGCC
AGAAGCAAGGTCTCTTGCAAGTTGGATTCAAAGTGAGTTCAACAAGGCTTGTGA
GCTGACAGATTCAAGCTGGATAGAGCTCGATGAAATTGGGGAGGATGTCGCCCC
AATAGAATACATTGCGAGCATGAGGAGAAATTTTACTGCTGAGATTTCCTCAT
TGTAGAGCAACAGAATATATAATGAAAGGAGTATACATCAACACTGCTCTACTC
AATGCATCCTGTGCTGCGATGGATGAATTTCAATTAATTCCGATGATAAGTAAAT
GCAGGACCAAGAAGGGAGAAGGAAAACAAATTTATATGGATTCAATAATAAG
GGAAGGTCCCATTTAAGAAATGATACTGACGTGGTGAACCTTTGTAAGTATGGAAT
TTTCTCTCACTGATCCAAGATTTGAGCCACACAAATGGGAAAAATACTGCGTTCT
AGAAATTGGAGACATGCTTCTAAGAACTGCTGTAGGTCAAGTGTCAAGACCCAT
ATTTTGTATGTAAGGACAAATGGAACCTCTAAAATTAATAATGAAATGGGGAAT
GGAAATGAGACGCTGCCTCCTTCAGTCTCTGCAACAGATTGAAAGCATGATCGA
AGCTGAGTCCTCAGTCAAAGAAAAGGACATGACCAAGAATTTTGTGAGAACAA
ATCAGAGACATGGCCTATAGGAGAGTCCCCCAAGGAGTGGAAGAGGGCTCAAT
CGGGAAGGTTTGAGGACCTTATTAGCAAAATCTGTGTTTAACAGTTTATATGCA
TCTCCACAACCTGGAAGGATTTTCAGCTGAATCTAGGAAATTAATTCTCATTGTTT
AGGCTCTTAGAGATGACCTGGAACCTGGAACCTTTGATATTGGGGGGTTATATGA
ATCAATTGAGGAGTGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGT
TCAACTCCTTCCTACACATGCACTGAAGTAGTTGTGGCAATGCTACTATTTGTTA
TCCATACTGTCCA (SEQ ID NO: 11)

FIG. 11

PA - Amino

MEDFVRQCFNPMIVELAEKAMKEYGENPKIETNKFAAICTHLEVCFMYSDFHFINEL
GESVVIESGDPNALLKHRFEIIEGRDRTMAWTVVNSICNTTRAETPKFLPDLYDYKEN
RFVEIGVTRREVHIYYLEKANKIKSEKTHIHIFSFTGEEMATKADYTLDEESRARIKTR
LFTIRQEMASRGLWDSFRQSERGEETIEERFEITGTMRKLANYSLPPNFSSLENFRVYI
DGFEPNGCIESKLSQMSKEVNAKIEPFSKTTTPRLKMPGGPPCHQRSKFLLMDALKLS
IEDPSHEGEGIPLYDAIKCMKTFFGWKEPSIVKPHKKGINPNYLQTWKQVLEEIQDLE
NEERTPKTKNMKKTSQKWLALGENMAPEKVDFEDCKDINDLKQYDSDEPEARSLAS
WIQSEFNKACELTDSSWIELDEIGEDVAPIEYIASMRRNYFTAESHCRATEYIMKGVY
INTALLNASCAAMDEFQLIPMISKCRTKEGRRKTNLYGFIIKGRSII LRNDTDVVNFVS
MEFSLTDPRFEPHKWEKYCVLEIGDMLLRTAVGQVSRPIFLYVRTNGTSKIKMKWG
MEMRRCLLQSLQQIESMIEAESSVKEKDMTKEFFENKSETWPIGESPKGVEEGSIGKV
CRTLLAKSVFNSLYASPQLEGFSAESRKLLLVQALRDDLEPGTFDIGGLYESIEECLIN
DPWVLLNASWFNSFLTHALK (SEQ ID NO: 12)

FIG. 12

PBI

GAAAGCAGGCAAACCATTTGAATGGATGTCAATCCGACTCTACTTTTCTTAAAGG
TGCCAGCGCAAAATGCTATAAAGCACAAACATTCCCTTATACTGGAGATCCTCCCTA
CAGTCATGGAACAGGGACAGGATACACCATGGATACTGTCAACAGAACACACCA
ATATTCAGAAAAAGGGAAATGGACAACAAACACTGAGATTGGAGCACCACAACCT
TAATCCAATCGATGGACCACTTCCTGAAGACAATGAACCAAGTGGGTACGCCCCA
AACAGATTGTGTATTGGAAGCAATGGCTTTCCTTGAAGAATCCCATCCCGGAATC
TTTGAAAATTCTGTCTTTGAAACGATGGAGGTGATTACAGCAGACAAGAGTGGAC
AAACTAACACAAGGCCGACAAACTTATGATTGGACCTTGAATAGGAATCAACCT
GCCGCAACAGCACTTGCTAATACGATTGAAGTATTCAGATCAAATGGTCTGACTT
CCAATGAATCGGGGAGATTGATGGACTTCCTCAAAGATGTCATGGAGTCCATGA
ACAAAGGAGGAAATGGAAATAACAACACACTTCCAACGGAAGAGAAGAGTAAAG
GACAACATGACAAAGAGAATGATAACACAGAGAACCATAGGGAAGAAAAACA
ACGATTAAGCAGAAAGAGCTATCTAATCAGAACATTAACCCCTAAACACAATGAC
CAAGGACGCTGAAAGAGGGAAATTTGAAACGACGAGCAATTCGCTTACCCCAAGGGA
TGCAGATAAGAGGATTTGTATATTTTGTGAAACACTAGCTCGAAGAATATGTGA
AAAGCTTGAACAATCAGGATTGCCAGTTGGCGGTAATGAGAAAAAGGCCAAACT
GGCTAATGTCTCAGAAAAATGATGACTAATTCCCAAGACACTGAACTCTCCTTC
ACCATCACTGGGGACAATACCAAAATGGAATGAAAAATCAGAAACCCACGCATATTC
CTGGCAATGATCACATACATACTAGAAATCAGCCAGAATGGTTCAGAAATGTT
CTAAGCATTGCACCGATTATGTTCTCAAATAAAATGGCAAGACTGGGGAAAGGA
TATATGTTTGAAGCAAAAGTATGAAATTTGAGAACTCAAATACCAGCAGAAATG
CTAGCAAGCATTGACCTAAATATTTCAATGATTCAACAAAAAAGAAATTTGAA
AAGATACGACCACTCCTGGTTGACGGGACTGCTTCACTGAGTCTGOCATGATGA
TGGGAATGTTCAACATGTTGAGCACTGTGCTGGGTGTATCCATATTAACCTGGG
CCAGAGGAAATATACAAAGACCACATACTGGTGGGATGGTCTGCAATCATCCGA
TGACTTTGCTTTGATAGTGAATGCGCCTAATCATGAAGGAATACAAGCTGGAGTA
GACAGATTCTATAGAACTTGCAAACCTGGTCGGGATCAACATGAGCAAAAAGAAAG
TCCCTACATAAAATAGAACIGGAACATTCGAATTCACAAGCTTTTCTTACCGGATG
GTTTTGTAGCCAATTTTCAAGCATGGAACCTACCCAGTTTTTGGGGTTTTCCGGAATAAA
TGAATCTGCAGACATGAGCATTGGAGTGACAGTCATCAAAAACAACATGATAAA
TAATGATCTCGGTCTTGCACGGCACAAATGGYACTCCAACCTCTTCATTAAGGAT
TATCGGTACACATACCGGTGCCATAGAGGTGATACCCAGATACAAACCAGAAGA
TCTTTTGTAGTTGAAGAAACITGTGGGAACAGACTCGATCAAAGACTGGTCTTACITGG
TATCAGATGGGGGTCCAAACCTATATAACATCAGAAACCTACACATCCCGGAAG
TCTGTTTTAAATGGGAGCTAATGGATGAAGATTATAAGGGGAGGCTATGCAATC
CATTGAATCCTTTTCTGTTAGTCAAAAGAAATTGAATCAGTCAACAGTGCAGTAGT
AATGCCTGCGCATGGCCCTGCCAAAAGCATGGAGTATGATGCTGTGCAACAACA
CATTCTTGGATCCCCAAGAGGAACCGGTCCATATTGAACACAAGCCAAAGGGGA
ATACTAGAAGATGAGCAGATGTATCAGAAATGCTGCAACCTGTTTGAATAATTCT
TCCCCAGCAGCTCATACAGAAGACCAGTCGGAATTTCTAGTATGGTTGAGGCCAT
GGTATCCAGGGCCCCGATTGATGCACGAATTGACTTCGAATCTGGACGGATAAA
GAAGGATGAGTTCTGCTGAGATCATGAAGATCTGTTCCACCATTGAAGAGCTCAG
ACGGCAAAAATAGTGAA (SEQ ID NO: 13)

FIG. 13

PBI - Amino

MDVNPTLLFLKVPAQNAISTTFPYTGDPYPYSHGTGTGYTMDTVNRTHQYSEKGKWT
TNTEIGAPQLNPIDGPLPEDNEPSGYAQTDCVLEAMAFLEESHPIFENSCLTMEVIQ
QTRVDKLTQGRQTYDWTLNRNQPAATALANTIEVFRSNGLTSNESGRLMDFLKDV
MESMNKEEMEITTHFQRKRRVRDNMTKRMITQRTIGKKKQRLSRKSYLIRTLTLNT
MTKDAERGKLLKRRAIATPGMQIRGFVYFVETLARRICEKLEQSGLPVGGNEKKAKL
ANVVRKMMTNSQDTELSFTITGDNTKWNENQNPRIFLAMITYITRNQPEWFRNVLSI
APIMFSNKMARLGKGYMFESKSMKLRTQIPAEMLASIDLKYFNDSTKKKIEKIRPLLV
DGTASLSPGMMMGMFNMLSTVLGVSILNLGQRKYTKTTYWWDGLQSSDDFALIVN
APNHEGIQAGVDRFYRTCKLVGINMSKKKSYINRTGTFEFTSFFYRYGFVANFSMELP
SFGVSGINESADMSIGVTVIKNNMINNDLGPATQMXLQLFIKDYRYTYRCHRGDTQ
IQTRRSFELKKLWEQTRSKTGLLVSDGGPNLYNIRNLHIPEVCLKWELMDEDYKGRL
CNPLNPFVSHKEIESVNSAVVMPAHGPAKSMEYDAVATTHSWIPKRNRSLNTSQRGI
LEDEQMYQKCCNLFEKFFPSSSYRRPVGISSMVEAMVSRARIDARIDFESGRIKKDEF
AEIMKICSTIEELRRQK (SEQ ID NO: 14)

FIG. 14

PB2

TATTGGICTCAGGGAGCGAAAGCAGGTCAAAATATATTCAATATGGAGAGAATAA
AAGAACTGAGAGATCTGATGTTACAATCCCGCACCCGCGAGATACTAACAAAAA
CTACTGTGGACCACATGCCATAATCAAGAAATACACATCAGGAAGACAAGAGA
AGAACCCCTGCACTTAGGATGAAATGGATGATGGCAATGAAATACCCAAATTACAG
CAGATAAGAGGATAATGGAGATGATTCTGAGAGAAATGAACAGGGACAAACC
CTTTGGAGCAAAACGAACGATGCTGGCTCAGACCCGCGTAATGGTATCACCTCTGG
CAGTGACATGGTGGAATAGGAATGGACCAACAACGAACACAATTTCATTATCCGA
AAGTCTACAAAACCTTATTTTGAAGAGGTTGAAAGATTGAAACACGGAACCTTTG
GCCCCGTTTCAATTTAGGAATCAAGTCAAGATAAGACGAAGAGTTGATGTAAACC
CTGGTCACGCGGACCTCAGTGCTAAAGAAGCACAAGATGTGATCATGGAAGTTG
TTTTCCCAAATGAAGTGGGAGCCAGAATTCTAACATCAGAATCACAACTAACAAAT
AACCAAAAGAGAAAAAGGAAGAACCTCAGGACTGCAAAAATGCTCCCTTGAATGGT
AGCATACATGCTAGAAAGAGAGTTGGTCCGAAAAACAAGGTTCCCTCCAGTAGT
AGGCGGAACAAGCAGTGTATACATTGAAGTGTTCATCTGACTCAGGGAACATG
CTGGGAGCAAAATGTACACCCAGGAGGAGAAGTTAGAAACGATGATATTGATCA
AAGTTTAATTATTGCAGCCCGGAACATAGTGAGAAGAGCAACAGTATCAGCAGA
TCCACTAGCAATCCCTACTGGAAAATGTCACAGTACACAGATTTGGTGGAAACAAG
GATGGTAGACATCCCTTAAGCAGAACCCAACAGAGGAACAAGCTGTGGATATATG
CAAAGCAGCAATGGGATTGAGAATTAGCTCATCATTCAGCTTTGGTGGATTACC
TTCAAAAGGACAAGTGGATCATCAGTCAAGAGAGAAGAAGAAATGCTTACGGGC
AACCTTCAAAACATTGAAAATAAGAGTGCATGAGGGCTATGAAGAATTCACAATG
GTCGGAAGAAGAGCAACAGCCATTATCAGAAAGGCAACCAGAAGATTGATTCAA
TTGATAGTAAGTGGGAGAGATGAACAATCAATTGCTGAAGCAATAATTGTAGCC
ATGGTGTTCGCAAGAAGATTGCATGATAAAAGCAGTTCGAGGCGATTGAACT
TTGTTAATAGAGCAAAATCAGCGTTTGAACCCCATGCATCAACTCTTGAGGCATT
CCAAAAAGATGCAAAAGTGCCTTTCCAAAAATTTGGGGAAATGAACCCATCGACAA
TGTAATGGGGATGATTGGAATATTGCCTGACATGACCCCAAGCACCGAGATGTC
ATTGAGAGGAGTGAGAGTCAGCAAAATGGGAGTGGATGAGTACTCCAGCACTGA
GAGAGTGGTGGTGAGCATTGACCGTTTTTTAAGAGTTTCGGGATCAAAGGGGAAA
CATACTACTGTCCCCTGAAGAAGTCAGTGAAACACAAGGAACGGAAAAGCTGAC
AATAATTTATTCGTATCAATGATGTGGGAGATTAATGGTCCCGAATCAGTGTG
GTCAATACTTATCAATGGATCATCAGAAACTGGGAAATTGTAAAAATTCAGTGGT
CACAGGACCCCACAATGTTATACAATAAGATAGAATTTGAACCATTCATCCCT
GGTCCCTAGGGCCACCAGAAGCCAATACAGCGGTTTCGTAAGAACCCTGTTTCAG
CAAATGCGAGATGTACTTGGAACATTTGATACTGCTCAAATAATAAAAACTCCTCC
CTTTTGCCGCTGCTCCTCCGGAACAGAGTAGGATGCAGTTCTCTTCTTGAAGT
AATGTAAGAGGTTTCGGGAATGAGGATACCTTGTAAGAGGCAATTCCTCCGTTTC
AACTACAATAAAGTCACTAAAAGGCTCACAGTCTTCGGAAAGGATGCAGGTGCG
CTTACTGAGGACCCAGATGAAGGTACGGCTGGAGTAGAATCTGCTGTTCTAAGA
GGGTTTCTCATTTTATAGGTAAAGAAAAACAAGAGATATGGCCCAGCACTAAGCATC
AATGAACTTAGCAAACTTGCAAAAGGGGAGAAAGCCAATGTACTAATTGGGCAA
GGGGACGTAGTGTGGTAATGAAACGGAAACGTGACTCTAGCATACTTACTGAC
AGCCAGACAGCGACCAAAAGGATTTCGGATGGCCATCAATTAGTGTGTAATTGTTT
AAAAACGACCTTGTCTTCTACTAATACGAGACCATAT (SEQ ID NO: 15)

FIG. 15

PB2 - Amino

MERIKELRDLMLQSRTREILTKTTVDHMAIIKKYTSGRQEKNPALRMKWMMAMKY
PITADKRIMEMIPERNEQGQTLWSKTNDAGSDRVMVSPLAVTWNRNGPTTNTIHY
PKVYKTYFEKVERLKHGTFGPVHFRNQVKIRRRVDVNPGHADLSAKEAQDVIMEVV
FPNEVGARILTSESQLTITKEKKEELQDCKIAPLMVAYMLERELVRKTRFLPVVGGTS
SVYIEVLHLTQGTCTWEQMYTPGGEVRNDDIDQSLIIAARNIVRRATVSADPLASLE
MCHSTQIGGTRMVDILKQNPTEEQAVDICKAAMGLRISSSFSGGGFTFKRTSGSSVKR
EEEMLTGNLQTLKIRVHEGYEEFTMVGRRATAIIRKATRRLIQLIVSGRDEQSIAEAI
VAMVFSQEDCMIAVRGDLNFVNRRANQRLNPMHQLLRHFQKDAKVLFNWVGIEPI
DNVMGMIGIILPDMPSTEMSLRGVVRVSKMGVDEYSSTERVVVSDRFLRVDRQRGNI
LLSPEEVSETQGTEKLTIYSSSMMWEINGPESVLVNTYQWIIRNWEIVKIQWSQDPT
MLYNKIEFEPFQSLVPRATRSQYSGFVRTLFQQMRDVLGTFDTAQIIKLLPFAAAPPE
QSRMQFSSLTVNVRGSGMRILVRGNSPVFNYNKVTKRLTVLGKDGALTEDPDDEGT
AGVESAVLRGFLILGKENKRYGPALSINELSKLAKGEKANVLIGQGDVVLVMKRKR
DSSILTDSQTATKRIRMAIN (SEQ ID NO: 16)

FIG. 16

CANINE INFLUENZA VIRUS AND RELATED COMPOSITIONS AND METHODS OF USE

Matter enclosed in heavy brackets [] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue.

CROSS-REFERENCE TO RELATED PATENT APPLICATIONS

This application is a divisional of U.S. Non-Provisional patent application Ser. No. 11/539,123, filed Oct. 5, 2006, now issued as U.S. Pat. No. 7,468,187, which claims the benefit of U.S. Provisional Patent Application No. 60/727,808, filed Oct. 18, 2005, the contents of both the applications are incorporated herein by reference in their entirety.

TECHNICAL FIELD OF THE INVENTION

The present invention relates to the fields of virology, molecular biology, and immunology. In particular, the present invention relates to canine influenza virus, as well as related compositions and methods of use in inducing an immune response in animals.

BACKGROUND OF THE INVENTION

Influenza virus is an RNA virus belonging to the family Orthomyxoviridae. The viral RNA consists of eight independent segments, which easily recombine among influenza viruses to produce new subtypes.

Nucleoprotein (NP), which is the primary component of the nucleocapsid, is encoded in the fifth segment. The NP and the matrix protein are used to classify the influenza virus into group A, B or C. Since NP is an internal protein, it is not subject to the pressure of selection by a host's immune system. It binds RNA, is part of the transcriptase complex, and is involved in the nuclear-cytoplasmic transport of viral RNA (vRNA).

