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(54) Title: MATERIALS AND METHODS FOR RESPIRATORY DISEASE CONTROL IN CANINES

(57) Abstract: The subject invention pertains to isolated influenza virus that is capable of infecting canids and causing respiratory disease in the canid. The subject invention also pertains to compositions and methods for inducing an immune response against an influenza virus of the present invention. The subject invention also pertains to compositions and methods for identifying a virus of the invention and diagnosing infection of an animal with a virus of the invention.

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DESCRIPTION

MATERIALS AND METHODS FOR RESPIRATORY DISEASE
CONTROL IN CANINES

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CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application Serial No. 60/673,443, filed April 21, 2005, which is hereby incorporated by reference herein in its entirety, including any figures, tables, nucleic acid sequences, amino acid sequences, and drawings.

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BACKGROUND OF THE INVENTION

“Kennel cough” or infectious tracheobronchitis (ITB) is an acute, contagious respiratory infection in dogs characterized mainly by coughing (Ford *et al*, 1998). Canine ITB is considered one of the most prevalent infectious respiratory diseases of dogs worldwide, and outbreaks can reach epidemic proportions when dogs are housed in high-density population environments such as kennels. Most outbreaks are due to direct dog-to-dog contact or aerosolization of respiratory secretions (Ford *et al*, 1998). The clinical signs are caused by infection with one or a combination of bacterial and viral agents that colonize the epithelium of the upper and lower respiratory tract. Canine parainfluenza virus (CPiV) and *Bordetella bronchiseptica* bacteria are the most common organisms isolated from affected dogs, but several other viruses such as canine distemper virus (CDV) and canine adenoviruses-1 and -2 (CAV-1, CAV-2), along with bacteria such as *Streptococcus sp.*, *Pasteurella multocida* and *Escherichia coli*, can influence the clinical course and outcome (Ford *et al*, 1998). While outbreaks occur most efficiently and rapidly in high-density populations with high morbidity, complicated respiratory infections and death are uncommon. Although life-threatening secondary bacterial pneumonia can develop, the majority of ITB cases are self-limiting and resolve without any treatment (Ford *et al*, 1998).

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In July 1992, a respiratory infection presumed to be “kennel cough” became epidemic at several greyhound tracks in New England, Florida, West Virginia, Wisconsin, Kansas, Colorado, Oklahoma and Arizona. According to veterinarians, most of the affected dogs had a mild cough that resolved, but more than a dozen greyhounds developed an acute hemorrhagic pneumonia followed by rapid death (Greyhound Daily News, 1999).

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In late 1998 to early 1999, several outbreaks of “kennel cough” occurred in racing greyhound kennels across the country, resulting in mandatory closure of tracks and quarantine of all racing greyhounds in the U.S. for several weeks (Greyhound Daily News, 1999). At one track in Florida (Palm Beach Kennel Club), coughing was recorded in nearly 40% of the dog population on a single day (Personal communication from Dr. William Duggar). Similar to the outbreak in 1992, the coughing resolved in most greyhounds, but 10 dogs in Florida died from a hemorrhagic pneumonia syndrome uncharacteristic of “kennel cough” (Putnam, 1999).

In March-April 2003, another outbreak of “kennel cough” occurred at greyhound tracks in the eastern U.S. The outbreak is believed to have originated in kennels at four tracks in Florida and caused the suspension of racing and quarantine of dogs for almost three weeks. Nearly 25% of the dogs at the track in West Palm Beach were affected, while almost 50% of the 1400 dogs at Derby Lane in St. Petersburg developed coughing. Again, most dogs recovered, but several dogs have died from the respiratory infection. The estimated economic impact of the respiratory outbreak at the Derby Lane track alone was \$2 million.

There are no published reports documenting the etiology or clinicopathology of the “kennel cough” epidemics in racing greyhound kennels in 1992, 1998-1999, or 2003. The assumption has been that the infections were due to CPiV and/or *B. bronchiseptica*, the two most common causes of kennel cough. Unsubstantiated communications such as web sites have attributed the fatal hemorrhagic pneumonias reported in some of the coughing dogs to infection with β -hemolytic *Streptococcus equi* subspecies *zooepidemicus*, and refer to the syndrome as “canine streptococcal toxic shock.”

Transmission of virus from one host species to another is a crucial feature of the ecology and epidemiology of influenza virus (Webster, 1998). Two basic mechanisms of interspecies transmission of influenza virus are possible (Webster *et al.*, 1992; Lipatov *et al.*, 2004). One is the direct transfer of an essentially unaltered virus from one species to another. Examples of this mechanism include the recent human infections with the H5N1 subtype of avian influenza virus (Subbarao *et al.*, 1998; Peiris *et al.*, 2004; Guan *et al.*, 2004) and possibly the pandemic of 1918, known as Spanish flu (Reid *et al.*, 2004). The second mechanism is a consequence of the segmented nature of the influenza genome. Co-infection of a host with viruses from different species can result in reassortment of the segmented viral genes and the generation of a recombinant with the ability to infect other species. For example, novel viruses generated by gene reassortment between avian and human influenza

viruses resulted in human influenza pandemics in 1957 and 1968 (Webster *et al.*, 1992; Lipatov *et al.*, 2004; Kawaoka *et al.*, 1989).

Most direct transmissions of unaltered influenza viruses from the natural host species to a different species are terminal events because sustained transmission between individuals of the new species fails to occur. Multiple virus-host interactions are necessary for replication and horizontal transmission and provide a formidable barrier to perpetuation of influenza viruses in the new host (Webster *et al.*, 2004). Therefore, establishment of new host-specific lineages of influenza virus is uncommon and has only occurred in domestic poultry, pigs, horses, and humans (Webster *et al.*, 1992; Lipatov *et al.*, 2004).