Neuraminidase (NM), which splits the α -keto bond that joins a terminal sialic acid and the next sugar residue, thereby allowing the release of viral progeny from infected cells, is encoded by the sixth segment. Nine subtypes (N1-N9) of this enzyme have been identified. All subtypes have two structural regions—a stalk and a head. All N8 proteins have 470 amino acids, the first eight of which are highly conserved. The following region is rich in hydrophobic amino acids and is considered to be the transmembrane domain. The next 51 amino acids make up the stalk region, and the head region begins at Cys91. The last region contains the catalytic site of the enzyme. Cysteine residues in the head and stalk region tend to be highly conserved. There are 6-8 putative N-glycosylation sites.

Hemagglutinin (HA), which is a membrane glycoprotein responsible for the adsorption of the virus into the host cell, is the main antigen to which neutralizing antibodies are directed. Its antigenic variation is the major cause of influenza epidemics. It is encoded by the fourth segment. Sixteen different subtypes (H1-H16) have been identified. HA has a signal peptide of 16 amino acids and two polypeptides (HA1 and HA2) joined by disulfide bridges. HA1 has the amino terminal end, whereas HA2 has the carboxyl terminal end. A hydrophobic region in HA2 anchors HA to the viral membrane. Cysteine residues tend to be highly conserved. There

are six putative glycosylation sites, which enable the virus to mask its antigenic sites (Skehel et al., PNAS USA 81: 1779 (1984)).

Other proteins include matrix (M or M1 and M2), non-structural (NS or NS1 and NS2), PA, PB1, and PB2. The M1 protein is a major component of the virion that binds to the plasma membrane of infected cells by means of two hydrophobic regions at the N-terminus of the protein, whereas M2 is an ion channel and, therefore, an integral membrane protein. The NS1 protein is found in the nucleus and affects cellular RNA transport, splicing, and translation. The NS2 protein is found in the nucleus and cytoplasm and has unknown function. The PA protein is a transcriptase and may have protease activity, whereas the PB1 protein functions in transcription elongation and the PB2 protein functions in transcription cap binding.

Globally, influenza is the most economically significant respiratory disease in humans, pigs, horses and poultry (Wright et al., Orthomyxoviruses. In: Fields Virology, Knipe et al., eds. Lippincott Williams & Wilkins, Philadelphia, 2001, pp. 1533-1579.). Influenza virus is known for its continuous genetic and antigenic changes, which impede effective control of the virus (Wright et al. (2001), supra; Webster et al., Microbiol. Rev. 56: 152-179 (1992)). Of particular concern for prevention of epidemics and pandemics is the emergency of a new subtype of the virus by genetic re-assortment or inter-species transmission (Wright et al. (2001), supra).

Recently, influenza outbreaks have occurred in species, e.g., feline and canine, which historically do not carry influenza virus (Keawcharoen et al., Emerg. Infect. Dis. 10: 2189-2191 (2004); Crawford et al., Science 310: 398-485 (Oct. 21, 2005; published online Sep. 29, 2005); Dubovi et al., Isolation of equine influenza virus from racing greyhounds with fatal hemorrhagic pneumonia. In: Proceedings of the 47th Annual Meeting of American Association of Veterinary Laboratory Diagnosticians, Greensboro, N.C., Oct. 2005, p. 158; and Yoon et al., Emerg. Infect. Dis. 11(12): 1974-1976 (Dec. 2005)). Therefore, the host range of influenza virus is expanding.

Outbreaks of respiratory disease in racing greyhounds caused by infection with influenza virus have occurred in Florida in 2004, in eastern and western Iowa in April 2005, and in Texas in 2005. The disease was characterized by rapid onset of fever and cough, rapid respiration, and hemorrhagic nasal discharge. The morbidity was almost 100% in both race track compounds in Iowa, although the mortality was less than 5%. While a large percentage of affected dogs recovered, many succumbed to hemorrhagic pneumonia. Therapeutic administration of broad-spectrum antibiotics reduced the severity of the disease but could not control it.

In view of the above, it is an object of the present invention to provide the influenza virus that infects canines. It is another object of the present invention to provide materials and methods for inducing an immune response to the influenza virus in canines. These and other objects and advantages, as well as additional inventive features, will become apparent from the detailed description provided herein.

BRIEF SUMMARY OF THE INVENTION

The present invention provides an isolated canine influenza virus of subtype H3N8 comprising an HA having SEQ ID NO: 4 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4, with the proviso that the amino acids at positions 94 and 233 are identical to SEQ ID NO: 4. In particular, the present invention provides an isolated canine

influenza virus of subtype H3N8 deposited with the American Type Culture Collection (Manassas, Va.) on Jun. 29, 2006, as Patent Deposit No. PTA-7694. Accordingly, the present invention also provides a composition comprising attenuated virus as well as a composition comprising inactivated virus.

The present invention also provides isolated or purified proteins. In one embodiment, the present invention provides an isolated or purified HA, which (i) has the amino acid sequence of SEQ ID NO: 4 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 4 at amino acid positions 94 and 233, or a fragment of (i) or (ii), wherein the fragment comprises at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 94 or 233 of SEQ ID NO: 4.

In another embodiment, the present invention provides an isolated or purified NM, which (i) comprises the amino acid sequence of SEQ ID NO: 2 or (ii) is derived from an influenza virus and which comprises an amino acid sequence that is greater than 99% identical to SEQ ID NO: 2, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 2 at amino acid positions 68 and 134, or a fragment of (i) or (ii), wherein the fragment comprises at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 68 or 134 of SEQ ID NO: 2.

In yet another embodiment, the present invention provides an isolated or purified NP, which (i) has the amino acid sequence of SEQ ID NO: 6 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 6, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 6 at amino acid position 402, or a fragment of (i) or (ii), wherein the fragment comprises at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 402 of SEQ ID NO: 6.

In still yet another embodiment, the present invention provides an isolated or purified M1, which (i) has the amino acid sequence of SEQ ID NO: 8 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 8, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 8 at amino acid position 111, or a fragment of (i) or (ii), wherein the fragment comprises at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 111 of SEQ ID NO: 8.

Also provided is an isolated or purified NS1, which has the amino acid sequence of SEQ ID NO: 10.

Further provided is an isolated or purified PA protein, which (i) has the amino acid sequence of SEQ ID NO: 12 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 98% (or 99%) identical to SEQ ID NO: 12, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 12 at amino acid positions 233, 256, 327, and 561, or a fragment of (i) or (ii), wherein the fragment comprises at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 233, 256, 327, and 561, of SEQ ID NO: 12.

Still further provided is an isolated or purified PB1, which (i) has the amino acid sequence of SEQ ID NO: 14 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 14, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 14 at amino acid positions 200 and 213, or a fragment of (i) or (ii), wherein the fragment comprises at

least nine contiguous amino acids, at least one of which is identical to the amino acid at position 200 or 213 of SEQ ID NO: 14.

Even still further provided is an isolated or purified PB2, which (i) has the amino acid sequence of SEQ ID NO: 16 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 16, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 16 at amino acid positions 107, 221, 292, and 661, or a fragment of (i) or (ii), wherein the fragment comprises at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 107, 221, 292, or 661 of SEQ ID NO: 16.

In view of the above, the present invention further provides a composition comprising an above-described protein, such as HA or NM, or a fragment thereof in an amount sufficient to induce an immune response in an animal and a biologically acceptable carrier.

Also in view of the above, the present invention provides a method of inducing an immune response to canine influenza virus in an animal. The method comprises administering to the animal the composition comprising a protein or fragment thereof.

An isolated or purified nucleic acid encoding above-described protein or fragment thereof, optionally as part of a vector, is also provided, as is a composition comprising the isolated or purified nucleic acid, which expresses the protein, such as HA or NM, or a fragment thereof, in an amount sufficient to induce an immune response in an animal and a biologically acceptable carrier.

Accordingly, the present invention also provides another method of inducing an immune response to canine influenza virus in an animal. The method comprises administering to the animal the composition comprising a nucleic acid.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 is the partial nucleotide sequence (SEQ ID NO: 1; see also GenBank Acc. No. DQ146420) of the coding domain sequence (CDS) of the NM gene from subtype H3N8 of canine influenza virus. In accordance with convention, the sequence is presented from left to right and top to bottom.

FIG. 2 is the amino acid sequence (SEQ ID NO: 2; see also GenBank Acc. No. DQ146420) encoded by SEQ ID NO: 1. In accordance with convention the sequence is presented in single letter format from left to right and top to bottom.

FIG. 3 is the complete nucleotide sequence (SEQ ID NO: 3; see also GenBank Acc. No. DQ146419) of the CDS of the HA gene from subtype H3N8 of canine influenza virus.

FIG. 4 is the amino acid sequence (SEQ ID NO: 4; see also GenBank Acc. No. DQ146419) encoded by SEQ ID NO: 3.

FIG. 5 is the complete nucleotide sequence (SEQ ID NO: 5) of the CDS of the NP gene from subtype H3N8 of canine influenza virus.

FIG. 6 is the deduced amino acid sequence (SEQ ID NO: 6) encoded by SEQ ID NO: 5.

FIG. 7 is the complete nucleotide sequence (SEQ ID NO: 7) of the CDS of the M1 protein gene from subtype H3N8 of canine influenza virus.

FIG. 8 is the deduced amino acid sequence (SEQ ID NO: 8) encoded by SEQ ID NO: 7.

FIG. 9 is the complete nucleotide sequence (SEQ ID NO: 9) of the CDS of the NS1 protein gene from subtype H3N8 of canine influenza virus.

FIG. 10 is the deduced amino acid sequence (SEQ ID NO: 10) encoded by SEQ ID NO: 9.

FIG. 11 is the complete nucleotide sequence (SEQ ID NO: 11) of the CDS of the PA protein gene from subtype H3N8 of canine influenza virus.

FIG. 12 is the deduced amino acid sequence (SEQ ID NO: 12) encoded by SEQ ID NO: 11.

FIG. 13 is the complete nucleotide sequence (SEQ ID NO: 13) of the CDS of the PB1 protein gene from subtype H3N8 of canine influenza virus.

FIG. 14 is the deduced amino acid sequence (SEQ ID NO: 14) encoded by SEQ ID NO: 13.

FIG. 15 is the complete nucleotide sequence (SEQ ID NO: 15) of the CDS of the PB2 protein gene from subtype H3N8 of canine influenza virus.

FIG. 16 is the deduced amino acid sequence (SEQ ID NO: 16) encoded by SEQ ID NO: 15.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is predicated on the discovery of a strain of influenza virus in canines. The strain was isolated from racing greyhounds in eastern and western Iowa. The strain has been classified as an H3N8 subtype, and has been designated A/canine/Iowa/13628/2005. Accordingly, the present invention provides a virus comprising an HA having SEQ ID NO: 4 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4, with the proviso that the amino acids at positions 94 and 233 are identical to SEQ ID NO: 4. The virus can further comprise an NM comprising the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 2, with the proviso that the amino acids at positions 68 and 134 are identical to SEQ ID NO: 2. The virus comprising the aforementioned HA, alone or in further combination with the aforementioned NM, can further comprise at least one of the following: an NP having the amino acid sequence of SEQ ID NO: 6 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 6, with the proviso that amino acid 402 is identical to that of SEQ ID NO: 6; an M1 having the amino acid sequence of SEQ ID NO: 8 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 8, with the proviso that amino acid 111 is identical to that of SEQ ID NO: 8; an NS1 having the amino acid sequence of SEQ ID NO: 10; a PA protein having the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence that is greater than 98% (or 99%) identical to SEQ ID NO: 12, with the proviso that amino acids 233, 256, 327, and 561 are identical to SEQ ID NO: 12; a PB1 having the amino acid sequence of SEQ ID NO: 14 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 14, with the proviso that amino acids 200 and 213 are identical to SEQ ID NO: 14; and/or PB2 having the amino acid sequence of SEQ ID NO: 16 or an amino acid sequence that is greater than 99% identical to SEQ ID NO: 16, with the proviso that amino acids 107, 221, 292, and 661 are identical to SEQ ID NO: 16. In particular, the present invention provides an isolated canine influenza virus of subtype H3N8 deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, Va. 20110-2209, U.S.A., on Jun. 29, 2006, as Patent Deposit No. PTA-7694.

Influenza virus can be precipitated by subjecting the virus in aqueous medium to one or more insolubilizing steps brought about by the presence of up to 5% by weight of polyethylene glycol (PEG) having a molecular weight between 3,000 and 20,000 or another linear filamentary non-charged polymer in an amount equivalent to the solubilizing power of PEG, separating an insolubilized fraction from a non-insolubilized fraction, and recovering virus from one of

the fractions (see, e.g., U.S. Pat. No. 3,989,818). Preferably, the temperature does not exceed 35° C., the pH is between 6 and 9, and the ionic strength of the aqueous medium is below the salting out point for the virus. The concentration of the virus in the aqueous medium prior to insolubilizing corresponds to a hemagglutination titer of at least 1 in 32. Aggregated viral particles are obtained, which are believed to provide a better antigenic effect due to the slow release of viral particles after vaccination. If, however, non-aggregated or less aggregated particles are desired, they can be dissociated using any suitable method, such as sonication.

The virus can be attenuated by passaging in a cell system until the virus has lost its ability to produce disease, while fully retaining its immunogenic character. For example, the virus can be serially passaged in a culture of cells originating from a canine species or other suitable species at a temperature of about 37° C. At each passage, the virus is harvested from one culture and inoculated into a medium containing a fresh cell culture in accordance with methods known in the art. For example, the virus can be collected from tissue cell culture fluids and/or cells. Optionally, during harvesting, the cell culture can be sonicated to promote release of the virus. See, e.g., U.S. Pat. Nos. 5,698,433 and 6,455,298.

If desired, an influenza strain can be passaged at least once in the allantoic cavity of embryonated eggs, such as chicken eggs, in the presence of serum, to obtain serum-resistant virus (see, e.g., U.S. Pat. No. 3,953,592; Kilbourne et al., J. Exp. Med. 111: 387 (1960); Kilbourne, Science 160: 74-75 (April 1968); and Laver et al., Virology 30: 493-501 (1966)). High potency influenza vaccine with low pyrogenicity and low endotoxicity can be achieved by treating the concentrated allantoic fluid containing an attenuated virus sequentially with butyl acetate and ethyl acetate, followed by flash evaporation (see, e.g., U.S. Pat. No. 4,000,257). Such virus can be administered intranasally as a vaccine.

Once inoculated into the host, the virus multiplies to some extent so that only a small initial inoculum is required. The virus must be innocuous, and infection of susceptible contacts should be kept to a minimum.

Alternatively, the virus can be inactivated by abolishing replication and virulence. This can be done by chemical or physical means. Chemical inactivation can be carried out by treatment of the virus with an enzyme, formaldehyde, β -propiolactone or derivative thereof, ethyleneimine or derivative thereof, an organic solvent (e.g., halogenated hydrocarbon), and/or a detergent (e.g., Tween®, Triton X®, sodium desoxycholate, sulfobetain, or cetyltrimethylammonium salts). If necessary, chemically activated compositions can be neutralized. For example, if formaldehyde is used to deactivate the composition, the composition can be neutralized with thio-sulphate. If required, the pH subsequently can be returned to a value of about 7. Alternatively, the virus can be extracted with a mixture of ether and ethanol, the aqueous and organic phases can be separated, and residual ether can be removed from the viral suspension under reduced pressure (see, e.g., U.S. Pat. No. 4,431,633). Physical inactivation advantageously can be carried by subjecting the virus to energy-rich radiation, such as ultraviolet light, γ -radiation, or X-rays. Inactivated forms require a relatively high amount of inoculum and, therefore, a correspondingly large quantity of antigenic material, which has to be manufactured, tested, and distributed.

In view of the above, the present invention also provides a composition comprising an attenuated or inactivated virus. The virus should be present in an amount sufficient to induce an immune response and, desirably, should provide protection upon challenge. Generally, an adjuvant, such as Tween®,

Span®, Freund's complete adjuvant, saponin, *Corynebacterium parvum* (Coparvax®), aluminium phosphate, aluminium hydroxide, or a mixture thereof, is added to the composition, particularly if the composition comprises inactivated virus. Protein hydrolysates and/or amino acids can be added to stabilize the composition (see, e.g., U.S. Pat. No. 4,537,769). Alternatively, the composition can be formulated as an oil-in-water emulsion using oils such as Marcol and/or Arlacel.

Recombinant influenza strains also can be prepared, such as from the combination of an "over-attenuated" (i.e., the number of passages for attenuation is substantially greater than what is normally required to remove pathogenicity) influenza A parent strain, e.g., A2, with a virulent influenza strain as provided herein (see, e.g., U.S. Pat. No. 3,991,179; also, see U.S. Pat. Nos. 4,009,258; 4,278,662; 4,318,903; 4,338,296; and 4,693,893). A recombinant strain preferably has the growth characteristics of the over-attenuated strain coupled with the antigenic properties, e.g., the HA and NM proteins, of the virulent strain. The selection of strains of influenza virus for vaccine formulation is described in U.S. Pat. No. 5,162,112. Recombinant strains can be formulated as compositions for inducing an immune response.

Sucrose, arginine monohydrochloride, the monosodium monohydrate of glutamic acid, and gelatin hydrolysate can be used to stabilize an influenza virus composition for storage in a refrigerator. See, e.g., U.S. Pat. App. Pub. No. 2006/0110406.

In view of the above, the present invention also provides an isolated or purified HA. The HA either has the amino acid sequence of SEQ ID NO: 4 or is derived from an influenza virus and has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 4 at amino acid positions 94 and 233. A fragment of HA comprising at least nine (such as 9, 12, 15, 18, 21 or 24) contiguous amino acids, at least one of which is identical to the amino acid at position 94 or 233 of SEQ ID NO: 4, is also provided.

An isolated or purified NM is also provided. The NM comprises the amino acid sequence of SEQ ID NO: 2 or is derived from an influenza virus and comprises an amino acid sequence that is greater than 99% identical to SEQ ID NO: 2, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 2 at amino acid positions 68 and 134. A fragment of NM comprising at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 68 or 134 of SEQ ID NO: 2, is also provided.

Further provided is an isolated or purified NP. The NP has the amino acid sequence of SEQ ID NO: 6 or is derived from an influenza virus and has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 6, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 6 at amino acid position 402. A fragment of NP comprising at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 402 of SEQ ID NO: 6, is also provided.

Still further provided is an isolated or purified M1. The M1 has the amino acid sequence of SEQ ID NO: 8 or is derived from an influenza virus and has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 8, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 8 at amino acid position 111. A fragment of M1 comprising at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 111 of SEQ ID NO: 8, is also provided.

Even still further provided is an isolated or purified NS1, which has the amino acid sequence of SEQ ID NO: 10.

An isolated or purified PA protein is also provided. The PA has the amino acid sequence of SEQ ID NO: 12 or is derived from an influenza virus and has an amino acid sequence that is greater than 98% (or 99%) identical to SEQ ID NO: 12, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 12 at amino acid positions 233, 256, 327, and 561. A fragment of PA comprising at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 233, 256, 327, or 561 of SEQ ID NO: 12, is also provided.

An isolated or purified PB 1 is provided. The PB1 has the amino acid sequence of SEQ ID NO: 14 or is derived from an influenza virus and has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 14, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 14 at amino acid positions 200 and 213. A fragment of PB1 comprising at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 200 or 213 of SEQ ID NO: 14, is also provided.

Provided also is an isolated or purified PB2. The PB2 has the amino acid sequence of SEQ ID NO: 16 or is derived from an influenza virus and has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 16, with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 16 at amino acid positions 107, 221, 292, and 661. A fragment of PB2 comprising at least nine contiguous amino acids, at least one of which is identical to the amino acid at position 107, 221, 292, or 661 of SEQ ID NO: 16, is provided as well.

The above proteins and fragments thereof can be purified (coupled with chemical or physical fragmentation to generate fragments) or synthesized in accordance with methods known in the art. See, e.g., Meienhofer, *Hormonal Proteins and Peptides* 2: 46, Academic Press, NY (1973), for solid phase protein synthesis, and Schroder et al., *The Peptides*, vol. 1, Academic Press, NY (1965), for solution phase protein synthesis. Automated systems can be used to carry out such techniques in accordance with manufacturer's instructions. Therapeutic quantities can be recombinantly produced and purified.

Alternatively, proteins, in particular HA and NM, can be isolated by selective solubilization, while leaving residual subviral particles consisting of the intact lipid/protein membrane enclosing all other non-essential viral components. The difference in size/density of the solubilized proteins and the residual subviral particles allows separation based on differences in physical properties by gradient centrifugation and fractionation, sedimentation, molecular sieve chromatography, or pelleting in an ultracentrifuge. Selective solubilization of HA and NM can be achieved by treatment of the virus with a cationic detergent (see, e.g., U.S. Pat. No. 4,140,762; the '762 patent). The whole virus-containing fluid obtained from cell culture can be treated with a DNA-digesting enzyme followed by addition of a cationic detergent and isolation of surface-antigen proteins (see, e.g., U.S. Pat. No. 5,948,410). The fluid can be subjected to several ultracentrifugation steps, or the virus can be fragmented in the presence of an amphiphilic nonionic detergent followed by filtration to remove undesirable substances (see, e.g., U.S. Pat. No. 6,048,537). Alternatively, membrane filtration and chemical splitting can be used to obtain a viral protein (see, e.g., U.S. Pat. No. 4,327,182). Other procedures are described in U.S. Pat. Nos. 4,064,232 and 4,057,626. Preferably, the virus is multiplied before treatment as exemplified in the '762 patent (col. 2, 11, 10 et seq).

Mapping can be conducted to identify an immune response-inducing epitope of a viral protein, i.e., "epitope

mapping.” Such mapping involves fragmenting of a protein into overlapping peptides (such as peptides comprising 9, 12, 15, 18, 21 or 24 amino acids). The protein can be fragmented with a proteolytic enzyme. The individual peptides are then tested for their ability to bind to an antibody elicited by the native protein or to induce T-cell or B-cell activation. Alternatively, hydrophilic regions of the protein can be selected, since hydrophilic residues are often on the surface of the protein and, therefore, are accessible to the antibody. X-ray crystallographic analysis of the antigen-antibody complex also can be performed. Potential HLA anchor binding motifs, which are peptide sequences that are known to be likely to bind to MHC molecules, can be identified from the amino acid sequence of a protein. Preferably, the epitope selected is one that shares little to no sequence identity with sequences widely found in the animal to which a composition comprising or expressing a protein fragment will be administered.

An isolated or purified nucleic acid encoding an above-described protein or fragment thereof, optionally as part of a vector, is also provided. The nucleic acid encoding the HA can comprise the nucleotide sequence of SEQ ID NO: 3 or a fragment thereof encoding at least nine (9, 12, 15, 18, 21 or 24) contiguous amino acids. If desired, a trivalent vaccine based on HA can be prepared, wherein one of the HAs comprises the amino acid sequence of SEQ ID NO: 4 (see, e.g., U.S. Pat. Nos. 5,762,939 and 6,245,532; see, e.g., U.S. Pat. No. 6,740,325 for a tetravalent vaccine). The nucleic acid encoding the NM can have the nucleotide sequence of SEQ ID NO: 1 or a fragment thereof encoding at least nine contiguous amino acids (see, e.g., U.S. Pat. No. 6,605,457 and U.S. Pat. App. Pub. No. 2003/0129197), whereas the nucleic acid encoding the NP can have the nucleotide sequence of SEQ ID NO: 5 or a fragment thereof encoding at least nine contiguous amino acids, the nucleic acid encoding the M1 protein can have the nucleotide sequence of SEQ ID NO: 7 or a fragment thereof encoding at least nine contiguous amino acids, the nucleic acid encoding the NS1 protein can have the nucleotide sequence of SEQ ID NO: 9, the nucleic acid encoding the PA can have the nucleotide sequence of SEQ ID NO: 11 or a fragment thereof encoding at least nine contiguous amino acids, the nucleic acid encoding the PB1 can have the nucleotide sequence of SEQ ID NO: 13 or a fragment thereof encoding at least nine contiguous amino acids, and the nucleic acid encoding the PB2 can have the nucleotide sequence of SEQ ID NO: 15 or a fragment thereof encoding at least nine contiguous amino acids. One of ordinary skill in the art will appreciate, however, that due to the degeneracy of the genetic code, there are numerous other nucleotide sequences that can encode such amino acid sequences.

The above nucleic acids, which can be DNA or RNA, and fragments thereof can be synthesized (see, e.g., *Oligonucleotide Synthesis*, Gait, ed., 1984). Such molecules can include non-naturally occurring nucleotides/bases that encode the desired amino acid sequence. For example, the base or sugar can be methylated. In addition, the backbone of the nucleic acid molecule can be modified, e.g., a phosphorothioate backbone, methylphosphonate, methylphosphorothioate, phosphorodithioate, and combinations thereof.

Alternatively, isolated vRNA can be subjected to reverse transcriptase to produce an RNA/DNA hybrid, from which the RNA is digested away and the residual DNA is treated to produce a dsDNA having a hairpin end, which is treated with a single-strand-specific nuclease to produce a bimolecular double-stranded copy of the vRNA (see, e.g., U.S. Pat. No. 4,357,421). See, e.g., U.S. Pat. App. Pub. No. 2006/0166321 for the use of tandem transcription cassettes for the preparation of influenza in the absence of helper virus.

The nucleic acid is optionally part of a DNA vector comprising at least one promoter, in which case each nucleotide sequence is operably linked to a promoter, which can be the same or different. In addition to promoters, other control sequences, such as terminating signals and the like, can be part of the DNA vector.

For example, the nucleic acid can be introduced into a suitable recombinant expression vector, such as those adapted for bacteria, such as *E. coli* and *Salmonella typhi*, yeast, such as *Saccharomyces cerevisiae* or *Pichia pastoris*, or filamentous fungi, such as *Aspergillus nidulans*. The bacteria, yeast, or fungi can be grown in continuous culture. The polypeptide, which is produced during culture, then can be isolated and purified. Alternatively, the nucleic acid molecule can be introduced into Poxviridae (e.g., fowlpox-based vectors), Herpesviridae (e.g., pseudorabies virus-based vectors, turkey herpes virus-based vectors, feline herpes virus-based vectors, infectious laryngotracheitis virus-based vectors, and bovine herpes virus-based vectors), Adenoviridae (e.g., bovine adenovirus (e.g., serotype 3), human adenovirus (e.g., serotype 4 or 7), and canine adenovirus (e.g., serotype 2; CAV2; see, e.g., U.S. Pat. No. 6,090,393), or an insect virus expression vector, such as recombinant baculovirus (e.g., *Autographa californica* nuclear polyhydrosis virus (AcNPV)), which, in turn, can be used to infect susceptible cultured SF9 cells, which are derived from the insect *Spodoptera frugiperda*. Other viral vectors include vaccinia (see, e.g., U.S. Pat. No. 4,722,848), adenovirus, adeno-like virus, adeno-associated virus, retrovirus, and pox (see, e.g., Hruby, *Vet. Parasitol.* 29: 281-282 (1988); Uiu, “AIDS Research Reviews,” Dekker, Inc., 1991, 1: 403-416), which can be administered by a skin scratch or by injection, optionally as a liposomal formulation. Other vectors include Bacille-Calmette-Guerin (BCG; Stover et al., *Nature* 351: 456-460 (1991)), detoxified anthrax toxin vectors, and the like. Mammalian cells, such as Chinese hamster ovary (CHO) cells, and even plant cells can be used to express the polypeptide from the appropriate construct. One of ordinary skill in the art will appreciate that the choice of host cell will affect the nature of post-translational processing (e.g., glycosylation, folding, and the like), which, in turn, can impact the immunogenicity of the polypeptide, and subsequent purification techniques.

Expression can be achieved in any appropriate host cell transformed/transfected with the expression vector. Examples of suitable host cells include, but are not limited to, those described above. Thus, the present invention also provides a host cell transformed/transfected with an expression vector.

Supernatants from host/vector systems that secrete the protein or fragment thereof into culture media can be applied to a purification matrix, such as an affinity column or an ion exchange column. One or more reverse-phase HPLC steps can be employed to purify further the recombinant protein or fragment thereof.

Production of a protein or fragment thereof as a fusion protein can stabilize production. This can be accomplished by ligating polynucleotide sequences encoding two or more proteins (or fragments thereof) into an appropriate expression vector with or without a peptidic linker. Desirably, the reading frames of the polynucleotide sequences are in phase, so that a single fusion protein that retains the biological activity of each protein (or fragment thereof) is produced. A peptidic linker from 1 to about 50 amino acids can be used to separate the resultant proteins (or fragments thereof) so as to ensure that each protein (or fragment thereof) properly folds into its native secondary, tertiary, and quaternary structures (see, e.g., Maratea et al., *Gene* 49: 39-46 (1985); Murphy et al., *PNAS*

USA 83: 8258-8262 (1986); U.S. Pat. No. 4,935,233; and U.S. Pat. No. 4,751,180). The ability to adopt a flexible extended conformation, the inability to adopt a secondary structure that could interact with functional amino acids on either one or both of the proteins, and the lack of hydrophobic or charged residues that might react with either one or both of the proteins are factors, which are taken into consideration in selecting a peptide linker. Linkers are not required when the ends of the proteins to be joined do not contain essential regions, such that the ends can be used to separate functional domains and prevent steric interference. Preferred peptide linker sequences contain Gly, Asn, and Ser residues. Other near neutral residues, such as Thr and Ala, also can be used.

Other additional amino acid sequence(s) can be selected to enhance the expression and/or immunogenicity of the protein or fragment thereof. For example, the protein or fragment thereof can be fused to the heavy chain of immunoglobulin G (IgG) or an antigen-presenting cell (APC) binding protein or a dendritic cell binding protein, such as IL-D, GM-CSF, IL-1, TNF, IL-4, CD40L, CTLA4, CD28, or FLT-3 ligand. Techniques, such as the use of dehydrating agents, e.g., dicyclohexylcarbodiimide (DCCI), or the creation of linkages between sulfhydryl groups, epsilon amino groups, carboxyl groups, and the like, can be used. If desired, a cleavage site can be introduced into the fusion protein to enable separation of the protein (or fragment thereof) from the non-naturally occurring sequence(s). Examples of cleavage sites include a target sequence for a proteolytic enzyme or, if methionine is not present in the protein (or fragment thereof), methionine, which, in turn, is cleaved by cyanogen bromide. Such methods are known in the art. The protein or fragment thereof can be modified by glycosylation or other derivatization (e.g., acetylation or carboxylation), also in accordance with methods known in the art.

The protein (or fragment thereof) can be expressed in situ from a suitable expression system. Any DNA construct, which is effective in producing the encoded protein or fragment thereof in the desired environment, can be used to express the protein or fragment thereof as described above.

Alternatively, the nucleic acid molecule can behave as an effective expression system in situ when injected into an animal as "naked DNA" (see, e.g., Ulmer et al., *Science* 259: 1745-1749 (1993); and Cohen, *Science* 259: 1691-1692 (1993)). DNA delivery also can be facilitated through the use of bupivacaine, polymers, and peptides; alternatively, cationic lipid complexes, particles, or pressure (see, e.g., U.S. Pat. No. 5,922,687) can be used.

Examples of amino acid sequences that are at least about or greater than 95% identical to, such as at least about or greater than 96%, 97%, 98%, or 99% identical to, SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, or 16 include amino acid sequences that contain one or more substitutions, insertions, additions and/or deletions. Sequence identity can be determined by aligning polypeptide sequences and applying publicly available computer algorithms, such as BLASTP (Pearson et al., *PNAS* USA 85: 2444-2448 (1988); Pearson, *Methods Enzymol.* 183: 63-98 (1990); and Altschul et al., *Nucl. Acids Res.* 25: 3389-3402 (1997)). The software for BLASTP is available on the FTP server of the National Center for Biotechnology Information (NCBI) or NCBI, National Library of Medicine, Building 38A, Room 8N805, Bethesda, Md. 20894. Once the polypeptide sequences are aligned, the number of identical amino acids over the aligned portions is identified, the number of identical amino acids is divided by the total number of amino acids of the polypeptide of interest, and the result is multiplied by 100 to determine the percentage sequence identity.

In this regard, one of ordinary skill in the art will appreciate that a fragment of a given amino acid sequence can be at least about or greater than 95% identical to, such as 96%, 97%, 98% or 99% identical to, the amino acid sequence. Thus, fragments are intended to be encompassed by "an amino acid sequence that is at least about or greater than 95% (or 96%, 97%, 98% or 99%) identical to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, or 16." Such fragments desirably retain the immunogenicity of the full-length protein. Functional fragments can be generated by mutational analysis of the nucleic acid encoding the protein and subsequent expression of the resulting mutant protein or by chemical/enzymatic digestion of the protein, itself.

Modifications, such as substitutions, insertions, additions and/or deletions, can be introduced into the nucleic acid or the protein (or fragment thereof) in accordance with methods known in the art (see, e.g., Adelman et al., *DNA* 2: 183 (1983), for oligonucleotide-directed site-specific mutagenesis). Desirably, the modification does not substantially diminish the immunogenicity of the protein fragment; rather, it is preferred that the immunogenicity remains substantially the same or increases relative to the unmodified protein.

A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, i.e., similar secondary structure and hydrophobic nature. Amino acid substitutions can be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids, such as aspartic acid and glutamic acid, can be interchanged, whereas positively charged amino acids, such as lysine and arginine, can be interchanged, and amino acids with uncharged polar head groups having similar hydrophilicity values can be interchanged. In this regard, leucine, isoleucine and valine can be interchanged, glycine and alanine can be interchanged, asparagine and glutamine can be interchanged, and serine, threonine, phenylalanine, and tyrosine can be interchanged. Other groups of amino acids that can be interchanged include: (1) ala, pro, gly, glu, asp, gln, asn, ser and thr; (2) cys, ser, tyr and thr; (3) val, ile, leu, met, ala and phe; (4) lys, arg and his; and (5) phe, tyr, trp, and his.

In view of the above, a composition comprising the isolated or purified protein/nucleic acid or fragment of either of the foregoing and a biologically acceptable carrier is also provided. The nucleic acid or fragment thereof can be part of a vector. See, for example, U.S. Pat. No. 4,029,763, which is directed to an influenza vaccine comprising, as an active ingredient, NM, and U.S. Pat. No. 4,140,762, which is directed to an influenza vaccine comprising, as active ingredients, HA and NM. U.S. Pat. No. 4,826,687 describes the addition of muramyl dipeptide to a vaccine comprising HA and NM. If desired, polypeptides corresponding substantially to amino acids 148-162, 163-166, and/or 215-239 of M1 can be added to a composition of a protein/nucleic acid or fragment thereof (see, e.g., U.S. Pat. Nos. 5,136,019; 5,616,327; and 5,741,493). Any suitable biologically acceptable carrier can be used in the composition. For example, the protein(s)/nucleic acid(s)/fragments thereof can be resuspended in a diluent, e.g., 0.9% sodium chloride solution, which is optionally buffered with, for example, a phosphate buffer. Any sucrose that remains from purification of the virus can be reduced by dialysis. Dialysis or gel chromatography can be used to remove any remaining cationic detergent. Preferably, the protein or fragment thereof is present in an amount sufficient to induce an immune response (i.e., cellular or humoral) in an animal. A frequently selected carrier for pharmaceuticals and antigens is poly(D,L-lactide-co-glycolide) (PLGA).

PLGA is a biodegradable polyester, and can be used for the controlled release of antigen (Eldridge et al., *Curr. Topics Micro. Immuno.* 146: 59-66 (1989); see also U.S. Pat. No. 6,090,393). The entrapment of antigens in PLGA microspheres of 1-10 μ in diameter has been shown to have a remarkable adjuvant effect when administered orally.

If desired, a preserving agent or an inactivating agent, such as formaldehyde, can be added. A conventional amount of preserving/inactivating agent is 1 part per 10,000 parts.

If desired, one or more proteins (or immunogenic fragments thereof), such as the above-described HA, can be combined with proteosomes. See, e.g., U.S. Pat. No. 6,743,900 and U.S. Pat. App. Pub. No. 2004/0156867.

Immunogenicity can be improved by inclusion of conventional immunological adjuvants, such as aluminium hydroxide (e.g., about 0.2%) or aluminium phosphate, aluminium (see, e.g., U.S. Pat. Nos. 6,372,223, 6,635,246, 6,861,244 and 7,052,701 and U.S. Pat. App. Pub. Nos. 2004/0096464 and 2006/0147468), chitosan (see, e.g., U.S. Pat. Nos. 6,136,606 and 6,534,065), alum, such as in the form of aluminum hydroxide, aluminum phosphate or aluminum oxide, mineral oils (e.g., Bayol F® and Marcol 52®), Freund's complete adjuvant, Freund's incomplete adjuvant, muramyl dipeptide, monophosphoryl lipid A, and saponins, including the Quil A component. Immunogenicity also can be improved by adding a cytokine, such as an interleukin, or by conjugating proteins or fragments thereof. Preferably, the protein or fragment thereof is conjugated with a macromolecular carrier, such as a protein (e.g., serum albumin, keyhole limpet hemocyanin, immunoglobulin, thyroglobulin, and ovalbumin), polysaccharide (e.g., latex-functionalized sepharose, agarose, cellulose beads, and the like), phospholipid, polymeric amino acids (e.g., polyglutamic acid, polylysine, and the like), or amino acid co-polymers (see, e.g., U.S. Pat. Nos. 5,136,019 and 5,612,037). Alternatively, the protein or fragment thereof can be encapsulated with a proteoliposome or lipid vesicle.

The composition, which can induce an immune response, can be prepared in the form of a suspension or can be lyophilized. If lyophilized, it is preferable to add one or more stabilizers. Suitable stabilizers are, for example, sucrose, phosphate, glutamate, and albumin (SPGA; Bovarnick, J. *Bacteriol.* 59: 509 (1950)), carbohydrates (e.g., sorbitol, mannitol, starch, dextran, and glucose), proteins (e.g., albumin and casein) or degradation products thereof, protein-containing agents (e.g., bovine serum or skim milk), and buffers (e.g., alkali metal phosphates).

Alternatively, the composition can be formulated as a controlled-release composition. The attenuated/inactivated virus or recombinant vector can be microencapsulated with polymers, such as polycarbonates, polyesters, polyurethanes, polyorthoesters, and polyamides. The particular polymer selected depends on a number of factors including reproducibility of polymer synthesis and microencapsulation, cost of materials and process, toxicological profile, requirements for variable release kinetics, and the physicochemical compatibility of the polymer and the virus/vector.