Because of the serious nature of influenza virus infection, there remains a need for methods for diagnosing, preventing, and treating infection by influenza virus.

BRIEF SUMMARY OF THE INVENTION

The subject invention pertains to isolated influenza virus that is capable of infecting canids and causing respiratory disease in the canid. The subject invention also pertains to compositions and methods for inducing an immune response against an influenza virus of the present invention. The subject invention also pertains to compositions and methods for identifying a virus of the invention and diagnosing infection of an animal with a virus of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the Patent Office upon request and payment of the necessary fee.

Figures 1A-1B show phylogenetic relationships among the hemagglutinin genes. **Figure 1A** shows a tree of HA genes from representative canine, human, avian, swine, and equine isolates, including A/Budgerigar/Hokkaido/1/77 (H4) as outgroup. **Figure 1B** shows a tree of the canine influenza virus HA genes with contemporary and older equine HA genes, using A/Duck/Ukraine/63 (H3) as outgroup. Phylogenetic trees were inferred from nucleotide sequences by the neighbor joining method and bootstrap analysis values $\geq 90\%$ are shown. The bar denotes the number of nucleotide changes per unit length of the horizontal tree branches.

Figures 2A-2B show immunohistochemical detection of influenza H3 antigen in the lungs. Lung tissue sections were probed with a mouse monoclonal antibody to H3 hemagglutinin and binding was detected by immunoperoxidase reaction (brown precipitate). **Figure 2A** shows bronchial epithelium from a greyhound with spontaneous disease. Viral H3 antigen was detected in bronchial epithelial cell cytoplasm and in macrophages in airway lumens and in alveolar spaces. **Figure 2B** shows bronchial epithelium from a dog 5 days after inoculation with A/canine/Florida/43/04 (H3N8). Viral H3 antigen was detected in bronchial epithelial cell cytoplasm. Scale bar, 66 μ m.

Figure 3 shows the characteristic histological changes in the bronchi of greyhounds that died from hemorrhagic pneumonia associated with influenza virus infection. The tissues are stained with H&E. Upper panel: Normal bronchus with ciliated epithelial cells, mucous cells, and basal cells. Lower panel: Bronchus from a greyhound with spontaneous influenza. There is necrosis and erosion of the bronchial ciliated epithelial cells. Scale bar, 100 μ m.

Figures 4A-4B shows phylogenetic relationships among the H3 hemagglutinin genes. **Figure 4A** shows a phylogenetic tree of the canine influenza virus HA genes with contemporary and older equine HA genes. **Figure 4B** shows a phylogenetic tree of the canine influenza virus HA protein with contemporary and older equine HA. Phylogenetic trees were inferred from genetic or amino acid sequences by the neighbor joining method and bootstrap analysis values $\geq 80\%$ are shown. The bar denotes the number of amino acid changes per unit length of the horizontal tree branches.

Figure 5 shows Influenza virus H3 protein in epithelial cells of bronchi and bronchial glands in lungs of dogs that died of pneumonia associated with influenza virus infection. Upper panels: Erosion of ciliated bronchial epithelial cells in bronchi. Tissues were stained with H&E. Lower panels: Influenza virus H3 protein in the cytoplasm of bronchial (left) and bronchial gland (right) epithelial cells. Tissues were stained with a monoclonal antibody to influenza H3 detected by immunoperoxidase reaction (brown precipitate) and counterstained with hematoxylin.

Figures 6A-6D show amplification plots of H3 and Matrix genes (**Figure 6A** and **Figure 6B**) obtained from the amplification of 10-fold serially diluted *in vitro* transcribed RNA standards. Standard curves of H3 and Matrix genes (**Figure 6C** and **Figure 6D**) constructed by plotting the log of starting RNA concentrations against the threshold cycle (Ct) obtained from each dilution.

Figure 7 shows sensitivity of Directigen Flu A was tested with 10-fold serially diluted virus stocks including A/Wyoming/3/2003 and A/canine/FL/242/2003. The purple triangle indicates positive result.

5 BRIEF DESCRIPTION OF THE SEQUENCES

SEQ ID NO: 1 is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding a PB2 protein that can be used according to the present invention.

SEQ ID NO: 2 is the amino acid sequence encoded by SEQ ID NO: 1.

10 **SEQ ID NO: 3** is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding a PB1 protein that can be used according to the present invention.

SEQ ID NO: 4 is the amino acid sequence encoded by SEQ ID NO: 3.

SEQ ID NO: 5 is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding a PA protein that can be used according to the present invention.

SEQ ID NO: 6 is the amino acid sequence encoded by SEQ ID NO: 5.

15 **SEQ ID NO: 7** is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding an NS protein that can be used according to the present invention.

SEQ ID NO: 8 is the amino acid sequence encoded by SEQ ID NO: 7.

SEQ ID NO: 9 is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding an NP protein that can be used according to the present invention.

20 **SEQ ID NO: 10** is the amino acid sequence encoded by SEQ ID NO: 9.

SEQ ID NO: 11 is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding an NA protein that can be used according to the present invention.

SEQ ID NO: 12 is the amino acid sequence encoded by SEQ ID NO: 11.

25 **SEQ ID NO: 13** is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding an MA protein that can be used according to the present invention.

SEQ ID NO: 14 is the amino acid sequence encoded by SEQ ID NO: 13.

SEQ ID NO: 15 is a nucleotide sequence of a canine influenza virus (Florida/43/04) encoding an HA protein that can be used according to the present invention.

SEQ ID NO: 16 is the amino acid sequence encoded by SEQ ID NO: 15.

30 **SEQ ID NO: 17** is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding a PB2 protein that can be used according to the present invention.

SEQ ID NO: 18 is the amino acid sequence encoded by SEQ ID NO: 17.

SEQ ID NO: 19 is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding a PB1 protein that can be used according to the present invention.