The compositions described herein can be used alone or in combination with other active ingredients/compositions. Examples include compositions, which can induce an immune response against canine distemper, infectious canine hepatitis (CAV-1 and CAV-2), rabies, parainfluenza, canine corona virus, measles, leptospirosis, and Bordetella. Polyphenols have been disclosed to inhibit influenza infection in humans (see, e.g., U.S. Pat. No. 5,173,922; the '922 patent). Accordingly, the addition of a polyphenol, such as epigallocatechin gallate, epicatechin gallate, epigallocatechin, epicatechin, free theaflavin, theaflavin monogallate A,

theaflavin monogallate B, and/or theaflavin digallate may be beneficial (see the '922 patent). Inhibitors of NM are disclosed in U.S. Pat. No. 5,453,533. The use of cytokines as immunopotentiators and liposomal encapsulation are described in U.S. Pat. No. 5,919,480.

The amount of nucleic acid in the composition can vary widely. For example, the concentration can range from less than about 0.1% to as much as about 20-50% or more by weight, usually at least about 2%. The concentration of protein in the composition also can vary widely. For example, the concentration can range from less than about 0.1% to as much as about 20-50% or more by weight, usually at least about 2%. Fluid volume and viscosity are taken into consideration when determining the final concentration.

Accordingly, a method of inducing an immune response to canine influenza virus in an animal is also provided. The susceptibility of an animal to infection can be assessed using the plaque reduction neutralization test (U.S. Pat. No. 4,315,073) or the hemagglutination test. The method comprises administering to the animal an above-described composition comprising an isolated or purified protein/nucleic acid or fragment thereof. If the composition comprises a nucleic acid (or fragment thereof) as part of a vector, preferably the protein (or fragment thereof) is expressed in an amount sufficient to induce an immune response in an animal. For example, a single dose of from about 9 to about 43 international units per kg of animal body weight can be administered. For larger mammals, a single dose can comprise from about 600 to about 3,000 international units per kg of body weight. For vaccine compositions prepared by culturing virus in the allantoic cavity of fertile eggs, harvesting the virus, and, if desired, stabilizing the harvested virus with a stabilizer, such as a peptone or sucrose, and then distribution into glass vials for subsequent freeze-drying, an effective vaccine dosage unit can contain at least 10^7 EID₅₀ (50% egg-infective dose) of virus. In the latter situation, the freeze-dried vaccine is reconstituted by addition of water or another pharmaceutically acceptable diluent prior to administration, such as in the form of a nasal spray or nasal drops. If desired, the vaccine can be administered in two successive dosages at a one-week interval.

The composition can be administered to puppies as a single dose at the age of 12 weeks, or repeatedly starting from the age of 6 weeks (e.g., at 6, 9 and 12 weeks), or weekly from 4 weeks on. The effective dosage and route of administration are determined by the nature of the composition, the nature of the expression product, LD₅₀, and, if recombinant vector is used, the expression level of the vector, as well as the breed of dog and its age, sex, weight, and condition. Dosages of expressed product can range from a few to a few hundred micrograms, e.g., 5-500 μ g. Preferred dosages of virus or recombinant vector can range from about 10^3 to about 10^6 pfu. The dose for the live attenuated strain can be at least about 10^3 TCID₅₀.

The compositions can be administered parenterally (i.e., by injection (e.g., intradermal, subcutaneous, or intramuscular) or by the route of infection, such as nasally) or enterally (i.e., by oral administration). The use of a gelling agent and a muco- or bio-adhesive to enhance the immune response against an intradermally administered immunogenic composition is described in U.S. Pat. App. Pub. No. 2005/0255121. If desired, the composition for inducing an immune response can be administered through drinking water or syrup in accordance with Chu et al. (U.S. Pat. App. Pub. No. 2006/0171960, which was published on Aug. 3, 2006). Oral administration is advantageous inasmuch as it avoids time-consuming and labor-intensive intramuscular injection, which, in turn, can

15

create stress for the animal and discomfort. Discomfort, in turn, can affect the performance of race dogs. Alternatively, the composition comprising a recombinant vector expressing at least one immune response-inducing epitope can be applied directly to the skin for localized expression and induction of an immune response.

Efficacy of the composition, which can induce an immune response, can be demonstrated by exposing puppies to a virulent strain of canine influenza virus. Untreated dogs should develop clinical signs characteristic of canine influenza viral infection, whereas treated dogs should not.

The recombinant vectors and the products expressed from them can be used to produce antibodies, such as polyclonal antibodies (pAb) and monoclonal antibodies (mAb), in accordance with methods known in the art (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1988); Harlow and Lane, *Using Antibodies: A Laboratory Manual* (1998), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1998); Shepherd and Dean, *Monoclonal Antibodies: A Practical Approach*, Oxford University Press, U.S.A. (2000)); and Harris and Adair, *Antibody Therapeutics*, CRC Press, Inc., Boca Raton, Fla. (1997)). The antibodies, in particular mAbs, can be used in binding assays and diagnostic kits/tests to determine the presence/absence of an antigen of canine influenza virus or whether or not an immune response to the virus has been stimulated. The antibodies also can be used to recover material by immuno-adsorption chromatography.

Antibodies also can provide passive immunization. For example, partially purified immune sera from host animals or from hybridoma cell lines can be injected into an animal. The antibodies provide a therapeutic effect by binding to and neutralizing an infectious influenza virus.

A composition comprising an anti-idiotypic antibody having an internal image of an epitope of an above-described protein, such as a protein consisting of the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 3, is also provided.

One of ordinary skill in the art will appreciate that an anti-idiotypic antibody, which bears an internal image of an epitope, such as those described herein, can be prepared. See, e.g., Herlyn et al., *Science* 232: 100-102 (1986)). Methods of preparing monoclonal and polyclonal anti-idiotypic antibodies, which bear the internal image of the polypeptide, are described in U.S. Pat. No. 5,053,224, for example. Briefly, polyclonal anti-idiotypic antibodies can be produced by immunizing animals with monoclonal idiotype antibodies raised against the polypeptide and screened for reactivity with the polypeptide and screening for antisera, which react with idiotype antibodies to the polypeptide. Monoclonal antibodies (mAbs) also can be prepared from such animals using standard techniques of immortalizing the antibody-secreting cells of the animal and screening cultures with idiotype antibodies in competition with the polypeptide. While mAbs are preferred, polyclonal antibodies (pAbs), which are prepared in a variety of mammalian systems, also can be used.

Another method for inducing an immune response to CIV in a canine is also provided. This method comprises administering to the canine an effective amount of a composition comprising an anti-idiotypic antibody as described above.

The isolated or purified nucleic acid molecules or vectors comprising them can be used to generate DNA for probes/primers, which can be used to detect the presence or absence of hybridizable DNA or to amplify DNA, such as cDNA.

Labeled proteins or fragments thereof, as well as labeled nucleic acids or fragments thereof, can be used in assays. Assay methods include fluoroimmunoassays (Smith et al., *Ann. Clin. Biochem.* 18: 253-275 (1981)), radioimmunoas-

16

says (RIA), enzyme-linked immunosorbent assays (ELISA), and enzyme-multiplied immunoassay technique (EMIT; see *Enzyme Immunoassay*, Maggio, ed., CRC Press, Inc., Boca Raton, Fla., 1980. pp. 141-150; 234-235, and 242-243). Such methods can be used to detect the presence of the virus and to diagnose the state of infection.

The virus, itself, can be used as a vector. The use of viruses as vectors is within the skill in the art.

EXAMPLE

The following example serves to illustrate the present invention. The example is not intended to limit the scope of the invention in any way. The example describes the identification and partial characterization of a canine influenza virus.

Outbreaks of acute respiratory disease, characterized by cough, fever, rapid respiration, and hemorrhagic nasal discharge, occurred among greyhounds within two race track compounds located in eastern and western Iowa in Apr. 2005. While a large percentage of affected dogs recovered, many succumbed to hemorrhagic pneumonia.

Lungs of affected dogs exhibited extensive red to red-black discoloration with moderate to marked palpable firmness and mild fibrinous pleuritis. Lung sections were characterized by severe hemorrhagic interstitial to bronchointerstitial pneumonia. Patchy interstitial change with alveolar septal thickening, coagulum of debris in alveoli, and associated atelectasis were evident. Focally extensive pyogranulomatous bronchointerstitial pneumonia with dilatation of airways by degenerate cells and debris was observed. Scattered vasculitis and vascular thrombi were apparent.

Microbiological testing for conventional viral and bacterial agents did not reveal any significant pathogens except *Streptococcus equi* subsp. *zooepidemicus*, which was present in lung tissues from all animals examined. Two of four lung samples tested positive for influenza virus using real-time reverse transcriptase-polymerase chain reaction (RT-PCR; Harmon et al., Development of a PCR-based differential test for H1N1 and H3N2 swine influenza viruses. In: Proceedings of the 42nd Annual Meeting of American Association of Veterinary Laboratory Diagnosticians. San Diego, Calif. Oct. 1999. p. 44.). Immunohistochemistry using monoclonal antibody (mAb) specific for the NP of influenza virus (Vincent et al., *J. Vet. Diagn. Invest.* 9: 191-195 (1997)) was also positive within viral pneumonic lesions of both lungs as was antigen-capturing ELISA (Directgen™ Flu A, Becton/Dickinson, Sparks, Md.) testing on the samples. Bronchioalveolar lavage samples from the two positive lungs tested positive for influenza virus by PCR.

Virus isolation was attempted because the detection of influenza virus in canine lungs was an unexpected observation, since only a single report of influenza virus infection in dogs existed (Dubovi et al., Isolation of equine influenza virus from racing greyhounds with fatal hemorrhagic pneumonia. In: Proceedings of the 47th Annual Meeting of American Association of Veterinary Laboratory Diagnosticians. Greensboro, N.C. Oct. 2004. p. 158.). A virus that was able to agglutinate rooster red blood cells was isolated in Madin-Darby canine kidney (MDCK) cells from lung and bronchioalveolar lavage fluid of one of the two animals in which influenza virus was detected by immunohistochemical (IHC) assay and PCR. The isolate was determined by PCR to be influenza virus of H3 subtype. The virus isolate was subtyped as H3N8 using HA-inhibition and NM-inhibition assays. The virus isolate was recognized by antisera raised against various H3 equine influenza viruses, including Miami ((A/Eq/MI/1/

63-H3N8) 640-1280), AK((A/Eq/AK/29759/91-H3N8) 320-640), and Kentucky ((A/Eq/Kentucky/81-H3N8) 160-320).

Sequencing of HA and NA genes of both isolates revealed 100% and 99.8% identity, respectively, between the two isolates. Phylogenetically, the HA gene of the isolates was genetically close (96-98% nucleotide homology) to the HA gene of recent H3N8 equine influenza viruses (Macken et al., The value of a database in surveillance and vaccine selection. In: Options for the Control of Influenza IV. Osterhaus et al., eds. Elsevier Science, Amsterdam. 2001. pp. 103-106.). The NA gene of the isolates also showed 96-98% homology with the NA gene of recent H3N8 equine influenza viruses. Since greyhounds in two different race tracks, which are geographically remote in Iowa, simultaneously succumbed to the disease without the involvement of sick horses indicates that the influenza virus isolate is a canine-adapted strain that can perpetuate in and spread among dogs. S. zooepidemicus, which has been implicated in respiratory disease and septicemia-associated problems in many different animal species (Wood et al., J. Clin. Microbiol. 43: 120-126 (2005); and Gillespie et al., The General Staphylococcus and Streptococcus. In: Hagan and Bruner's Infectious Diseases of Domestic Animals. 7th ed. Comstock/Cornell University Press. Ithaca, N.Y. 1981. pp. 164-180)), probably contributed to the severity of the disease.

All references, including publications, patent applications, and patents, cited herein are hereby incorporated by reference

to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

The use of the terms "a," "an," "the," and similar referents in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to illuminate better the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

Preferred embodiments of this invention are described herein, including the best mode known to the inventors for carrying out the invention. It should be understood that the illustrated embodiments are exemplary only, and should not be taken as limiting the scope of the invention.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 16

<210> SEQ ID NO 1

<211> LENGTH: 1450

<212> TYPE: DNA

<213> ORGANISM: Influenza A virus

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (9)..(1418)

<400> SEQUENCE: 1

```

agtttaaa atg aat cca aat caa aag ata ata gca att gga ttt gca tca      50
      Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser
          1             5             10

ttg ggg ata tta atc att aat gtc att ctc cat gta gtc agc att ata      98
      Leu Gly Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile
          15             20             25             30

gta aca gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa      146
      Val Thr Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys
          35             40             45

ggg acg atc ata aga gaa tac aat gaa aca gta aga gta gaa aaa ctt      194
      Gly Thr Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu
          50             55             60

act caa tgg tat aat acc agt aca att aag tac ata gag aga cct tca      242
      Thr Gln Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser
          65             70             75

aat gaa tac tac atg aat aac act gaa cca ctt tgt gag gcc caa ggc      290
      Asn Glu Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly
          80             85             90

ttt gca cca ttt tcc aaa gat aat gga ata cga att ggg tcg aga ggc      338
      Phe Ala Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly
          95             100             105             110

cat gtt ttt gtg ata aga gaa cct ttt gta tca tgt tcg ccc tca gaa      386
      His Val Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu

```

-continued

115					120					125							
tgt	aga	acc	ttt	ttc	ctc	aca	cag	ggc	tca	tta	ctc	aat	gac	aaa	cat		434
Cys	Arg	Thr	Phe	Phe	Leu	Thr	Gln	Gly	Ser	Leu	Leu	Asn	Asp	Lys	His		
			130					135					140				
tct	aac	ggc	aca	ata	aag	gat	cga	agc	ccg	tat	agg	act	ttg	atg	agt		482
Ser	Asn	Gly	Thr	Ile	Lys	Asp	Arg	Ser	Pro	Tyr	Arg	Thr	Leu	Met	Ser		
		145				150					155						
gtc	aaa	ata	ggg	caa	tca	ccc	aat	gta	tat	caa	gct	agg	ttt	gaa	tcg		530
Val	Lys	Ile	Gly	Gln	Ser	Pro	Asn	Val	Tyr	Gln	Ala	Arg	Phe	Glu	Ser		
	160					165				170							
gtg	gca	tgg	tca	gca	aca	gca	tgc	cat	gat	gga	aaa	aaa	tgg	atg	aca		578
Val	Ala	Trp	Ser	Ala	Thr	Ala	Cys	His	Asp	Gly	Lys	Lys	Trp	Met	Thr		
	175				180					185					190		
gtt	gga	gtc	aca	ggg	ccc	gac	aat	caa	gca	att	gca	gta	gtg	aac	tat		626
Val	Gly	Val	Thr	Gly	Pro	Asp	Asn	Gln	Ala	Ile	Ala	Val	Val	Asn	Tyr		
			195					200						205			
gga	ggt	gtt	ccg	gtt	gat	act	att	aat	tca	tgg	gca	ggg	gat	att	tta		674
Gly	Gly	Val	Pro	Val	Asp	Thr	Ile	Asn	Ser	Trp	Ala	Gly	Asp	Ile	Leu		
			210					215						220			
aga	acc	caa	gaa	tca	tca	tgc	acc	tgc	att	aaa	gga	gac	tgt	tat	tgg		722
Arg	Thr	Gln	Glu	Ser	Ser	Cys	Thr	Cys	Ile	Lys	Gly	Asp	Cys	Tyr	Trp		
			225				230					235					
gta	atg	act	gat	gga	ccg	gca	aat	agg	caa	gct	aaa	tat	agg	ata	ttc		770
Val	Met	Thr	Asp	Gly	Pro	Ala	Asn	Arg	Gln	Ala	Lys	Tyr	Arg	Ile	Phe		
	240					245					250						
aaa	gca	aaa	gat	gga	aga	gta	att	gga	caa	act	gat	ata	agt	ttc	aat		818
Lys	Ala	Lys	Asp	Gly	Arg	Val	Ile	Gly	Gln	Thr	Asp	Ile	Ser	Phe	Asn		
	255				260				265					270			
ggg	gga	cac	ata	gag	gag	tgt	tct	tgt	tac	ccc	aat	gaa	ggg	aag	gtg		866
Gly	Gly	His	Ile	Glu	Glu	Cys	Ser	Cys	Tyr	Pro	Asn	Glu	Gly	Lys	Val		
			275						280					285			
gaa	tgc	ata	tgc	agg	gac	aat	tgg	act	gga	aca	aat	aga	cca	att	ctg		914
Glu	Cys	Ile	Cys	Arg	Asp	Asn	Trp	Thr	Gly	Thr	Asn	Arg	Pro	Ile	Leu		
		290					295						300				
gta	ata	tct	tct	gat	cta	tcg	tac	aca	gtt	gga	tat	ttg	tgt	gct	ggc		962
Val	Ile	Ser	Ser	Asp	Leu	Ser	Tyr	Thr	Val	Gly	Tyr	Leu	Cys	Ala	Gly		
		305					310						315				
att	ccc	act	gac	act	cct	agg	gga	gag	gat	agt	caa	ttc	aca	ggc	tca		1010
Ile	Pro	Thr	Asp	Thr	Pro	Arg	Gly	Glu	Asp	Ser	Gln	Phe	Thr	Gly	Ser		
		320				325					330						
tgt	aca	agt	cct	ttg	gga	aat	aaa	gga	tac	ggt	gta	aaa	ggc	ttc	ggg		1058
Cys	Thr	Ser	Pro	Leu	Gly	Asn	Lys	Gly	Tyr	Gly	Val	Lys	Gly	Phe	Gly		
	335				340				345					350			
ttt	cga	caa	gga	act	gac	gta	tgg	gcc	gga	agg	aca	att	agt	agg	act		1106
Phe	Arg	Gln	Gly	Thr	Asp	Val	Trp	Ala	Gly	Arg	Thr	Ile	Ser	Arg	Thr		
			355					360						365			
tca	aga	tca	gga	ttc	gaa	ata	ata	aaa	atc	agg	aat	ggt	tgg	aca	cag		1154
Ser	Arg	Ser	Gly	Phe	Glu	Ile	Ile	Lys	Ile	Arg	Asn	Gly	Trp	Thr	Gln		
			370					375						380			
aac	agt	aag	gac	caa	atc	agg	agg	caa	gtg	att	atc	gat	gac	cca	aat		1202
Asn	Ser	Lys	Asp	Gln	Ile	Arg	Arg	Gln	Val	Ile	Ile	Asp	Asp	Pro	Asn		
		385				390						395					
tgg	tca	gga	tat	agc	ggg	tct	ttc	aca	ttg	ccg	gtt	gaa	ctg	aca	aaa		1250
Trp	Ser	Gly	Tyr	Ser	Gly	Ser	Phe	Thr	Leu	Pro	Val	Glu	Leu	Thr	Lys		
		400				405					410						
aag	gga	tgt	ttg	gtc	ccc	tgt	ttc	tgg	gtt	gaa	atg	att	aga	ggt	aaa		1298
Lys	Gly	Cys	Leu	Val	Pro	Cys	Phe	Trp	Val	Glu	Met	Ile	Arg	Gly	Lys		
	415				420				425					430			
cct	gaa	gaa	aca	aca	ata	tgg	acc	tct	agc	agc	tcc	att	gtg	atg	tgt		1346
Pro	Glu	Glu	Thr	Thr	Ile	Trp	Thr	Ser	Ser	Ser	Ser	Ile	Val	Met	Cys		

-continued

	435	440	445	
gga gta gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att				1394
Gly Val Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile				
	450	455	460	
ctt ccc ttt gac atc gat aag atg taatttacga aaaaaactcc ttgtttctac				1448
Leu Pro Phe Asp Ile Asp Lys Met				
	465	470		
ta				1450

<210> SEQ ID NO 2

<211> LENGTH: 470

<212> TYPE: PRT

<213> ORGANISM: Influenza A virus

<400> SEQUENCE: 2

Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly			
1 5 10 15			
Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr			
20 25 30			
Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr			
35 40 45			
Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu Thr Gln			
50 55 60			
Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu			
65 70 75 80			
Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala			
85 90 95			
Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val			
100 105 110			
Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg			
115 120 125			
Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn			
130 135 140			
Gly Thr Ile Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys			
145 150 155 160			
Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala			
165 170 175			
Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly			
180 185 190			
Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly			
195 200 205			
Val Pro Val Asp Thr Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr			
210 215 220			
Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met			
225 230 235 240			
Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala			
245 250 255			
Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly			
260 265 270			
His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys			
275 280 285			
Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile			
290 295 300			
Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro			
305 310 315 320			

-continued

gcc tgc aaa agg gga tca gcc gat agt ttc ttt agc cga ctg aat tgg Ala Cys Lys Arg Gly Ser Ala Asp Ser Phe Phe Ser Arg Leu Asn Trp 155 160 165	533
cta aca aaa tct gga agc tct tac ccc aca ttg aat gtg aca atg cct Leu Thr Lys Ser Gly Ser Ser Tyr Pro Thr Leu Asn Val Thr Met Pro 170 175 180	581
aac aat aaa aat ttc gac aag cta tac atc tgg ggg att cat cac ccg Asn Asn Lys Asn Phe Asp Lys Leu Tyr Ile Trp Gly Ile His His Pro 185 190 195 200	629
agc tca aat caa gag cag aca aaa ttg tac atc caa gaa tca gga cga Ser Ser Asn Gln Glu Gln Thr Lys Leu Tyr Ile Gln Glu Ser Gly Arg 205 210 215	677
gta aca gtc tca aca aaa aga agt caa caa aca ata atc cct aac atc Val Thr Val Ser Thr Lys Arg Ser Gln Gln Thr Ile Ile Pro Asn Ile 220 225 230	725
gaa tct aga ccg ttg gtc aga ggt caa tca ggc agg ata agc ata tac Glu Ser Arg Pro Leu Val Arg Gly Gln Ser Gly Arg Ile Ser Ile Tyr 235 240 245	773
tggt acc att gta aaa cct gga gat atc cta atg ata aac agt aat ggc Trp Thr Ile Val Lys Pro Gly Asp Ile Leu Met Ile Asn Ser Asn Gly 250 255 260	821
aac tta gtt gca ccg cgg gga tat ttt aaa ttg aac aca ggg aaa agc Asn Leu Val Ala Pro Arg Gly Tyr Phe Lys Leu Asn Thr Gly Lys Ser 265 270 275 280	869
tct gta atg aga tcc gat gta ccc ata gac att tgt gtg tct gaa tgt Ser Val Met Arg Ser Asp Val Pro Ile Asp Ile Cys Val Ser Glu Cys 285 290 295	917
att aca cca aat gga agc atc tcc aac gac aag cca ttc caa aat gtg Ile Thr Pro Asn Gly Ser Ile Ser Asn Asp Lys Pro Phe Gln Asn Val 300 305 310	965
aac aaa gtt aca tat gga aaa tgc ccc aag tat atc agg caa aac act Asn Lys Val Thr Tyr Gly Lys Cys Pro Lys Tyr Ile Arg Gln Asn Thr 315 320 325	1013
tta aag ctg gcc act ggg atg agg aat gta cca gaa aag caa acc aga Leu Lys Leu Ala Thr Gly Met Arg Asn Val Pro Glu Lys Gln Thr Arg 330 335 340	1061
gga atc ttt gga gca ata gcg gga ttc atc gaa aac ggc ttg gaa gga Gly Ile Phe Gly Ala Ile Ala Gly Phe Ile Glu Asn Gly Trp Glu Gly 345 350 355 360	1109
atg gtt gat ggg ttg tat ggg ttc cga tat caa aac tct gaa gga aca Met Val Asp Gly Trp Tyr Gly Phe Arg Tyr Gln Asn Ser Glu Gly Thr 365 370 375	1157
ggg caa gct gca gat cta aag agc act caa gca gcc att gac cag att Gly Gln Ala Ala Asp Leu Lys Ser Thr Gln Ala Ala Ile Asp Gln Ile 380 385 390	1205
aat gga aag tta aac aga gtg att gaa aga acc aat gag aaa ttc cat Asn Gly Lys Leu Asn Arg Val Ile Glu Arg Thr Asn Glu Lys Phe His 395 400 405	1253
caa ata gag aag gaa ttc tca gaa gta gaa gga aga att cag gac ttg Gln Ile Glu Lys Glu Phe Ser Glu Val Glu Gly Arg Ile Gln Asp Leu 410 415 420	1301
gag aaa tat gta gaa gac acc aaa ata gac cta tgg tcc tac aat gca Glu Lys Tyr Val Glu Asp Thr Lys Ile Asp Leu Trp Ser Tyr Asn Ala 425 430 435 440	1349
gaa ttg ctg gtg gct cta gaa aat caa cat aca att gac tta aca gat Glu Leu Leu Val Ala Leu Glu Asn Gln His Thr Ile Asp Leu Thr Asp 445 450 455	1397
gca gaa atg aat aaa tta ttt gag aag act aga cgc cag tta aga gaa Ala Glu Met Asn Lys Leu Phe Glu Lys Thr Arg Arg Gln Leu Arg Glu 460 465 470	1445

-continued

```

aac gca gaa gac atg gga ggt gga tgt ttc aag att tac cac aaa tgt      1493
Asn Ala Glu Asp Met Gly Gly Gly Cys Phe Lys Ile Tyr His Lys Cys
   475                               480                               485

gat aat gca tgc att gaa tca ata aga act ggg aca tat gac cat tac      1541
Asp Asn Ala Cys Ile Glu Ser Ile Arg Thr Gly Thr Tyr Asp His Tyr
   490                               495                               500

ata tac aga gat gaa gca tta aac aac cga ttt cag atc aaa ggt gta      1589
Ile Tyr Arg Asp Glu Ala Leu Asn Asn Arg Phe Gln Ile Lys Gly Val
  505                               510                               515                               520

gag ttg aaa tca ggc tac aaa gat tgg ata ctg tgg att tca ttc gcc      1637
Glu Leu Lys Ser Gly Tyr Lys Asp Trp Ile Leu Trp Ile Ser Phe Ala
   525                               530                               535

ata tca tgc ttc tta att tgc gtt gtt cta ttg ggt ttc att atg tgg      1685
Ile Ser Cys Phe Leu Ile Cys Val Val Leu Leu Gly Phe Ile Met Trp
   540                               545                               550

gct tgc caa aaa ggc aac atc aga tgc aac att tgc att tgagtaaaact      1734
Ala Cys Gln Lys Gly Asn Ile Arg Cys Asn Ile Cys Ile
   555                               560                               565

gatagttaaa aacacccttg tttctact      1762

```

```

<210> SEQ ID NO 4
<211> LENGTH: 565
<212> TYPE: PRT
<213> ORGANISM: Influenza A Virus

```

```

<400> SEQUENCE: 4

```

```

Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser
 1                               5                               10                               15

Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His
   20                               25                               30

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln
  35                               40                               45

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
  50                               55                               60

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 65                               70                               75                               80

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Leu Gln Tyr
   85                               90                               95

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
 100                               105                               110

Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
 115                               120                               125

Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
 130                               135                               140

Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp
 145                               150                               155                               160

Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr
 165                               170                               175

Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu
 180                               185                               190

Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys
 195                               200                               205

Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser
 210                               215                               220

Gln Gln Thr Ile Ile Pro Asn Ile Glu Ser Arg Pro Leu Val Arg Gly
 225                               230                               235                               240

```

-continued

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

<210> SEQ ID NO 5
 <211> LENGTH: 1585
 <212> TYPE: DNA
 <213> ORGANISM: Influenza A Virus
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (51)..(1544)

<400> SEQUENCE: 5

cagggagcaa aagcagggtgataatcact cactgagtga catcaaagtc atg gcg 56
 Met Ala
 1

tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat ggg gaa 104
 Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp Gly Glu

-continued

5	10	15	
cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg gtg gga Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met Val Gly 20 25 30			152
gga atc gga cgg ttt tat gtc cag atg tgt act gag ctt aaa cta aac Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys Leu Asn 35 40 45 50			200
gac cat gaa ggg cgg ctg att cag aac agc ata aca ata gaa agg atg Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu Arg Met 55 60 65			248
gta ctt tca gca ttc gac gaa aga aga aac aag tat ctc gag gag cat Val Leu Ser Ala Phe Asp Glu Arg Asn Lys Tyr Leu Glu Glu His 70 75 80			296
ccc agt gct ggg aaa gac cct aag aaa acg gga ggc ccg ata tac aga Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile Tyr Arg 85 90 95			344
aga aaa gat ggg aaa tgg atg agg gaa ctc atc ctc cat gat aaa gaa Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp Lys Glu 100 105 110			392
gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac gct act Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp Ala Thr 115 120 125 130			440
gct ggt ctt act cat atg atg atc tgg cac tcc aat ctc aat gac acc Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn Asp Thr 135 140 145			488
aca tac caa aga aca agg gct ctt gtt cgg act ggg atg gat ccc aga Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp Pro Arg 150 155 160			536
atg tgc tct ctg atg caa ggc tca acc ctc cca cgg aga tct gga gcc Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser Gly Ala 165 170 175			584
gct ggt gct gca gta aaa ggt gtt gga aca atg gta atg gaa ctc atc Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu Leu Ile 180 185 190			632
agg atg atc aaa cgc gga ata aat gat cgg aat ttc tgg aga ggt gaa Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg Gly Glu 195 200 205 210			680
aat ggt cga aga acc aga att gct tat gaa aga atg tgc aat atc ctc Asn Gly Arg Arg Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn Ile Leu 215 220 225			728
aaa ggg aaa ttt cag aca gca gca caa cgg gct atg atg gac cag gtg Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp Gln Val 230 235 240			776
agg gaa ggc cgc aat cct gga aac gct gag att gag gat ctc att ttc Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu Ile Phe 245 250 255			824
ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat aaa tca Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His Lys Ser 260 265 270			872
tgc cta cct gcc tgt gtt tat ggc ctt gca gta acc agt ggg tat gac Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly Tyr Asp 275 280 285 290			920
ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc aaa cta Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe Lys Leu 295 300 305			968
ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa aac cca Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu Asn Pro 310 315 320			1016
gca cac aaa agc cag ttg gtg tgg atg gca tgc cat tct gca gca ttt Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala Ala Phe 325 330 335 340			1064

-continued

325	330	335	
gag gat ctg aga gtt tta aat ttc att aga gga acc aaa gta atc cca Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val Ile Pro 340 345 350			1112
aga gga cag tta aca acc aga gga gtt caa att gct tca aat gaa aac Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn Glu Asn 355 360 365 370			1160
atg gag aca ata aat tct agc aca ctt gaa ctg aga agc aaa tat tgg Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys Tyr Trp 375 380 385			1208
gca ata agg acc aga agc gga gga aac acc agt caa cag aga gca ttt Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg Ala Phe 390 395 400			1256
gca gga cag ata agt gtg caa cct act ttc tca gta cag aga aat ctt Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg Asn Leu 405 410 415			1304
ccc ttt gag aga gca acc att atg gct gca ttc act ggt aac act gaa Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn Thr Glu 420 425 430			1352
ggg agg act tcc gac atg aga acg gaa atc ata agg atg atg gaa aat Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met Glu Asn 435 440 445 450			1400
gcc aaa tca gaa gat gtg tct ttc cag ggg cgg gga gtc ttc gag ctc Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe Glu Leu 455 460 465			1448
tcg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac atg agc Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp Met Ser 470 475 480			1496
aat gaa ggg tct tat ttc ttc gga gac aat gct gag gag ttt gac agt Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe Asp Ser 485 490 495			1544
taaagaaaaa tacccttggt tctactaata cgagacgata t			1585
<210> SEQ ID NO 6			
<211> LENGTH: 498			
<212> TYPE: PRT			
<213> ORGANISM: Influenza A Virus			
<400> SEQUENCE: 6			
Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp 1 5 10 15			
Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met 20 25 30			
Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys 35 40 45			
Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu 50 55 60			
Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu 65 70 75 80			
Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile 85 90 95			
Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp 100 105 110			
Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp 115 120 125			
Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn 130 135 140			
Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp			

-continued

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

<210> SEQ ID NO 7
 <211> LENGTH: 1056
 <212> TYPE: DNA
 <213> ORGANISM: Influenza A virus
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (40)..(795)

<400> SEQUENCE: 7

tattcgtctc agggagcaaa agcaggtaga tatttaaag atg agt ctt cta acc
 Met Ser Leu Leu Thr

-continued

															1						5																																																									
gag gtc gaa acg tac gtt ctc tct atc gta cca tca ggc ccc ctc aaa															102																																																															
Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro Ser Gly Pro Leu Lys																																																																														
															10																15																20																															
gcc gag atc gcg cag aga ctt gaa gat gtc ttt gcg gga aag aac acc															150																																																															
Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe Ala Gly Lys Asn Thr																																																																														
															25																30																35																															
gat ctt gag gca ctc atg gaa tgg cta aag aca aga cca atc ctg tca															198																																																															
Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr Arg Pro Ile Leu Ser																																																																														
															40																45																50																															
cct ctg act aaa ggg att tta gga ttt gta ttc acg ctc acc gtg ccc															246																																																															
Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe Thr Leu Thr Val Pro																																																																														
															55																60																65																															
agt gag cga gga ctg cag cgt aga cgc ttt gtc caa aat gcc ctt agt															294																																																															
Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val Gln Asn Ala Leu Ser																																																																														
															70																75																80																85															
gga aac gga gat cca aac aac atg gac aga gca gta aaa ctg tac agg															342																																																															
Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala Val Lys Leu Tyr Arg																																																																														
															90																95																100																															
aag ctt aaa aga gaa ata aca ttc cat gag gca aaa gag gtg gca ctc															390																																																															
Lys Leu Lys Arg Glu Ile Thr Phe His Glu Ala Lys Glu Val Ala Leu																																																																														
															105																110																115																															
agc tat tcc act ggt gca cta gcc agc tgc atg gga ctc ata tac aac															438																																																															
Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met Gly Leu Ile Tyr Asn																																																																														
															120																125																130																															
aga atg gga act gtt aca acc gaa gtg gca ttt ggc ctg gta tgc gcc															486																																																															
Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe Gly Leu Val Cys Ala																																																																														
															135																140																145																															
aca tgt gaa cag att gct gat tcc cag cat cga tct cac agg cag atg															534																																																															
Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg Ser His Arg Gln Met																																																																														
															150																155																160																165															
gtg aca aca acc aac cca tta atc aga cat gaa aac aga atg gta tta															582																																																															
Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu Asn Arg Met Val Leu																																																																														
															170																175																180																															
gcc agt acc acg gct aaa gcc atg gaa cag atg gca gga tcg agt gag															630																																																															
Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met Ala Gly Ser Ser Glu																																																																														
															185																190																195																															
cag gca gca gag gcc atg gag gtt gct agt agg gct agg cag atg gta															678																																																															
Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg Ala Arg Gln Met Val																																																																														
															200																205																210																															
cag gca atg aga acc att ggg acc cac cct agc tcc agt gcc ggt ttg															726																																																															
Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser Ser Ser Ala Gly Leu																																																																														
															215																220																225																															
aaa gat gat ctc ctt gaa aat tta cag gcc tac cag aaa cgg atg gga															774																																																															
Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr Gln Lys Arg Met Gly																																																																														
															230																235																240																245															
gtg caa atg cag cga ttc aag tgatcctctc gttattgcag caagtatcat															825																																																															
Val Gln Met Gln Arg Phe Lys																																																																														
															250																																																															
tggaatcttg cacttgatat tgtggattct tgatcgtctt ttcttcaaat tcatttatcg															885																																																															
tcgccttaaaa tacgggttga aaagagggcc ttctacggaa ggagtacctg agtctatgag															945																																																															
ggaagaatat cggcaggaac agcagaatgc tgtggatggt gacgatggtc attttgtcaa															1005																																																															
catagagctg gagtaaaaaa ctaccttggt tctactaata cgagacgata t															1056																																																															

<210> SEQ ID NO 8

<211> LENGTH: 252

<212> TYPE: PRT

<213> ORGANISM: Influenza A virus

-continued

<400> SEQUENCE: 8

```

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

```

<210> SEQ ID NO 9

<211> LENGTH: 870

<212> TYPE: DNA

<213> ORGANISM: Influenza A virus

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (29) .. (718)

<400> SEQUENCE: 9

```

ggagcaaaag caggggtgaca aaaacata atg gat tcc aac act gtg tca agc      52
          Met Asp Ser Asn Thr Val Ser Ser
          1          5
ttt cag gta gac tgt ttt ctt tgg cat gtc cgc aaa cga ttc gca gac      100
Phe Gln Val Asp Cys Phe Leu Trp His Val Arg Lys Arg Phe Ala Asp
10          15          20
caa gaa ctg ggt gat gcc cca ttc ctt gac cgg ctt cgc cga gac cag      148
Gln Glu Leu Gly Asp Ala Pro Phe Leu Asp Arg Leu Arg Arg Asp Gln
25          30          35          40
aag tcc cta agg gga aga ggt agc act ctt ggt ctg gac atc gaa aca      196
Lys Ser Leu Arg Gly Arg Gly Ser Thr Leu Gly Leu Asp Ile Glu Thr
45          50          55
gcc act cat gca gga aag cag ata gtg gag cag att ctg gaa aag gaa      244
Ala Thr His Ala Gly Lys Gln Ile Val Glu Gln Ile Leu Glu Lys Glu
60          65          70

```

-continued

tca gat gag gca ctt aaa atg acc att gcc tct gtt cct gct tca cgc	292
Ser Asp Glu Ala Leu Lys Met Thr Ile Ala Ser Val Pro Ala Ser Arg	
75 80 85	
tac tta act gac atg act ctt gat gag atg tca aga gac tgg ttc atg	340
Tyr Leu Thr Asp Met Thr Leu Asp Glu Met Ser Arg Asp Trp Phe Met	
90 95 100	
ctc atg ccc aag caa aaa gta aca gcc tcc cta tgt ata aga atg gac	388
Leu Met Pro Lys Gln Lys Val Thr Gly Ser Leu Cys Ile Arg Met Asp	
105 110 115 120	
caa gca atc atg gat aag aac atc ata ctt aaa gca aac ttt agt gtg	436
Gln Ala Ile Met Asp Lys Asn Ile Ile Leu Lys Ala Asn Phe Thr Val	
125 130 135	
att ttc gaa agg ctg gaa aca cta ata cta ctt aga gcc ttc acc gaa	484
Ile Phe Glu Arg Leu Glu Thr Leu Ile Leu Leu Arg Ala Phe Thr Glu	
140 145 150	
gaa gga gca gtc gtt ggc gaa att tca cca tta cct tct ctt cca gga	532
Glu Gly Ala Val Val Gly Glu Ile Ser Pro Leu Pro Ser Leu Pro Gly	
155 160 165	
cat act aat gag gat gtc aaa aat gca att ggg gtc ctc atc gga gga	580
His Thr Asn Glu Asp Val Lys Asn Ala Ile Gly Val Leu Ile Gly Gly	
170 175 180	
ctt aaa tgg aat gat aat acg gtt aga atc tct gaa act cta cag aga	628
Leu Lys Trp Asn Asp Asn Thr Val Arg Ile Ser Glu Thr Leu Gln Arg	
185 190 195 200	
ttc gct tgg aga agc agt cat gaa aat ggg aga cct tca ttc cct tca	676
Phe Ala Trp Arg Ser Ser His Glu Asn Gly Arg Pro Ser Phe Pro Ser	
205 210 215	
aag cag aaa cga aaa atg gag aga aca att aag cca gaa att	718
Lys Gln Lys Arg Lys Met Glu Arg Thr Ile Lys Pro Glu Ile	
220 225 230	
tgaagaaata agatgggtga ttgaagaagt gcgacataga ttgaaaaata cagaaaatag	778
ttttgaacaa ataacattta tgcaagcctt acaactattg cttgaagtag aacaagagat	838
aagaactttc tcgtttcagc ttatttaatg at	870