SEQ ID NO: 20 is the amino acid sequence encoded by SEQ ID NO: 19.

5 **SEQ ID NO: 21** is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding a PA protein that can be used according to the present invention.

SEQ ID NO: 22 is the amino acid sequence encoded by SEQ ID NO: 21.

SEQ ID NO: 23 is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding an NS protein that can be used according to the present invention.

SEQ ID NO: 24 is the amino acid sequence encoded by SEQ ID NO: 23.

10 **SEQ ID NO: 25** is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding an NP protein that can be used according to the present invention.

SEQ ID NO: 26 is the amino acid sequence encoded by SEQ ID NO: 25.

SEQ ID NO: 27 is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding an NA protein that can be used according to the present invention.

15 **SEQ ID NO: 28** is the amino acid sequence encoded by SEQ ID NO: 27.

SEQ ID NO: 29 is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding an MA protein that can be used according to the present invention.

SEQ ID NO: 30 is the amino acid sequence encoded by SEQ ID NO: 29.

20 **SEQ ID NO: 31** is a nucleotide sequence of a canine influenza virus (FL/242/03) encoding an HA protein that can be used according to the present invention.

SEQ ID NO: 32 is the amino acid sequence encoded by SEQ ID NO: 31.

SEQ ID NO: 33 is the mature form of the HA protein shown in SEQ ID NO: 16 wherein the N-terminal 16 amino acid signal sequence has been removed.

25 **SEQ ID NO: 34** is the mature form of the HA protein shown in SEQ ID NO: 32 wherein the N-terminal 16 amino acid signal sequence has been removed.

SEQ ID NO: 35 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 36 is an oligonucleotide that can be used according to the present invention.

30 **SEQ ID NO: 37** is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 38 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 39 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 41 is an oligonucleotide that can be used according to the present invention.

5 **SEQ ID NO: 42** is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 43 is an oligonucleotide that can be used according to the present invention.

10 **SEQ ID NO: 44** is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 45 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 46 is an oligonucleotide that can be used according to the present invention.

15 **SEQ ID NO: 47** is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding a PB2 protein that can be used according to the present invention.

SEQ ID NO: 48 is the amino acid sequence encoded by SEQ ID NO: 47.

SEQ ID NO: 49 is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding a PB1 protein that can be used according to the present invention.

20 **SEQ ID NO: 50** is the amino acid sequence encoded by SEQ ID NO: 49.

SEQ ID NO: 51 is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding a PA protein that can be used according to the present invention.

SEQ ID NO: 52 is the amino acid sequence encoded by SEQ ID NO: 51.

25 **SEQ ID NO: 53** is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding an NS protein that can be used according to the present invention.

SEQ ID NO: 54 is the amino acid sequence encoded by SEQ ID NO: 53.

SEQ ID NO: 55 is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding an NP protein that can be used according to the present invention.

SEQ ID NO: 56 is the amino acid sequence encoded by SEQ ID NO: 55.

30 **SEQ ID NO: 57** is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding an NA protein that can be used according to the present invention.

SEQ ID NO: 58 is the amino acid sequence encoded by SEQ ID NO: 57.

SEQ ID NO: 59 is a nucleotide sequence of a canine influenza virus (Miami/2005) encoding an MA protein that can be used according to the present invention.

SEQ ID NO: 60 is the amino acid sequence encoded by SEQ ID NO: 59.

SEQ ID NO: 61 is a nucleotide sequence of a canine influenza virus (Miami/2005)
5 encoding an HA protein that can be used according to the present invention.

SEQ ID NO: 62 is the amino acid sequence encoded by SEQ ID NO: 61.

SEQ ID NO: 63 is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding a PB2 protein that can be used according to the present invention.

10 **SEQ ID NO: 64** is the amino acid sequence encoded by SEQ ID NO: 63.

SEQ ID NO: 65 is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding a PB1 protein that can be used according to the present invention.

SEQ ID NO: 66 is the amino acid sequence encoded by SEQ ID NO: 65.

15 **SEQ ID NO: 67** is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding a PA protein that can be used according to the present invention.

SEQ ID NO: 68 is the amino acid sequence encoded by SEQ ID NO: 67.

SEQ ID NO: 69 is a nucleotide sequence of a canine influenza virus
20 (Jacksonville/2005) encoding an NS protein that can be used according to the present invention.

SEQ ID NO: 70 is the amino acid sequence encoded by SEQ ID NO: 69.

SEQ ID NO: 71 is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding an NP protein that can be used according to the present
25 invention.

SEQ ID NO: 72 is the amino acid sequence encoded by SEQ ID NO: 71.

SEQ ID NO: 73 is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding an NA protein that can be used according to the present invention.

30 **SEQ ID NO: 74** is the amino acid sequence encoded by SEQ ID NO: 73.

SEQ ID NO: 75 is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding an MA protein that can be used according to the present invention.

SEQ ID NO: 76 is the amino acid sequence encoded by SEQ ID NO: 75.

SEQ ID NO: 77 is a nucleotide sequence of a canine influenza virus (Jacksonville/2005) encoding an HA protein that can be used according to the present invention.

5 SEQ ID NO: 78 is the amino acid sequence encoded by SEQ ID NO: 77.

SEQ ID NO: 79 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 80 is an oligonucleotide that can be used according to the present invention.

10 SEQ ID NO: 81 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 82 is an oligonucleotide that can be used according to the present invention.

15 SEQ ID NO: 83 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 84 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 85 is an oligonucleotide that can be used according to the present invention.

20 SEQ ID NO: 86 is an oligonucleotide that can be used according to the present invention.

SEQ ID NO: 87 is an oligonucleotide that can be used according to the present invention.