<210> SEQ ID NO 10

<211> LENGTH: 230

<212> TYPE: PRT

<213> ORGANISM: Influenza A virus

<400> SEQUENCE: 10

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

-continued

130	135	140	
Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile 145 150 155 160			
Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn 165 170 175			
Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val 180 185 190			
Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu 195 200 205			
Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg 210 215 220			
Thr Ile Lys Pro Glu Ile 225 230			
<210> SEQ ID NO 11			
<211> LENGTH: 2191			
<212> TYPE: DNA			
<213> ORGANISM: Influenza A virus			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (4)..(2151)			
<400> SEQUENCE: 11			
taa atg gaa gac ttt gtg cga cag tgc ttc aat cca atg atc gtc gag Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu 1 5 10 15			48
ctt gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa Leu Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu 20 25 30			96
aca aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg Thr Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met 35 40 45			144
tac tcg gat ttc cac ttt ata aat gaa ctg ggt gag tca gtg gtc ata Tyr Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile 50 55 60			192
gag tct ggt gac cca aat gct ctt ttg aaa cac aga ttt gaa atc att Glu Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile 65 70 75			240
gag ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc Glu Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys 80 85 90 95			288
aac acc aca aga gct gaa aaa cct aaa ttt ctt cca gat tta tac gac Asn Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp 100 105 110			336
tat aag gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt Tyr Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val 115 120 125			384
cac ata tac tac ctg gag aaa gcc aac aaa ata aag tct gag aaa aca His Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr 130 135 140			432
cat atc cac att ttc tca ttt aca gga gaa gaa atg gct aca aaa gcg His Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala 145 150 155			480
gac tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta Asp Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu 160 165 170 175			528
ttc act ata aga caa gaa atg gcc agt aga ggc ctc tgg gat tcc ttt Phe Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe 180 185 190			576
cgt cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa atc			624

Arg	Gln	Ser	Glu	Arg	Gly	Glu	Glu	Thr	Ile	Glu	Glu	Arg	Phe	Glu	Ile		
			195					200					205				
aca	gga	acg	atg	cgc	aag	ctt	gcc	aat	tac	agt	ctc	cca	ccg	aac	ttc	672	
Thr	Gly	Thr	Met	Arg	Lys	Leu	Ala	Asn	Tyr	Ser	Leu	Pro	Pro	Asn	Phe		
			210					215					220				
tcc	agc	ctt	gaa	aat	ttt	aga	gtc	tat	ata	gat	gga	ttc	gaa	ccg	aac	720	
Ser	Ser	Leu	Glu	Asn	Phe	Arg	Val	Tyr	Ile	Asp	Gly	Phe	Glu	Pro	Asn		
			225					230					235				
ggc	tgc	att	gag	agt	aag	ctt	tct	caa	atg	tcc	aaa	gaa	gta	aat	gcc	768	
Gly	Cys	Ile	Glu	Ser	Lys	Leu	Ser	Gln	Met	Ser	Lys	Glu	Val	Asn	Ala		
						245				250					255		
aaa	atc	gaa	cca	ttt	tca	aag	aca	aca	ccc	cga	cca	ctc	aaa	atg	cca	816	
Lys	Ile	Glu	Pro	Phe	Ser	Lys	Thr	Thr	Pro	Arg	Pro	Leu	Lys	Met	Pro		
						260				265					270		
ggg	ggg	cca	ccc	tgc	cat	cag	cga	tcc	aaa	ttc	ttg	cta	atg	gat	gct	864	
Gly	Gly	Pro	Pro	Cys	His	Gln	Arg	Ser	Lys	Phe	Leu	Leu	Met	Asp	Ala		
								280							285		
ctg	aaa	ctg	agc	att	gag	gac	cca	agt	cac	gag	gga	gag	ggg	ata	cca	912	
Leu	Lys	Leu	Ser	Ile	Glu	Asp	Pro	Ser	His	Glu	Gly	Glu	Gly	Ile	Pro		
								295							300		
cta	tat	gat	gca	atc	aaa	tgc	atg	aaa	act	ttc	ttt	gga	tgg	aaa	gag	960	
Leu	Tyr	Asp	Ala	Ile	Lys	Cys	Met	Lys	Thr	Phe	Phe	Gly	Trp	Lys	Glu		
								310							315		
ccc	agt	att	gtt	aaa	cca	cat	aaa	aag	ggg	ata	aac	ccg	aac	tat	ctc	1008	
Pro	Ser	Ile	Val	Lys	Pro	His	Lys	Lys	Gly	Ile	Asn	Pro	Asn	Tyr	Leu		
															335		
caa	act	tgg	aag	caa	gta	tta	gaa	gaa	ata	caa	gac	ctt	gag	aac	gaa	1056	
Gln	Thr	Trp	Lys	Gln	Val	Leu	Glu	Glu	Ile	Gln	Asp	Leu	Glu	Asn	Glu		
															350		
gaa	agg	acc	ccc	aag	acc	aag	aat	atg	aaa	aaa	aca	agc	caa	ttg	aaa	1104	
Glu	Arg	Thr	Pro	Lys	Thr	Lys	Asn	Met	Lys	Lys	Thr	Ser	Gln	Leu	Lys		
															365		
tgg	gca	cta	ggg	gaa	aat	atg	gca	cca	gag	aaa	gtg	gat	ttt	gag	gat	1152	
Trp	Ala	Leu	Gly	Glu	Asn	Met	Ala	Pro	Glu	Lys	Val	Asp	Phe	Glu	Asp		
															380		
tgt	aaa	gac	atc	aat	gat	tta	aaa	caa	tat	gac	agt	gat	gag	cca	gaa	1200	
Cys	Lys	Asp	Ile	Asn	Asp	Leu	Lys	Gln	Tyr	Asp	Ser	Asp	Glu	Pro	Glu		
															395		
gca	agg	tct	ctt	gca	agt	tgg	att	caa	agt	gag	ttc	aac	aag	gct	tgt	1248	
Al																	

-continued

Arg	Asn	Asp	Thr	Asp	Val	Val	Asn	Phe	Val	Ser	Met	Glu	Phe	Ser	Leu	
			515					520					525			
act	gat	cca	aga	ttt	gag	cca	cac	aaa	tg	gaa	aaa	tac	tgc	gtt	cta	1632
Thr	Asp	Pro	Arg	Phe	Glu	Pro	His	Lys	Trp	Glu	Lys	Tyr	Cys	Val	Leu	
		530					535					540				
gaa	att	gga	gac	atg	ctt	cta	aga	act	gct	gta	gg	caa	gtg	tca	aga	1680
Glu	Ile	Gly	Asp	Met	Leu	Leu	Arg	Thr	Ala	Val	Gly	Gln	Val	Ser	Arg	
		545					550				555					
ccc	ata	ttt	ttg	tat	gta	agg	aca	aat	gga	acc	tct	aaa	att	aaa	atg	1728
Pro	Ile	Phe	Leu	Tyr	Val	Arg	Thr	Asn	Gly	Thr	Ser	Lys	Ile	Lys	Met	
		560				565				570					575	
aaa	tg	gga	atg	gaa	atg	aga	cgc	tgc	ctc	ctt	cag	tct	ctg	caa	cag	1776
Lys	Trp	Gly	Met	Glu	Met	Arg	Arg	Cys	Leu	Leu	Gln	Ser	Leu	Gln	Gln	
			580						585					590		
att	gaa	agc	atg	atc	gaa	gct	gag	tcc	tca	gtc	aaa	gaa	aag	gac	atg	1824
Ile	Glu	Ser	Met	Ile	Glu	Ala	Glu	Ser	Ser	Val	Lys	Glu	Lys	Asp	Met	
			595					600					605			
acc	aaa	gaa	ttt	ttt	gag	aac	aaa	tca	gag	aca	tg	cct	ata	gga	gag	1872
Thr	Lys	Glu	Phe	Phe	Glu	Asn	Lys	Ser	Glu	Thr	Trp	Pro	Ile	Gly	Glu	
			610				615					620				
tcc	ccc	aaa	gga	gtg	gaa	gag	ggc	tca	atc	ggg	aag	gtt	tgc	agg	acc	1920
Ser	Pro	Lys	Gly	Val	Glu	Glu	Gly	Ser	Ile	Gly	Lys	Val	Cys	Arg	Thr	
		625				630				635						
tta	tta	gca	aaa	tct	gtg	ttt	aac	agt	tta	tat	gca	tct	cca	caa	ctg	1968
Leu	Leu	Ala	Lys	Ser	Val	Phe	Asn	Ser	Leu	Tyr	Ala	Ser	Pro	Gln	Leu	
		640				645				650					655	
gaa	gga	ttt	tca	gct	gaa	tct	agg	aaa	tta	ctt	ctc	att	gtt	cag	gct	2016
Glu	Gly	Phe	Ser	Ala	Glu	Ser	Arg	Lys	Leu	Leu	Leu	Ile	Val	Gln	Ala	
			660						665					670		
ctt	aga	gat	gac	ctg	gaa	cct	gga	acc	ttt	gat	att	ggg	ggg	tta	tat	2064
Leu	Arg	Asp	Asp	Leu	Glu	Pro	Gly	Thr	Phe	Asp	Ile	Gly	Gly	Leu	Tyr	
			675					680						685		
gaa	tca	att	gag	gag	tgc	ctg	att	aat	gat	ccc	tg	gtt	ttg	ctt	aat	2112
Glu	Ser	Ile	Glu	Glu	Cys	Leu	Ile	Asn	Asp	Pro	Trp	Val	Leu	Leu	Asn	
		690					695					700				
gca	tct	tg	ttc	aac	tcc	ttc	ctc	aca	cat	gca	ctg	aag	tagt	gtg	ggc	2161
Ala	Ser	Trp	Phe	Asn	Ser	Phe	Leu	Thr	His	Ala	Leu	Lys				
		705					710				715					
aatgctacta	ttt	gttatcc	ata	ctgtcca												2191

<210> SEQ ID NO 12

<211> LENGTH: 716

<212> TYPE: PRT

<213> ORGANISM: Influenza A virus

<400> SEQUENCE: 12

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

-continued

100						105						110					
Lys	Glu	Asn	Arg	Phe	Val	Glu	Ile	Gly	Val	Thr	Arg	Arg	Glu	Val	His		
115						120						125					
Ile	Tyr	Tyr	Leu	Glu	Lys	Ala	Asn	Lys	Ile	Lys	Ser	Glu	Lys	Thr	His		
130						135						140					
Ile	His	Ile	Phe	Ser	Phe	Thr	Gly	Glu	Glu	Met	Ala	Thr	Lys	Ala	Asp		
145						150						155					
Tyr	Thr	Leu	Asp	Glu	Glu	Ser	Arg	Ala	Arg	Ile	Lys	Thr	Arg	Leu	Phe		
165						170						175					
Thr	Ile	Arg	Gln	Glu	Met	Ala	Ser	Arg	Gly	Leu	Trp	Asp	Ser	Phe	Arg		
180						185						190					
Gln	Ser	Glu	Arg	Gly	Glu	Glu	Thr	Ile	Glu	Glu	Arg	Phe	Glu	Ile	Thr		
195						200						205					
Gly	Thr	Met	Arg	Lys	Leu	Ala	Asn	Tyr	Ser	Leu	Pro	Pro	Asn	Phe	Ser		
210						215						220					
Ser	Leu	Glu	Asn	Phe	Arg	Val	Tyr	Ile	Asp	Gly	Phe	Glu	Pro	Asn	Gly		
225						230						235					
Cys	Ile	Glu	Ser	Lys	Leu	Ser	Gln	Met	Ser	Lys	Glu	Val	Asn	Ala	Lys		
245						250						255					
Ile	Glu	Pro	Phe	Ser	Lys	Thr	Thr	Pro	Arg	Pro	Leu	Lys	Met	Pro	Gly		
260						265						270					
Gly	Pro	Pro	Cys	His	Gln	Arg	Ser	Lys	Phe	Leu	Leu	Met	Asp	Ala	Leu		
275						280						285					
Lys	Leu	Ser	Ile	Glu	Asp	Pro	Ser	His	Glu	Gly	Glu	Gly	Ile	Pro	Leu		
290						295						300					
Tyr	Asp	Ala	Ile	Lys	Cys	Met	Lys	Thr	Phe	Phe	Gly	Trp	Lys	Glu	Pro		
305						310						315					
Ser	Ile	Val	Lys	Pro	His	Lys	Lys	Gly	Ile	Asn	Pro	Asn	Tyr	Leu	Gln		
325						330						335					
Thr	Trp	Lys	Gln	Val	Leu	Glu	Glu	Ile	Gln	Asp	Leu	Glu	Asn	Glu	Glu		
340						345						350					
Arg	Thr	Pro	Lys	Thr	Lys	Asn	Met	Lys	Lys	Thr	Ser	Gln	Leu	Lys	Trp		
355						360						365					
Ala	Leu	Gly	Glu	Asn	Met	Ala	Pro	Glu	Lys	Val	Asp	Phe	Glu	Asp	Cys		
370						375						380					
Lys	Asp	Ile	Asn	Asp	Leu	Lys	Gln	Tyr	Asp	Ser	Asp	Glu	Pro	Glu	Ala		
385						390						395					
Arg	Ser	Leu	Ala	Ser	Trp	Ile	Gln	Ser	Glu	Phe	Asn	Lys	Ala	Cys	Glu		
405						410						415					
Leu	Thr	Asp	Ser	Ser	Trp	Ile	Glu	Leu	Asp	Glu	Ile	Gly	Glu	Asp	Val		
420						425						430					
Ala	Pro	Ile	Glu	Tyr	Ile	Ala	Ser	Met	Arg	Arg	Asn	Tyr	Phe	Thr	Ala		
435						440						445					
Glu	Ile	Ser	His	Cys	Arg	Ala	Thr	Glu	Tyr	Ile	Met	Lys	Gly	Val	Tyr		
450						455						460					
Ile	Asn	Thr	Ala	Leu	Leu	Asn	Ala	Ser	Cys	Ala	Ala	Met	Asp	Glu	Phe		
465						470						475					
Gln	Leu	Ile	Pro	Met	Ile	Ser	Lys	Cys	Arg	Thr	Lys	Glu	Gly	Arg	Arg		
485						490						495					
Lys	Thr	Asn	Leu	Tyr	Gly	Phe	Ile	Ile	Lys	Gly	Arg	Ser	His	Leu	Arg		
500						505						510					
Asn	Asp	Thr	Asp	Val	Val	Asn	Phe	Val	Ser	Met	Glu	Phe	Ser	Leu	Thr		
515						520						525					

-continued

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

<210> SEQ ID NO 13
 <211> LENGTH: 2299
 <212> TYPE: DNA
 <213> ORGANISM: Influenza A virus
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (22)..(2292)
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (547)..(547)
 <223> OTHER INFORMATION: Xaa stands for Ala or Val

<400> SEQUENCE: 13

gaaagcaggc aaaccatttg a atg gat gtc aat ccg act cta ctt ttc tta	51
Met Asp Val Asn Pro Thr Leu Leu Phe Leu	
1 5 10	
aag gtg cca gcg caa aat gct ata agc aca aca ttc cct tat act gga	99
Lys Val Pro Ala Gln Asn Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly	
15 20 25	
gat cct ccc tac agt cat gga aca ggg aca gga tac acc atg gat act	147
Asp Pro Pro Tyr Ser His Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr	
30 35 40	
gtc aac aga aca cac caa tat tca gaa aaa ggg aaa tgg aca aca aac	195
Val Asn Arg Thr His Gln Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn	
45 50 55	
act gag att gga gca cca caa ctt aat cca atc gat gga cca ctt cct	243
Thr Glu Ile Gly Ala Pro Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro	
60 65 70	
gaa gac aat gaa cca agt ggg tac gcc caa aca gat tgt gta ttg gaa	291
Glu Asp Asn Glu Pro Ser Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu	
75 80 85 90	
gca atg gct ttc ctt gaa gaa tcc cat ccc gga atc ttt gaa aat tcg	339
Ala Met Ala Phe Leu Glu Glu Ser His Pro Gly Ile Phe Glu Asn Ser	
95 100 105	
tgt ctt gaa acg atg gag gtg att cag cag aca aga gtg gac aaa cta	387

-continued

Cys	Leu	Glu	Thr	Met	Glu	Val	Ile	Gln	Gln	Thr	Arg	Val	Asp	Lys	Leu	
			110					115					120			
aca	caa	ggc	cga	caa	act	tat	gat	tgg	acc	ttg	aat	agg	aat	caa	cct	435
Thr	Gln	Gly	Arg	Gln	Thr	Tyr	Asp	Trp	Thr	Leu	Asn	Arg	Asn	Gln	Pro	
		125					130					135				
gcc	gca	aca	gca	ctt	gct	aat	acg	att	gaa	gta	ttc	aga	tca	aat	ggc	483
Ala	Ala	Thr	Ala	Leu	Ala	Asn	Thr	Ile	Glu	Val	Phe	Arg	Ser	Asn	Gly	
		140					145					150				
ctg	act	tcc	aat	gaa	tgc	ggg	aga	ttg	atg	gac	ttc	ctc	aaa	gat	gtc	531
Leu	Thr	Ser	Asn	Glu	Ser	Gly	Arg	Leu	Met	Asp	Phe	Leu	Lys	Asp	Val	
		155				160				165					170	
atg	gag	tcc	atg	aac	aag	gag	gaa	atg	gaa	ata	aca	aca	cac	ttc	caa	579
Met	Glu	Ser	Met	Asn	Lys	Glu	Glu	Met	Glu	Ile	Thr	Thr	His	Phe	Gln	
				175						180					185	
cgg	aag	aga	aga	gta	aga	gac	aac	atg	aca	aag	aga	atg	ata	aca	cag	627
Arg	Lys	Arg	Arg	Val	Arg	Asp	Asn	Met	Thr	Lys	Arg	Met	Ile	Thr	Gln	
				190				195					200			
aga	acc	ata	ggg	aag	aaa	aaa	caa	cga	tta	agc	aga	aag	agc	tat	cta	675
Arg	Thr	Ile	Gly	Lys	Lys	Lys	Gln	Arg	Leu	Ser	Arg	Lys	Ser	Tyr	Leu	
		205					210						215			
atc	aga	aca	tta	acc	cta	aac	aca	atg	acc	aag	gac	gct	gaa	aga	ggg	723
Ile	Arg	Thr	Leu	Thr	Leu	Asn	Thr	Met	Thr	Lys	Asp	Ala	Glu	Arg	Gly	
		220					225					230				
aaa	ttg	aaa	cga	cga	gca	atc	gct	acc	cca	ggg	atg	cag	ata	aga	gga	771
Lys	Leu	Lys	Arg	Arg	Ala	Ile	Ala	Thr	Pro	Gly	Met	Gln	Ile	Arg	Gly	
		235				240				245					250	
ttt	gta	tat	ttt	gtt	gaa	aca	cta	gct	cga	aga	ata	tgt	gaa	aag	ctt	819
Phe	Val	Tyr	Phe	Glu	Glu	Thr	Leu	Ala	Arg	Arg	Ile	Cys	Glu	Lys	Leu	
				255					260					265		
gaa	caa	tca	gga	ttg	cca	gtt	ggc	ggc	aat	gag	aaa	aag	gcc	aaa	ctg	867
Glu	Gln	Ser	Gly	Leu	Pro	Val	Gly	Gly	Asn	Glu	Lys	Lys	Ala	Lys	Leu	
		270					275						280			
gct	aat	gtc	gtc	aga	aaa	atg	atg	act	aat	tcc	caa	gac	act	gaa	ctc	915
Ala	Asn	Val	Val	Arg	Lys	Met	Met	Thr	Asn	Ser	Gln	Asp	Thr	Glu	Leu	
		285					290					295				
tcc	ttc	acc	atc	act	ggg	gac	aat	acc	aaa	tgg	aat	gaa	aat	cag	aac	963
Ser	Phe	Thr	Ile	Thr	Gly	Asp	Asn	Thr	Lys	Trp	Asn	Glu	Asn	Gln	Asn	
		300				305					310					
cca	cgc	ata	ttc	ctg	gca	atg	atc	aca	tac	ata	act	aga	aat	cag	cca	1011
Pro	Arg	Ile	Phe	Leu	Ala	Met	Ile	Thr	Tyr	Ile	Thr	Arg	Asn	Gln	Pro	
		315				320				325					330	
gaa	tgg	ttc	aga	aat	gtt	cta	agc	att	gca	ccg	att	atg	ttc	tca	aat	1059
Glu	Trp	Phe	Arg	Asn	Val	Leu	Ser	Ile	Ala	Pro	Ile	Met	Phe	Ser	Asn	
				335					340					345		
aaa	atg	gca	aga	ctg	ggg	aaa	gga	tat	atg	ttt	gaa	agc	aaa	agt	atg	1107
Lys	Met	Ala	Arg	Leu	Gly	Lys	Gly	Tyr	Met	Phe	Glu	Ser	Lys	Ser	Met	
			350					355					360			
aaa	ttg	aga	act	caa	ata	cca	gca	gaa	atg	cta	gca	agc	att	gac	cta	1155
Lys	Leu	Arg	Thr	Gln	Ile	Pro	Ala	Glu	Met	Leu	Ala	Ser	Ile	Asp	Leu	
		365					370					375				
aaa	tat	ttc	aat	gat	tca	aca	aaa	aag	aaa	att	gaa	aag	ata	cga	cca	1203
Lys	Tyr	Phe	Asn	Asp	Ser	Thr	Lys	Lys	Lys	Ile	Glu	Lys	Ile	Arg	Pro	
		380				385					390					
ctc	ctg	gtt	gac	ggg	act	gct	tca	ctg	agt	cct	ggc	atg	atg	atg	gga	1251
Leu	Leu	Val	Asp	Gly	Thr	Ala	Ser	Leu	Ser	Pro	Gly	Met	Met	Met	Gly	
		395				400				405					410	
atg	ttc	aac	atg	ttg	agc	act	gtg	ctg	ggc	gta	tcc	ata	tta	aac	ctg	1299
Met	Phe	Asn	Met	Leu	Ser	Thr	Val	Leu	Gly	Val	Ser	Ile	Leu	Asn	Leu	
				415					420					425		
ggc	cag	agg	aaa	tat	aca	aag	acc	aca	tac	tgg	tgg	gat	ggc	ctg	caa	1347

-continued

Gly	Gln	Arg	Lys	Tyr	Thr	Lys	Thr	Thr	Tyr	Trp	Trp	Asp	Gly	Leu	Gln	
			430					435					440			
tca	tcc	gat	gac	ttt	gct	ttg	ata	gtg	aat	gcg	cct	aat	cat	gaa	gga	1395
Ser	Ser	Asp	Asp	Phe	Ala	Leu	Ile	Val	Asn	Ala	Pro	Asn	His	Glu	Gly	
		445					450				455					
ata	caa	gct	gga	gta	gac	aga	ttc	tat	aga	act	tgc	aaa	ctg	gtc	ggg	1443
Ile	Gln	Ala	Gly	Val	Asp	Arg	Phe	Tyr	Arg	Thr	Cys	Lys	Leu	Val	Gly	
	460					465					470					
atc	aac	atg	agc	aaa	aag	aag	tcc	tac	ata	aat	aga	act	gga	aca	ttc	1491
Ile	Asn	Met	Ser	Lys	Lys	Lys	Ser	Tyr	Ile	Asn	Arg	Thr	Gly	Thr	Phe	
	475				480					485				490		
gaa	ttc	aca	agc	ttt	ttc	tac	cgg	tat	ggg	ttt	gta	gcc	aat	ttc	agc	1539
Glu	Phe	Thr	Ser	Phe	Phe	Tyr	Arg	Tyr	Gly	Phe	Val	Ala	Asn	Phe	Ser	
			495					500					505			
atg	gaa	cta	ccc	agt	ttt	ggg	gtt	tcc	gga	ata	aat	gaa	tct	gca	gac	1587
Met	Glu	Leu	Pro	Ser	Phe	Gly	Val	Ser	Gly	Ile	Asn	Glu	Ser	Ala	Asp	
			510					515					520			
atg	agc	att	gga	gtg	aca	gtc	atc	aaa	aac	aac	atg	ata	aat	aat	gat	1635
Met	Ser	Ile	Gly	Val	Thr	Val	Ile	Lys	Asn	Asn	Met	Ile	Asn	Asn	Asp	
		525					530					535				
ctc	ggg	cct	gcc	acg	gca	caa	atg	gya	ctc	caa	ctc	ttc	att	aag	gat	1683
Leu	Gly	Pro	Ala	Thr	Ala	Gln	Met	Xaa	Leu	Gln	Leu	Phe	Ile	Lys	Asp	
	540					545					550					
tat	cgg	tac	aca	tac	cgg	tgc	cat	aga	ggg	gat	acc	cag	ata	caa	acc	1731
Tyr	Arg	Tyr	Thr	Tyr	Arg	Cys	His	Arg	Gly	Asp	Thr	Gln	Ile	Gln	Thr	
	555				560					565					570	
aga	aga	tct	ttt	gag	ttg	aag	aaa	ctg	tgg	gaa	cag	act	cga	tca	aag	1779
Arg	Arg	Ser	Phe	Glu	Leu	Lys	Lys	Leu	Trp	Glu	Gln	Thr	Arg	Ser	Lys	
			575						580				585			
act	ggg	cta	ctg	gta	tca	gat	ggg	ggg	cca	aac	cta	tat	aac	atc	aga	1827
Thr	Gly	Leu	Leu	Val	Ser	Asp	Gly	Gly	Pro	Asn	Leu	Tyr	Asn	Ile	Arg	
		590					595						600			
aac	cta	cac	atc	ccg	gaa	gtc	tgt	tta	aaa	tgg	gag	cta	atg	gat	gaa	1875
Asn	Leu	His	Ile	Pro	Glu	Val	Cys	Leu	Lys	Trp	Glu	Leu	Met	Asp	Glu	
	605					610						615				
gat	tat	aag	ggg	agg	cta	tgc	aat	cca	ttg	aat	cct	ttc	gtt	agt	cac	1923
Asp	Tyr	Lys	Gly	Arg	Leu	Cys	Asn	Pro	Leu	Asn	Pro	Phe	Val	Ser	His	
	620					625					630					
aaa	gaa	att	gaa	tca	gtc	aac	agt	gca	gta	gta	atg	cct	gcg	cat	ggc	1971
Lys	Glu	Ile	Glu	Ser	Val	Asn	Ser	Ala	Val	Val	Met	Pro	Ala	His	Gly	
	635				640				645					650		
cct	gcc	aaa	agc	atg	gag	tat	gat	gct	gtt	gca	aca	aca	cat	tct	tgg	2019
Pro	Ala	Lys	Ser	Met	Glu	Tyr	Asp	Ala	Val	Ala	Thr	Thr	His	Ser	Trp	
			655					660						665		
atc	ccc	aag	agg	aac	cgg	tcc	ata	ttg	aac	aca	agc	caa	agg	gga	ata	2067
Ile	Pro	Lys	Arg	Asn	Arg	Ser	Ile	Leu	Asn	Thr	Ser	Gln	Arg	Gly	Ile	
		670					675						680			
cta	gaa	gat	gag	cag	atg	tat	cag	aaa	tgc	tgc	aac	ctg	ttt	gaa	aaa	2115
Leu	Glu	Asp	Glu	Gln	Met	Tyr	Gln	Lys	Cys	Cys	Asn	Leu	Phe	Glu	Lys	
		685				690						695				
ttc	ttc	ccc	agc	agc	tca	tac	aga	aga	cca	gtc	gga	att	tct	agt	atg	2163
Phe	Phe	Pro	Ser	Ser	Ser	Tyr	Arg	Arg	Pro	Val	Gly	Ile	Ser	Ser	Met	
	700					705					710					
gtt	gag	gcc	atg	gta	tcc	agg	gcc	cgc	att	gat	gca	cga	att	gac	ttc	2211
Val	Glu	Ala	Met	Val	Ser	Arg	Ala	Arg	Ile	Asp	Ala	Arg	Ile	Asp	Phe	
	715				720				725					730		
gaa	tct	gga	cgg	ata	aag	aag	gat	gag	ttc	gct	gag	atc	atg	aag	atc	2259
Glu	Ser	Gly	Arg	Ile	Lys	Lys	Asp	Glu	Phe	Ala	Glu	Ile	Met	Lys	Ile	
			735				740						745			
tgt	tcc	acc	att	gaa	gag	ctc	aga	cgg	caa	aaa	tagtgaa					2299

-continued

Cys Ser Thr Ile Glu Glu Leu Arg Arg Gln Lys
750 755

<210> SEQ ID NO 14
 <211> LENGTH: 757
 <212> TYPE: PRT
 <213> ORGANISM: Influenza A virus
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (547)..(547)
 <223> OTHER INFORMATION: The 'Xaa' at location 547 stands for Ala, or Val.

<400> SEQUENCE: 14

Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn
 1 5 10 15
 Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His
 20 25 30
 Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln
 35 40 45
 Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro
 50 55 60
 Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser
 65 70 75 80
 Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu
 85 90 95
 Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu
 100 105 110
 Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr
 115 120 125
 Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala
 130 135 140
 Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser
 145 150 155 160
 Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys
 165 170 175
 Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg
 180 185 190
 Asp Asn Met Thr Lys Arg Met Ile Thr Gln Arg Thr Ile Gly Lys Lys
 195 200 205
 Lys Gln Arg Leu Ser Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu
 210 215 220
 Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala
 225 230 235 240
 Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu
 245 250 255
 Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro
 260 265 270
 Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys
 275 280 285
 Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly
 290 295 300
 Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala
 305 310 315 320
 Met Ile Thr Tyr Ile Thr Arg Asn Gln Pro Glu Trp Phe Arg Asn Val
 325 330 335
 Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly

340										345					350					
Lys	Gly	Tyr	Met	Phe	Glu	Ser	Lys	Ser	Met	Lys	Leu	Arg	Thr	Gln	Ile					
355							360			365										
Pro	Ala	Glu	Met	Leu	Ala	Ser	Ile	Asp	Leu	Lys	Tyr	Phe	Asn	Asp	Ser					
370							375			380										
Thr	Lys	Lys	Lys	Ile	Glu	Lys	Ile	Arg	Pro	Leu	Leu	Val	Asp	Gly	Thr					
385							390			395					400					
Ala	Ser	Leu	Ser	Pro	Gly	Met	Met	Met	Gly	Met	Phe	Asn	Met	Leu	Ser					
405							410			415										
Thr	Val	Leu	Gly	Val	Ser	Ile	Leu	Asn	Leu	Gly	Gln	Arg	Lys	Tyr	Thr					
420							425			430										
Lys	Thr	Thr	Tyr	Trp	Trp	Asp	Gly	Leu	Gln	Ser	Ser	Asp	Asp	Phe	Ala					
435							440			445										
Leu	Ile	Val	Asn	Ala	Pro	Asn	His	Glu	Gly	Ile	Gln	Ala	Gly	Val	Asp					
450							455			460										
Arg	Phe	Tyr	Arg	Thr	Cys	Lys	Leu	Val	Gly	Ile	Asn	Met	Ser	Lys	Lys					
465							470			475					480					
Lys	Ser	Tyr	Ile	Asn	Arg	Thr	Gly	Thr	Phe	Glu	Phe	Thr	Ser	Phe	Phe					
485							490			495										
Tyr	Arg	Tyr	Gly	Phe	Val	Ala	Asn	Phe	Ser	Met	Glu	Leu	Pro	Ser	Phe					
500							505			510										
Gly	Val	Ser	Gly	Ile	Asn	Glu	Ser	Ala	Asp	Met	Ser	Ile	Gly	Val	Thr					
515							520			525										
Val	Ile	Lys	Asn	Asn	Met	Ile	Asn	Asn	Asp	Leu	Gly	Pro	Ala	Thr	Ala					
530							535			540										
Gln	Met	Xaa	Leu	Gln	Leu	Phe	Ile	Lys	Asp	Tyr	Arg	Tyr	Thr	Tyr	Arg					
545							550			555					560					
Cys	His	Arg	Gly	Asp	Thr	Gln	Ile	Gln	Thr	Arg	Arg	Ser	Phe	Glu	Leu					
565							570			575										
Lys	Lys	Leu	Trp	Glu	Gln	Thr	Arg	Ser	Lys	Thr	Gly	Leu	Leu	Val	Ser					
580							585			590										
Asp	Gly	Gly	Pro	Asn	Leu	Tyr	Asn	Ile	Arg	Asn	Leu	His	Ile	Pro	Glu					
595							600			605										
Val	Cys	Leu	Lys	Trp	Glu	Leu	Met	Asp	Glu	Asp	Tyr	Lys	Gly	Arg	Leu					
610							615			620										
Cys	Asn	Pro	Leu	Asn	Pro	Phe	Val	Ser	His	Lys	Glu	Ile	Glu	Ser	Val					
625							630			635					640					
Asn	Ser	Ala	Val	Val	Met	Pro	Ala	His	Gly	Pro	Ala	Lys	Ser	Met	Glu					
645							650			655										
Tyr	Asp	Ala	Val	Ala	Thr	Thr	His	Ser	Trp	Ile	Pro	Lys	Arg	Asn	Arg					
660							665			670										
Ser	Ile	Leu	Asn	Thr	Ser	Gln	Arg	Gly	Ile	Leu	Glu	Asp	Glu	Gln	Met					
675							680			685										
Tyr	Gln	Lys	Cys	Cys	Asn	Leu	Phe	Glu	Lys	Phe	Phe	Pro	Ser	Ser	Ser					
690							695			700										
Tyr	Arg	Arg	Pro	Val	Gly	Ile	Ser	Ser	Met	Val	Glu	Ala	Met	Val	Ser					
705							710			715					720					
Arg	Ala	Arg	Ile	Asp	Ala	Arg	Ile	Asp	Phe	Glu	Ser	Gly	Arg	Ile	Lys					
725							730			735										
Lys	Asp	Glu	P																	

-continued

```

<210> SEQ ID NO 15
<211> LENGTH: 2370
<212> TYPE: DNA
<213> ORGANISM: Influenza A virus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (42)..(2318)

<400> SEQUENCE: 15

tattggtctc agggagcgaa agcaggtcaa atatattcaa t atg gag aga ata aaa      56
                                         Met Glu Arg Ile Lys
                                         1             5

gaa ctg aga gat ctg atg tta caa tcc cgc acc cgc gag ata cta aca      104
Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr Arg Glu Ile Leu Thr
                        10             15             20

aaa act act gtg gac cac atg gcc ata atc aag aaa tac aca tca gga      152
Lys Thr Thr Val Asp His Met Ala Ile Ile Lys Lys Tyr Thr Ser Gly
                        25             30             35

aga caa gag aag aac cct gca ctt agg atg aaa tgg atg atg gca atg      200
Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys Trp Met Met Ala Met
                        40             45             50

aaa tac cca att aca gca gat aag agg ata atg gag atg att cct gag      248
Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met Glu Met Ile Pro Glu
                        55             60             65

aga aat gaa cag gga caa acc ctt tgg agc aaa acg aac gat gct ggc      296
Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys Thr Asn Asp Ala Gly
                        70             75             80             85

tca gac cgc gta atg gta tca cct ctg gca gtg aca tgg tgg aat agg      344
Ser Asp Arg Val Met Val Ser Pro Leu Ala Val Thr Trp Trp Asn Arg
                        90             95             100

aat gga cca aca acg aac aca att cat tat ccg aaa gtc tac aaa act      392
Asn Gly Pro Thr Thr Asn Thr Ile His Tyr Pro Lys Val Tyr Lys Thr
                        105             110             115

tat ttt gaa aag gtt gaa aga ttg aaa cac gga acc ttt ggc ccc gtt      440
Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly Thr Phe Gly Pro Val
                        120             125             130

cat ttt agg aat caa gtc aag ata aga cga aga gtt gat gta aac cct      488
His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg Val Asp Val Asn Pro
                        135             140             145

ggg cac gcg gac ctc agt gct aaa gaa gca caa gat gtg atc atg gaa      536
Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln Asp Val Ile Met Glu
                        150             155             160             165

gtt gtt ttc cca aat gaa gtg gga gcc aga att cta aca tca gaa tca      584
Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile Leu Thr Ser Glu Ser
                        170             175             180

caa cta aca ata acc aaa gag aaa aag gaa gaa ctt cag gac tgc aaa      632
Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu Leu Gln Asp Cys Lys
                        185             190             195

att gct ccc ttg atg gta gca tac atg cta gaa aga gag ttg gtc cga      680
Ile Ala Pro Leu Met Val Ala Tyr Met Leu Glu Arg Glu Leu Val Arg
                        200             205             210

aaa aca agg ttc ctc cca gta gta ggc gga aca agc agt gta tac att      728
Lys Thr Arg Phe Leu Pro Val Val Gly Gly Thr Ser Ser Val Tyr Ile
                        215             220             225

gaa gtg ttg cat ctg act cag gga aca tgc tgg gag caa atg tac acc      776
Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp Glu Gln Met Tyr Thr
                        230             235             240             245

cca gga gga gaa gtt aga aac gat gat att gat caa agt tta att att      824
Pro Gly Gly Glu Val Arg Asn Asp Asp Ile Asp Gln Ser Leu Ile Ile
                        250             255             260

gca gcc cgg aac ata gtg aga aga gca aca gta tca gca gat cca cta      872