25 SEQ ID NO: 88 is an oligonucleotide that can be used according to the present invention.

DETAILED DISCLOSURE OF THE INVENTION

The subject invention concerns isolated influenza virus that is capable of infecting canids and causing respiratory disease. In one embodiment, an influenza virus of the invention comprises a polynucleotide which encodes a protein having an amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment or variant thereof. In a specific embodiment, the

polynucleotide comprises the nucleotide sequence shown in any of SEQ ID Nos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or a fragment or variant thereof. In a specific embodiment, an influenza virus of the present invention is a subtype H3. Virus can be isolated from infected dogs and cultured in cells or eggs according to methods described herein. In an exemplified embodiment, the influenza virus is an influenza A virus.

The subject invention also concerns polynucleotides that comprise all or part of a gene or genes or a genomic segment of an influenza virus of the present invention. In one embodiment, a polynucleotide of the invention comprises an influenza hemagglutinin (HA) gene, neuraminidase (NA) gene, nucleoprotein (NP) gene, matrix protein (MA or M) gene, polymerase basic (PB) protein gene, polymerase acidic (PA) protein gene, non-structural (NS) protein gene, or a functional fragment or variant of any of these genes. In a specific embodiment, a polynucleotide of the invention comprises the hemagglutinin (HA) gene, or a functional fragment or variant thereof. In a further embodiment, the HA gene encodes a hemagglutinin protein having one or more of the following: a serine at position 83; a leucine at position 222; a threonine at position 328; and/or a threonine at position 483, versus the amino acid sequence of equine H3 consensus sequence. In one embodiment, the HA gene encodes a polypeptide having an amino acid sequence shown in SEQ ID NOs: 16, 32, 62, or 78, or a functional and/or immunogenic fragment or variant thereof. In a specific embodiment, the HA gene comprises a nucleotide sequence shown in SEQ ID NOs: 15, 31, 61, or 77.

In one embodiment, a polynucleotide of the invention encodes a polypeptide having the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment or variant thereof. In a specific embodiment, the polynucleotide encoding the amino acid sequence shown in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, comprises the nucleotide sequence shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, respectively, or a sequence encoding a functional and/or immunogenic fragment or variant of any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78. Thus, the subject invention concerns polynucleotide sequences comprising the nucleotide sequence shown in any of SEQ

ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or a fragment or variant, including a degenerate variant, of any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77. In a further specific embodiment, a polynucleotide of the invention can comprise: Nucleotides 1-2271 of SEQ ID NO: 3; Nucleotides 1-2148 of SEQ ID NO: 5; Nucleotides 1-657 of SEQ ID NO: 7; Nucleotides 1-1494 of SEQ ID NO: 9; Nucleotides 1-1410 of SEQ ID NO: 11; Nucleotides 1-756 of SEQ ID NO: 13; Nucleotides 1-1695 of SEQ ID NO: 15; Nucleotides 1-2271 of SEQ ID NO: 19; Nucleotides 1-2148 of SEQ ID NO: 21; Nucleotides 1-657 of SEQ ID NO: 23; Nucleotides 1-1494 of SEQ ID NO: 25; Nucleotides 1-756 of SEQ ID NO: 29; Nucleotides 1-1695 of SEQ ID NO: 31; Nucleotides 1-2277 of SEQ ID NO: 47; Nucleotides 1-2271 of SEQ ID NO: 49; Nucleotides 1-2148 of SEQ ID NO: 51; Nucleotides 1-690 of SEQ ID NO: 53; Nucleotides 1-1494 of SEQ ID NO: 55; Nucleotides 1-1410 of SEQ ID NO: 57; Nucleotides 1-756 of SEQ ID NO: 59; Nucleotides 1-1695 of SEQ ID NO: 61; Nucleotides 1-2277 of SEQ ID NO: 63; Nucleotides 1-2271 of SEQ ID NO: 65; Nucleotides 1-2148 of SEQ ID NO: 67; Nucleotides 1-690 of SEQ ID NO: 69; Nucleotides 1-1494 of SEQ ID NO: 71; Nucleotides 1-1410 of SEQ ID NO: 73; Nucleotides 1-756 of SEQ ID NO: 75; and Nucleotides 1-1695 of SEQ ID NO: 77. Nucleotide and amino acid sequences of viral polynucleotide and polypeptide sequences contemplated within the scope of the present invention have also been deposited with GenBank at accession Nos. DQ124147 through DQ124161 and DQ124190, the disclosure of which is incorporated herein by reference.

The subject invention also concerns polypeptides encoded by polynucleotides of an influenza virus of the present invention. The subject invention also concerns functional and/or immunogenic fragments and variants of the subject polypeptides. Polypeptides contemplated include HA protein, NA protein, NS protein, nucleoprotein, polymerase basic protein, polymerase acidic protein, and matrix protein of an influenza virus of the invention. In an exemplified embodiment, a polypeptide of the invention has an amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment or variant thereof.

The subject invention also concerns polynucleotide expression constructs comprising a polynucleotide sequence of the present invention. In one embodiment, an expression construct of the invention comprises a polynucleotide sequence encoding a polypeptide

comprising an amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment or variant thereof. In a specific embodiment, the polynucleotide encoding the amino acid sequence shown in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78 comprises the nucleotide sequence shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, respectively, or a sequence encoding a functional and/or immunogenic fragment or variant of any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78. Thus, the subject invention concerns expression constructs comprising a polynucleotide sequence comprising the nucleotide sequence shown in any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or a fragment or variant, including a degenerate variant, of any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77. In a preferred embodiment, an expression construct of the present invention provides for overexpression of an operably linked polynucleotide of the invention.

Expression constructs of the invention generally include regulatory elements that are functional in the intended host cell in which the expression construct is to be expressed. Thus, a person of ordinary skill in the art can select regulatory elements for use in, for example, human host cells, mammalian host cells, insect host cells, yeast host cells, bacterial host cells, and plant host cells. In one embodiment, the regulatory elements are ones that are functional in canine cells. Regulatory elements include promoters, transcription termination sequences, translation termination sequences, enhancers, and polyadenylation elements. As used herein, the term "expression construct" refers to a combination of nucleic acid sequences that provides for transcription of an operably linked nucleic acid sequence. As used herein, the term "operably linked" refers to a juxtaposition of the components described wherein the components are in a relationship that permits them to function in their intended manner. In general, operably linked components are in contiguous relation.

An expression construct of the invention can comprise a promoter sequence operably linked to a polynucleotide sequence encoding a polypeptide of the invention. Promoters can be incorporated into a polynucleotide using standard techniques known in the art. Multiple copies of promoters or multiple promoters can be used in an expression construct of the

invention. In a preferred embodiment, a promoter can be positioned about the same distance from the transcription start site in the expression construct as it is from the transcription start site in its natural genetic environment. Some variation in this distance is permitted without substantial decrease in promoter activity. A transcription start site is typically included in the expression construct. Preferably, the promoter associated with an expression construct of the invention provides for overexpression of an operably linked polynucleotide of the invention.

Promoters for use with an expression construct of the invention in eukaryotic cells can be of viral or cellular origin. Viral promoters include, but are not limited to, cytomegalovirus (CMV) gene promoters, SV40 early or late promoters, or Rous sarcoma virus (RSV) gene promoters. Promoters of cellular origin include, but are not limited to, desmin gene promoter and actin gene promoter. Promoters suitable for use with an expression construct of the invention in yeast cells include, but are not limited to, 3-phosphoglycerate kinase promoter, glyceraldehyde-3-phosphate dehydrogenase promoter, metallothionein promoter, alcohol dehydrogenase-2 promoter, and hexokinase promoter.

If the expression construct is to be provided in or introduced into a plant cell, then plant viral promoters, such as, for example, a cauliflower mosaic virus (CaMV) 35S (including the enhanced CaMV 35S promoter (see, for example U.S. Patent No. 5,106,739 and An, 1997)) or a CaMV 19S promoter can be used. Other promoters that can be used for expression constructs in plants include, for example, prolifera promoter, Ap3 promoter, heat shock promoters, T-DNA 1'- or 2'-promoter of *A. tumefaciens*, polygalacturonase promoter, chalcone synthase A (CHS-A) promoter from petunia, tobacco PR-1a promoter, ubiquitin promoter, actin promoter, alcA gene promoter, pin2 promoter (Xu *et al.*, 1993), maize WipI promoter, maize trpA gene promoter (U.S. Patent No. 5,625,136), maize CDPK gene promoter, and RUBISCO SSU promoter (U.S. Patent No. 5,034,322) can also be used. Root-specific promoters, such as any of the promoter sequences described in U.S. Patent No. 6,455,760 or U.S. Patent No. 6,696,623, or in published U.S. patent application Nos. 20040078841; 20040067506; 20040019934; 20030177536; 20030084486; or 20040123349, can be used with an expression construct of the invention. Constitutive promoters (such as the CaMV, ubiquitin, actin, or NOS promoter), developmentally-regulated promoters, and inducible promoters (such as those promoters that can be induced by heat, light, hormones, or chemicals) are also contemplated for use with polynucleotide expression constructs of the invention. Tissue-specific promoters, for example fruit-specific promoters, such as the E8 promoter of tomato (accession number: AF515784; Good *et al.* (1994)) can also be used.

Seed-specific promoters such as the promoter from a β -phaseolin gene (for example, of kidney bean) or a glycinin gene (for example, of soybean), and others, can also be used.

For expression in prokaryotic systems, an expression construct of the invention can comprise promoters such as, for example, alkaline phosphatase promoter, tryptophan (trp) promoter, lambda P_L promoter, β -lactamase promoter, lactose promoter, phoA promoter, T3 promoter, T7 promoter, or tac promoter (de Boer *et al.*, 1983).

Expression constructs of the invention may optionally contain a transcription termination sequence, a translation termination sequence, a sequence encoding a signal peptide, and/or enhancer elements. Transcription termination regions can typically be obtained from the 3' untranslated region of a eukaryotic or viral gene sequence. Transcription termination sequences can be positioned downstream of a coding sequence to provide for efficient termination. A signal peptide sequence is a short amino acid sequence typically present at the amino terminus of a protein that is responsible for the relocation of an operably linked mature polypeptide to a wide range of post-translational cellular destinations, ranging from a specific organelle compartment to sites of protein action and the extracellular environment. Targeting gene products to an intended cellular and/or extracellular destination through the use of an operably linked signal peptide sequence is contemplated for use with the polypeptides of the invention. Classical enhancers are cis-acting elements that increase gene transcription and can also be included in the expression construct. Classical enhancer elements are known in the art, and include, but are not limited to, the CaMV 35S enhancer element, cytomegalovirus (CMV) early promoter enhancer element, and the SV40 enhancer element. Intron-mediated enhancer elements that enhance gene expression are also known in the art. These elements must be present within the transcribed region and are orientation dependent.

DNA sequences which direct polyadenylation of mRNA transcribed from the expression construct can also be included in the expression construct, and include, but are not limited to, an octopine synthase or nopaline synthase signal.

Expression constructs can also include one or more dominant selectable marker genes, including, for example, genes encoding antibiotic resistance and/or herbicide-resistance for selecting transformed cells. Antibiotic-resistance genes can provide for resistance to one or more of the following antibiotics: hygromycin, kanamycin, bleomycin, G418, streptomycin, paromomycin, neomycin, and spectinomycin. Kanamycin resistance can be provided by neomycin phosphotransferase (NPT II). Herbicide-resistance genes can provide for

resistance to phosphinothricin acetyltransferase or glyphosate. Other markers used for cell transformation screening include, but are not limited to, genes encoding β -glucuronidase (GUS), β -galactosidase, luciferase, nopaline synthase, chloramphenicol acetyltransferase (CAT), green fluorescence protein (GFP), or enhanced GFP (Yang *et al.*, 1996).