```

-continued

Ala	Ala	Arg	Asn	Ile	Val	Arg	Arg	Ala	Thr	Val	Ser	Ala	Asp	Pro	Leu	
			265					270					275			
gca	tcc	cta	ctg	gaa	atg	tgc	cac	agt	aca	cag	att	ggg	gga	aca	agg	920
Ala	Ser	Leu	Leu	Glu	Met	Cys	His	Ser	Thr	Gln	Ile	Gly	Gly	Thr	Arg	
		280					285					290				
atg	gta	gac	atc	ctt	aag	cag	aac	cca	aca	gag	gaa	caa	gct	gtg	gat	968
Met	Val	Asp	Ile	Leu	Lys	Gln	Asn	Pro	Thr	Glu	Glu	Gln	Ala	Val	Asp	
		295				300					305					
ata	tgc	aaa	gca	gca	atg	gga	ttg	aga	att	agc	tca	tca	ttc	agc	ttt	1016
Ile	Cys	Lys	Ala	Ala	Met	Gly	Leu	Arg	Ile	Ser	Ser	Ser	Phe	Ser	Phe	
310					315				320					325		
ggg	gga	ttc	acc	ttc	aaa	agg	aca	agt	gga	tca	tca	gtc	aag	aga	gaa	1064
Gly	Gly	Phe	Thr	Phe	Lys	Arg	Thr	Ser	Gly	Ser	Ser	Val	Lys	Arg	Glu	
			330					335					340			
gaa	gaa	atg	ctt	acg	ggc	aac	ctt	caa	aca	ttg	aaa	ata	aga	gtg	cat	1112
Glu	Glu	Met	Leu	Thr	Gly	Asn	Leu	Gln	Thr	Leu	Lys	Ile	Arg	Val	His	
			345				350					355				
gag	ggc	tat	gaa	gaa	ttc	aca	atg	gtc	gga	aga	aga	gca	aca	gcc	att	1160
Glu	Gly	Tyr	Glu	Glu	Phe	Thr	Met	Val	Gly	Arg	Arg	Ala	Thr	Ala	Ile	
		360				365						370				
atc	aga	aag	gca	acc	aga	aga	ttg	att	caa	ttg	ata	gta	agt	ggg	aga	1208
Ile	Arg	Lys	Ala	Thr	Arg	Arg	Leu	Ile	Gln	Leu	Ile	Val	Ser	Gly	Arg	
		375			380				385							
gat	gaa	caa	tca	att	gct	gaa	gca	ata	att	gta	gcc	atg	gtg	ttt	tcg	1256
Asp	Glu	Gln	Ser	Ile	Ala	Glu	Ala	Ile	Ile	Val	Ala	Met	Val	Phe	Ser	
390					395				400					405		
caa	gaa	gat	tgc	atg	ata	aaa	gca	gtt	cga	ggc	gat	ttg	aac	ttt	gtt	1304
Gln	Glu	Asp	Cys	Met	Ile	Lys	Ala	Val	Arg	Gly	Asp	Leu	Asn	Phe	Val	
			410					415				420				
aat	aga	gca	aat	cag	cgt	ttg	aac	ccc	atg	cat	caa	ctc	ttg	agg	cat	1352
Asn	Arg	Ala	Asn	Gln	Arg	Leu	Asn	Pro	Met	His	Gln	Leu	Leu	Arg	His	
		425					430					435				
ttc	caa	aaa	gat	gca	aaa	gtg	ctt	ttc	caa	aat	tgg	gga	att	gaa	ccc	1400
Phe	Gln	Lys	Asp	Ala	Lys	Val	Leu	Phe	Gln	Asn	Trp	Gly	Ile	Glu	Pro	
		440				445					450					
atc	gac	aat	gta	atg	ggg	atg	att	gga	ata	ttg	cct	gac	atg	acc	cca	1448
Ile	Asp	Asn	Val	Met	Gly	Met	Ile	Gly	Ile	Leu	Pro	Asp	Met	Thr	Pro	
		455				460					465					
agc	acc	gag	atg	tca	ttg	aga	gga	gtg	aga	gtc	agc	aaa	atg	gga	gtg	1496
Ser	Thr	Glu	Met	Ser	Leu	Arg	Gly	Val	Arg	Val	Ser	Lys	Met	Gly	Val	
470					475				480					485		
gat	gag	tac	tcc	agc	act	gag	aga	gtg	gtg	gtg	agc	att	gac	cgt	ttt	1544
Asp	Glu	Tyr	Ser	Ser	Thr	Glu	Arg	Val	Val	Val	Ser	Ile	Asp	Arg	Phe	
			490					495						500		
tta	aga	gtt	cgg	gat	caa	agg	gga	aac	ata	cta	ctg	tcc	cct	gaa	gaa	1592
Leu	Arg	Val	Arg	Asp	Gln	Arg	Gly	Asn	Ile	Leu	Leu	Ser	Pro	Glu	Glu	
			505					510					515			
gtc	agt	gaa	aca	caa	gga	acg	gaa	aag	ctg	aca	ata	att	tat	tcg	tca	1640
Val	Ser	Glu	Thr	Gln	Gly	Thr	Glu	Lys	Leu	Thr	Ile	Ile	Tyr	Ser	Ser	
		520				525						530				
tca	atg	atg	tggt	gag	att	aat	ggg	ccc	gaa	tca	gtg	ttg	gtc	aat	act	1688
Ser	Met	Met	Trp	Glu	Ile	Asn	Gly	Pro	Glu	Ser	Val	Leu	Val	Asn	Thr	
		535			540						545					
tat	caa	tggt	atc	atc	aga	aac	tggt	gaa	att	gta	aaa	att	cag	tggt	tca	1736
Tyr	Gln	Trp	Ile	Ile	Arg	Asn	Trp	Glu	Ile	Val	Lys	Ile	Gln	Trp	Ser	
550					555				560					565		
cag	gac	ccc	aca	atg	tta	tac	aat	aag	ata	gaa	ttt	gaa	cca	ttc	caa	1784
Gln	Asp	Pro	Thr	Met	Leu	Tyr	Asn	Lys	Ile	Glu	Phe	Glu	Pro	Phe	Gln	
			570					575					580			
tcc	ctg	gtc	cct	agg	gcc	acc	aga	agc	caa	tac	agc	ggg	ttc	gta	aga	1832

-continued

Ser	Leu	Val	Pro	Arg	Ala	Thr	Arg	Ser	Gln	Tyr	Ser	Gly	Phe	Val	Arg		
			585					590					595				
acc	ctg	ttt	cag	caa	atg	cga	gat	gta	ctt	gga	aca	ttt	gat	act	gct		1880
Thr	Leu	Phe	Gln	Gln	Met	Arg	Asp	Val	Leu	Gly	Thr	Phe	Asp	Thr	Ala		
	600						605					610					
caa	ata	ata	aaa	ctc	ctc	cct	ttt	gcc	gct	gct	cct	ccg	gaa	cag	agt		1928
Gln	Ile	Ile	Lys	Leu	Leu	Pro	Phe	Ala	Ala	Ala	Pro	Pro	Glu	Gln	Ser		
	615					620					625						
agg	atg	cag	ttc	tct	tct	ttg	act	gtt	aat	gta	aga	ggg	tcg	gga	atg		1976
Arg	Met	Gln	Phe	Ser	Ser	Leu	Thr	Val	Asn	Val	Arg	Gly	Ser	Gly	Met		
	630				635				640					645			
agg	ata	ctt	gta	aga	ggc	aat	tcc	ccg	gtg	ttc	aac	tac	aat	aaa	gtc		2024
Arg	Ile	Leu	Val	Arg	Gly	Asn	Ser	Pro	Val	Phe	Asn	Tyr	Asn	Lys	Val		
				650				655						660			
act	aaa	agg	ctc	aca	gtc	ctc	gga	aag	gat	gca	ggg	gcg	ctt	act	gag		2072
Thr	Lys	Arg	Leu	Thr	Val	Leu	Gly	Lys	Asp	Ala	Gly	Ala	Leu	Thr	Glu		
			665				670					675					
gac	cca	gat	gaa	ggg	acg	gct	gga	gta	gaa	tct	gct	gtt	cta	aga	ggg		2120
Asp	Pro	Asp	Glu	Gly	Thr	Ala	Gly	Val	Glu	Ser	Ala	Val	Leu	Arg	Gly		
		680				685						690					
ttt	ctc	att	tta	ggg	aaa	gaa	aac	aag	aga	tat	ggc	cca	gca	cta	agc		2168
Phe	Leu	Ile	Leu	Gly	Lys	Glu	Asn	Lys	Arg	Tyr	Gly	Pro	Ala	Leu	Ser		
	695				700				705								
atc	aat	gaa	ctt	agc	aaa	ctt	gca	aaa	ggg	gag	aaa	gcc	aat	gta	cta		2216
Ile	Asn	Glu	Leu	Ser	Lys	Leu	Ala	Lys	Gly	Glu	Lys	Ala	Asn	Val	Leu		
	710				715				720					725			
att	ggg	caa	ggg	gac	gta	gtg	ttg	gta	atg	aaa	cgg	aaa	cgt	gac	tct		2264
Ile	Gly	Gln	Gly	Asp	Val	Val	Leu	Val	Met	Lys	Arg	Lys	Arg	Asp	Ser		
				730				735						740			
agc	ata	ctt	act	gac	agc	cag	aca	gcg	acc	aaa	agg	att	cgg	atg	gcc		2312
Ser	Ile	Leu	Thr	Asp	Ser	Gln	Thr	Ala	Thr	Lys	Arg	Ile	Arg	Met	Ala		
			745				750						755				
atc	aat	tagtg	ttgaa	ttgttta	aaaa	acgac	cttgt	ttctact	aat	acgag	accat	at					2370
Ile	Asn																

<210> SEQ ID NO 16

<211> LENGTH: 759

<212> TYPE: PRT

<213> ORGANISM: Influenza A virus

<400> SEQUENCE: 16

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

-continued

Val	Asp	Val	Asn	Pro	Gly	His	Ala	Asp	Leu	Ser	Ala	Lys	Glu	Ala	Gln	145	150	155	160
Asp	Val	Ile	Met	Glu	Val	Val	Phe	Pro	Asn	Glu	Val	Gly	Ala	Arg	Ile	165	170	175	
Leu	Thr	Ser	Glu	Ser	Gln	Leu	Thr	Ile	Thr	Lys	Glu	Lys	Lys	Glu	Glu	180	185	190	
Leu	Gln	Asp	Cys	Lys	Ile	Ala	Pro	Leu	Met	Val	Ala	Tyr	Met	Leu	Glu	195	200	205	
Arg	Glu	Leu	Val	Arg	Lys	Thr	Arg	Phe	Leu	Pro	Val	Val	Gly	Gly	Thr	210	215	220	
Ser	Ser	Val	Tyr	Ile	Glu	Val	Leu	His	Leu	Thr	Gln	Gly	Thr	Cys	Trp	225	230	235	240
Glu	Gln	Met	Tyr	Thr	Pro	Gly	Gly	Glu	Val	Arg	Asn	Asp	Asp	Ile	Asp	245	250	255	
Gln	Ser	Leu	Ile	Ile	Ala	Ala	Arg	Asn	Ile	Val	Arg	Arg	Ala	Thr	Val	260	265	270	
Ser	Ala	Asp	Pro	Leu	Ala	Ser	Leu	Leu	Glu	Met	Cys	His	Ser	Thr	Gln	275	280	285	
Ile	Gly	Gly	Thr	Arg	Met	Val	Asp	Ile	Leu	Lys	Gln	Asn	Pro	Thr	Glu	290	295	300	
Glu	Gln	Ala	Val	Asp	Ile	Cys	Lys	Ala	Ala	Met	Gly	Leu	Arg	Ile	Ser	305	310	315	320
Ser	Ser	Phe	Ser	Phe	Gly	Gly	Phe	Thr	Phe	Lys	Arg	Thr	Ser	Gly	Ser	325	330	335	
Ser	Val	Lys	Arg	Glu	Glu	Glu	Met	Leu	Thr	Gly	Asn	Leu	Gln	Thr	Leu	340	345	350	
Lys	Ile	Arg	Val	His	Glu	Gly	Tyr	Glu	Glu	Phe	Thr	Met	Val	Gly	Arg	355	360	365	
Arg	Ala	Thr	Ala	Ile	Ile	Arg	Lys	Ala	Thr	Arg	Arg	Leu	Ile	Gln	Leu	370	375	380	
Ile	Val	Ser	Gly	Arg	Asp	Glu	Gln	Ser	Ile	Ala	Glu	Ala	Ile	Ile	Val	385	390	395	400
Ala	Met	Val	Phe	Ser	Gln	Glu	Asp	Cys	Met	Ile	Lys	Ala	Val	Arg	Gly	405	410	415	
Asp	Leu	Asn	Phe	Val	Asn	Arg	Ala	Asn	Gln	Arg	Leu	Asn	Pro	Met	His	420	425	430	
Gln	Leu	Leu	Arg	His	Phe	Gln	Lys	Asp	Ala	Lys	Val	Leu	Phe	Gln	Asn	435	440	445	
Trp	Gly	Ile	Glu	Pro	Ile	Asp	Asn	Val	Met	Gly	Met	Ile	Gly	Ile	Leu	450	455	460	
Pro	Asp	Met	Thr	Pro	Ser	Thr	Glu	Met	Ser	Leu	Arg	Gly	Val	Arg	Val	465	470	475	480
Ser	Lys	Met	Gly	Val	Asp	Glu	Tyr	Ser	Ser	Thr	Glu	Arg	Val	Val	Val	485	490	495	
Ser	Ile	Asp	Arg	Phe	Leu	Arg	Val	Arg	Asp	Gln	Arg	Gly	Asn	Ile	Leu	500	505	510	
Leu	Ser	Pro	Glu	Glu	Val	Ser	Glu	Thr	Gln	Gly	Thr	Glu	Lys	Leu	Thr	515	520	525	
Ile	Ile	Tyr	Ser	Ser	Ser	Met	Met	Trp	Glu	Ile	Asn	Gly	Pro	Glu	Ser	530	535	540	
Val	Leu	Val	Asn	Thr	Tyr	Gln	Trp	Ile	Ile	Arg	Asn	Trp	Glu	Ile	Val	545	550	555	560
Lys	Ile	Gln	Trp	Ser	Gln	Asp	Pro	Thr	Met	Leu	Tyr	Asn	Lys	Ile	Glu				

-continued

565								570					575				
Phe	Glu	Pro	Phe	Gln	Ser	Leu	Val	Pro	Arg	Ala	Thr	Arg	Ser	Gln	Tyr		
580								585					590				
Ser	Gly	Phe	Val	Arg	Thr	Leu	Phe	Gln	Gln	Met	Arg	Asp	Val	Leu	Gly		
595								600					605				
Thr	Phe	Asp	Thr	Ala	Gln	Ile	Ile	Lys	Leu	Leu	Pro	Phe	Ala	Ala	Ala		
610								615					620				
Pro	Pro	Glu	Gln	Ser	Arg	Met	Gln	Phe	Ser	Ser	Leu	Thr	Val	Asn	Val		
625								630					635				
Arg	Gly	Ser	Gly	Met	Arg	Ile	Leu	Val	Arg	Gly	Asn	Ser	Pro	Val	Phe		
645								650					655				
Asn	Tyr	Asn	Lys	Val	Thr	Lys	Arg	Leu	Thr	Val	Leu	Gly	Lys	Asp	Ala		
660								665					670				
Gly	Ala	Leu	Thr	Glu	Asp	Pro	Asp	Glu	Gly	Thr	Ala	Gly	Val	Glu	Ser		
675								680					685				
Ala	Val	Leu	Arg	Gly	Phe	Leu	Ile	Leu	Gly	Lys	Glu	Asn	Lys	Arg	Tyr		
690								695					700				
Gly	Pro	Ala	Leu	Ser	Ile	Asn	Glu	Leu	Ser	Lys	Leu	Ala	Lys	Gly	Glu		
705								710					715				
Lys	Ala	Asn	Val	Leu	Ile	Gly	Gln	Gly	Asp	Val	Val	Leu	Val	Met	Lys		
725								730					735				
Arg	Lys	Arg	Asp	Ser	Ser	Ile	Leu	Thr	Asp	Ser	Gln	Thr	Ala	Thr	Lys		
740								745					750				
Arg	Ile	Arg	Met	Ala	Ile	Asn											
755																	

What is claimed is:

1. An isolated or purified *Hemagglutinin* HA, which (i) has the amino acid sequence of SEQ ID NO: 4 or (ii) is derived from an influenza virus and which has an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4, [with the proviso that the amino acid sequence is identical to that of SEQ ID NO: 4 at amino acid positions 94 and 233] and the isolated or purified HA has a leucine at position 94 and a glutamic acid at position 233, according to the numbering of SEQ ID NO: 4.

2. A composition comprising the isolated or purified HA of claim 1 in an amount sufficient to induce an immune response in an animal and a biologically acceptable carrier.

3. A method of inducing an immune response to a canine influenza H3 virus in an animal, which method comprises administering to the animal the composition of claim 2, [whereupon] where upon an immune response to canine influenza H3 virus is induced in the animal.

4. [An] A vector comprising the isolated or purified nucleic acid encoding the HA of claim 1, optionally as part of a vector].

5. [The isolated or purified nucleic acid] The vector of claim 4, wherein the nucleic acid encoding the HA comprises the nucleotide sequence of SEQ ID NO: 3.

6. A composition comprising the [isolated or purified nucleic acid] vector of claim 4, which expresses HA in an amount sufficient to induce an immune response in an animal, and a biologically acceptable carrier.

7. An isolated or purified HA peptide fragment comprising a contiguous nine amino acid fragment of [SEQ ID NO: 4, or a contiguous nine amino acid fragment of] an amino acid sequence that is greater than 99% identical to SEQ ID NO: 4,

that either includes the Leu at position 94 of SEQ ID NO: 4 or the Glu at position 233 of SEQ ID NO: 4, according to the numbering of SEQ ID NO: 4.

8. A composition comprising the isolated or purified HA peptide fragment of claim 7 in an amount sufficient to induce an immune response in an animal and a biologically acceptable carrier.

9. A method of inducing an immune response to a canine influenza H3 virus in an animal, which method comprises administering to the animal the composition of claim 8, [whereupon] where upon an immune response to canine influenza H3 virus is induced in the animal.

10. [An] A vector comprising an isolated or purified nucleic acid encoding the HA peptide fragment of claim 7, optionally as part of a vector].

11. A composition comprising the [isolated or purified nucleic acid] vector of claim 10, which expresses the HA peptide in an amount sufficient to induce an immune response in an animal, and a biologically acceptable carrier.

12. An isolated polypeptide that is 97% or greater identical to SEQ ID NO: 4 and has a leucine at position 94 and a glutamic acid at position 233, according to the numbering of SEQ ID NO: 4 and a biologically acceptable carrier.

13. An isolated DNA which encodes a polypeptide that is 97% or greater identical to SEQ ID NO: 4 and has a leucine at position 94 and a glutamic acid at position 233 according to the numbering of SEQ ID NO: 4.

14. An isolated polypeptide comprising a contiguous nine amino acid sequence that is greater than 97% identical to a sequence fragment of SEQ ID NO: 4, wherein said sequence fragment comprises either the Leu at position 94 or the Glu at position 233 of SEQ ID NO: 4, according to the numbering of SEQ ID NO: 4.

15. A method of inducing an immune response to a canine influenza H3 virus in an animal, which method comprises administering to the animal the composition of claim 4 or claim 12, where upon an immune response to a canine influenza H3 virus is induced in the animal.

5

* * * * *