5 The subject invention also concerns polynucleotide vectors comprising a polynucleotide sequence of the invention that encodes a polypeptide of the invention. Unique restriction enzyme sites can be included at the 5' and 3' ends of an expression construct or polynucleotide of the invention to allow for insertion into a polynucleotide vector. As used herein, the term "vector" refers to any genetic element, including for example, plasmids, 10 cosmids, chromosomes, phage, virus, and the like, which is capable of replication when associated with proper control elements and which can transfer polynucleotide sequences between cells. Vectors contain a nucleotide sequence that permits the vector to replicate in a selected host cell. A number of vectors are available for expression and/or cloning, and include, but are not limited to, pBR322, pUC series, M13 series, pGEM series, and 15 pBLUESCRIPT vectors (Stratagene, La Jolla, CA and Promega, Madison, WI).

 The subject invention also concerns oligonucleotide probes and primers, such as polymerase chain reaction (PCR) primers, that can hybridize to a coding or non-coding sequence of a polynucleotide of the present invention. Oligonucleotide probes of the invention can be used in methods for detecting influenza virus nucleic acid sequences. 20 Oligonucleotide primers of the invention can be used in PCR methods and other methods involving nucleic acid amplification. In a preferred embodiment, a probe or primer of the invention can hybridize to a polynucleotide of the invention under stringent conditions. Probes and primers of the invention can optionally comprise a detectable label or reporter molecule, such as fluorescent molecules, enzymes, radioactive moiety, and the like. Probes 25 and primers of the invention can be of any suitable length for the method or assay in which they are being employed. Typically, probes and primers of the invention will be 10 to 500 or more nucleotides in length. Probes and primers that are 10 to 20, 21 to 30, 31 to 40, 41 to 50, 51 to 60, 61 to 70, 71 to 80, 81 to 90, 91 to 100, or 101 or more nucleotides in length are contemplated within the scope of the invention. In one embodiment, probes and primers are 30 any of 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. Probes and primers of the invention can have complete (100%) nucleotide sequence identity with the polynucleotide sequence, or the sequence identity can be less than 100%. For example, sequence identity between a probe or primer and a sequence

can be 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75%, 70% or any other percentage sequence identity so long as the probe or primer can hybridize under stringent conditions to a nucleotide sequence of a polynucleotide of the invention. Exemplified probes and primers of the invention include those having the nucleotide sequence shown in any of SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, and SEQ ID NO: 46, or a functional fragment or variant of any of the SEQ ID NOs: 35-46.

As used herein, the terms "nucleic acid," "polynucleotide," and "oligonucleotide" refer to a deoxyribonucleotide, ribonucleotide, or a mixed deoxyribonucleotide and ribonucleotide polymer in either single- or double-stranded form, and unless otherwise limited, would encompass known analogs of natural nucleotides that can function in a similar manner as naturally-occurring nucleotides. Polynucleotide sequences include the DNA strand sequence that can be transcribed into RNA and the RNA strand that can be translated into protein. The complementary sequence of any nucleic acid, polynucleotide, or oligonucleotide of the present invention is also contemplated within the scope of the invention. Polynucleotide sequences also include both full-length sequences as well as shorter sequences derived from the full-length sequences. The subject invention also encompasses those polynucleotides that are complementary in sequence to the polynucleotides disclosed herein. Polynucleotides and polypeptides of the invention can be provided in purified or isolated form.

Because of the degeneracy of the genetic code, a variety of different polynucleotide sequences can encode a polypeptide of the present invention. A table showing all possible triplet codons (and where U also stands for T) and the amino acid encoded by each codon is described in Lewin (1985). In addition, it is well within the skill of a person trained in the art to create alternative polynucleotide sequences encoding the same, or essentially the same, polypeptides of the subject invention. These degenerate variant and alternative polynucleotide sequences are within the scope of the subject invention. As used herein, references to "essentially the same" sequence refers to sequences which encode amino acid substitutions, deletions, additions, or insertions which do not materially alter the functional and/or immunogenic activity of the polypeptide encoded by the polynucleotides of the present invention.

The subject invention also concerns variants of the polynucleotides of the present invention that encode polypeptides of the invention. Variant sequences include those

sequences wherein one or more nucleotides of the sequence have been substituted, deleted, and/or inserted. The nucleotides that can be substituted for natural nucleotides of DNA have a base moiety that can include, but is not limited to, inosine, 5-fluorouracil, 5-bromouracil, hypoxanthine, 1-methylguanine, 5-methylcytosine, and tritylated bases. The sugar moiety of the nucleotide in a sequence can also be modified and includes, but is not limited to, arabinose, xylulose, and hexose. In addition, the adenine, cytosine, guanine, thymine, and uracil bases of the nucleotides can be modified with acetyl, methyl, and/or thio groups. Sequences containing nucleotide substitutions, deletions, and/or insertions can be prepared and tested using standard techniques known in the art.

Substitution of amino acids other than those specifically exemplified or naturally present in a polypeptide of the invention are also contemplated within the scope of the present invention. For example, non-natural amino acids can be substituted for the amino acids of a polypeptide, so long as the polypeptide having the substituted amino acids retains substantially the same functional activity as the polypeptide in which amino acids have not been substituted. Examples of non-natural amino acids include, but are not limited to, ornithine, citrulline, hydroxyproline, homoserine, phenylglycine, taurine, iodotyrosine, 2,4-diaminobutyric acid, α -amino isobutyric acid, 4-aminobutyric acid, 2-amino butyric acid, γ -amino butyric acid, ϵ -amino hexanoic acid, 6-amino hexanoic acid, 2-amino isobutyric acid, 3-amino propionic acid, norleucine, norvaline, sarcosine, homocitrulline, cysteic acid, τ -butylglycine, τ -butylalanine, phenylglycine, cyclohexylalanine, β -alanine, fluoro-amino acids, designer amino acids such as β -methyl amino acids, C-methyl amino acids, N-methyl amino acids, and amino acid analogues in general. Non-natural amino acids also include amino acids having derivatized side groups. Furthermore, any of the amino acids in the protein can be of the D (dextrorotary) form or L (levorotary) form. Allelic variants of a protein sequence of a polypeptide of the present invention are also encompassed within the scope of the invention.

Amino acids can be generally categorized in the following classes: non-polar, uncharged polar, basic, and acidic. Conservative substitutions whereby a polypeptide of the present invention having an amino acid of one class is replaced with another amino acid of the same class fall within the scope of the subject invention so long as the polypeptide having the substitution still retains substantially the same functional activity as the polypeptide that does not have the substitution. Polynucleotides encoding a polypeptide having one or more amino acid substitutions in the sequence are contemplated within the scope of the present

invention. Table 11 below provides a listing of examples of amino acids belonging to each class. Single letter amino acid abbreviations are defined in Table 12.

Fragments and variants of polypeptides of influenza virus of the present invention can be generated using standard methods known in the art and tested for the presence of function or immunogenecity using standard techniques known in the art. For example, for testing fragments and/or variants of a neuraminidase polypeptide of the invention, enzymatic activity can be assayed. Thus, an ordinarily skilled artisan can readily prepare and test fragments and variants of a polypeptide of the invention and determine whether the fragment or variant retains activity relative to full-length or a non-variant polypeptide.

Polynucleotides and polypeptides contemplated within the scope of the subject invention can also be defined in terms of more particular identity and/or similarity ranges with those sequences of the invention specifically exemplified herein. The sequence identity will typically be greater than 60%, preferably greater than 75%, more preferably greater than 80%, even more preferably greater than 90%, and can be greater than 95%. The identity and/or similarity of a sequence can be 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% as compared to a sequence exemplified herein. Unless otherwise specified, as used herein percent sequence identity and/or similarity of two sequences can be determined using the algorithm of Karlin and Altschul (1990), modified as in Karlin and Altschul (1993). Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul *et al.* (1990). BLAST searches can be performed with the NBLAST program, score = 100, wordlength = 12, to obtain sequences with the desired percent sequence identity. To obtain gapped alignments for comparison purposes, Gapped BLAST can be used as described in Altschul *et al.* (1997). When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (NBLAST and XBLAST) can be used. See NCBI/NIH website.

The subject invention also contemplates those polynucleotide molecules having sequences which are sufficiently homologous with the polynucleotide sequences exemplified herein so as to permit hybridization with that sequence under standard stringent conditions and standard methods (Maniatis *et al.*, 1982). As used herein, "stringent" conditions for hybridization refers to conditions wherein hybridization is typically carried out overnight at 20-25 C below the melting temperature (T_m) of the DNA hybrid in 6x SSPE, 5x Denhardt's

solution, 0.1% SDS, 0.1 mg/ml denatured DNA. The melting temperature, T_m , is described by the following formula (Beltz *et al.*, 1983):

$$T_m = 81.5^\circ\text{C} + 16.6 \log[\text{Na}^+] + 0.41(\%G+C) - 0.61(\% \text{ formamide}) - 600/\text{length of duplex in base pairs}.$$

5 Washes are typically carried out as follows:

(1) Twice at room temperature for 15 minutes in 1x SSPE, 0.1% SDS (low stringency wash).

(2) Once at $T_m - 20^\circ\text{C}$ for 15 minutes in 0.2x SSPE, 0.1% SDS (moderate stringency wash).

10 The subject invention also concerns viral proteins and peptides encoded by the genes of an influenza virus of the present invention. In one embodiment, the viral protein is a mature HA protein. In a specific embodiment, the mature HA protein comprises one or more of the following: a serine at position 82; a leucine at position 221; a threonine at position 327; and/or a threonine at position 482. In an exemplified embodiment, the mature HA
15 protein has an amino acid sequence shown in SEQ ID NO: 33 or SEQ ID NO: 34, or a functional and/or immunogenic fragment or variant of SEQ ID NO: 33 or SEQ ID NO: 34. In another embodiment, the viral protein is an NA protein, NS protein, PB protein, PA protein, or MA protein. Viral proteins and peptides of the invention can be used to generate antibodies that bind specifically to the protein or peptide. Viral proteins and peptides of the
20 present invention can also be used as immunogens and in vaccine compositions.

The subject invention also concerns compositions and methods for inducing an immune response against an influenza virus that is capable of infecting a susceptible host animal and causing respiratory disease. The invention can be used to induce an immune response against an influenza virus of any subtype in a susceptible host animal. For example,
25 the influenza virus can be an HA subtype of H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15, or H16, and an NA subtype of N1, N2, N3, N4, N5, N6, N7, N8, or N9. In one embodiment, the HA subtype is H3 or H5. In a further embodiment, the NA subtype is N7 or N8. In a specific embodiment, an immune response is induced against an influenza virus of subtype H3N8. In one embodiment, the host animal is a canid. Canines include
30 wild, zoo, and domestic canines, such as wolves, coyotes, and foxes. Canines also include dogs, particularly domestic dogs, such as, for example, pure-bred and/or mongrel companion dogs, show dogs, working dogs, herding dogs, hunting dogs, guard dogs, police dogs, racing dogs, and/or laboratory dogs. In a specific embodiment, the host animal is a domesticated

dog, such as a greyhound. In one embodiment, an animal is administered an effective amount of an immunogenic composition of the present invention sufficient to induce an immune response against an influenza virus of the invention. The immune response can be a humoral and/or cellular immune response. In a specific embodiment, the immune response is a protective immune response that is capable of preventing or minimizing viral infection in the immunized host animal for some period of time subsequent to the immunization. Thus, the subject invention also concerns vaccine compositions and methods that can provide a vaccinated animal with a protective immune response to a virus of the present invention.

As described herein, the vaccine or immunogenic compositions of the subject invention may comprise cell-free whole virus, including attenuated or inactivated virus, or portions of the virus, including subviral particles (including "split vaccine" wherein a virion is treated to remove some or all viral lipids), viral proteins (including individual proteins and macromolecular complexes of multiple proteins), polypeptides, and peptides, as well as virus-infected cell lines, or a combination of any of these. Vaccine or immunogenic compositions comprising virus-infected cell lines may comprise multiple cell lines, each infected with a different viral strain.

The vaccine or immunogenic compositions of the subject invention also encompass recombinant viral vector-based constructs that may comprise, for example, genes encoding HA protein, NA protein, nucleoprotein, polymerase basic protein, polymerase acidic protein, and/or matrix protein of an influenza virus of the present invention. Any suitable viral vector that can be used to prepare a recombinant vector/virus construct is contemplated for use with the subject invention. For example, viral vectors derived from adenovirus, avipox, herpesvirus, vaccinia, canarypox, entomopox, swinepox, West Nile virus and others known in the art can be used with the compositions and methods of the present invention. Recombinant polynucleotide vectors that encode and express components can be constructed using standard genetic engineering techniques known in the art. In addition, the various vaccine compositions described herein can be used separately and in combination with each other. For example, primary immunizations of an animal may use recombinant vector-based constructs, having single or multiple strain components, followed by secondary boosts with vaccine compositions comprising inactivated virus or inactivated virus-infected cell lines. Other immunization protocols with the vaccine compositions of the invention are apparent to persons skilled in the art and are contemplated within the scope of the present invention.

The subject invention also concerns reassortant virus comprising at least one gene or genomic segment of an influenza virus of the present invention and the remainder of viral genes or genomic segments from a different influenza virus of the invention or from an influenza virus other than a virus of the present invention. Reassortant virus can be produced
5 by genetic reassortant of nucleic acid of a donor influenza virus of the present invention with nucleic acid of a recipient influenza virus and then selecting for reassortant virus that comprises the nucleic acid of the donor virus. Methods to produce and isolate reassortant virus are well known in the art (Fields *et al.*, 1996). In one embodiment, a reassortant virus of the invention comprises genes or genomic segments of a human, avian, swine, or equine
10 influenza virus. A reassortant virus of the present invention can include any combination of nucleic acid from donor and recipient influenza virus so long as the reassortant virus comprises at least one gene or genomic segment from a donor influenza virus of the present invention. In one embodiment, a recipient influenza virus can be an equine influenza virus.

Natural, recombinant or synthetic polypeptides of viral proteins, and peptide
15 fragments thereof, can also be used as vaccine compositions according to the subject methods. In one embodiment, viral polypeptides derived from multiple strains can be combined in a vaccine composition and are used to vaccinate a host animal. For example, polypeptides based on the viral HA protein from at least two different strains of influenza virus of the invention can be combined in the vaccine. The polypeptides may be homologous
20 to one strain or may comprise "hybrid" or "chimeric" polypeptides whose amino acid sequence is derived from joining or linking polypeptides from at least two distinct strains. Procedures for preparing viral polypeptides are well known in the art. For example, viral polypeptides and peptides can be synthesized using solid-phase synthesis methods (Merrifield, 1963). Viral polypeptides and peptides can also be produced using recombinant
25 DNA techniques wherein a polynucleotide molecule encoding an viral protein or peptide is expressed in a host cell, such as bacteria, yeast, or mammalian cell lines, and the expressed protein purified using standard techniques of the art.

Vaccine compositions of the present invention also include naked nucleic acid compositions. In one embodiment, a nucleic acid may comprise a nucleotide sequence
30 encoding an HA and/or an NA protein of an influenza virus of the present invention. Methods for nucleic acid vaccination are known in the art and are described, for example, in U.S. Patent Nos. 6,063,385 and 6,472,375. The nucleic acid can be in the form of a plasmid

or a gene expression cassette. In one embodiment, the nucleic acid is provided encapsulated in a liposome which is administered to an animal.

Vaccine compositions and immunogens, such as polypeptides and nucleic acids, that can be used in accordance with the present invention can be provided with a pharmaceutically-acceptable carrier or diluent. Compounds and compositions useful in the subject invention can be formulated according to known methods for preparing pharmaceutically useful compositions. Formulations are described in detail in a number of sources which are well known and readily available to those skilled in the art. For example, *Remington's Pharmaceutical Science* by E.W. Martin, Easton Pennsylvania, Mack Publishing Company, 19th ed., 1995, describes formulations which can be used in connection with the subject invention. In general, the compositions of the subject invention will be formulated such that an effective amount of an immunogen is combined with a suitable carrier in order to facilitate effective administration of the composition. The compositions used in the present methods can also be in a variety of forms. These include, for example, solid, semi-solid, and liquid dosage forms, such as tablets, pills, powders, liquid solutions or suspension, suppositories, injectable and infusible solutions, and sprays. The preferred form depends on the intended mode of administration and therapeutic application. The compositions also preferably include conventional pharmaceutically acceptable carriers and diluents which are known to those skilled in the art. Examples of carriers or diluents for use with the subject peptidomimetics include, but are not limited to, water, saline, oils including mineral oil, ethanol, dimethyl sulfoxide, gelatin, cyclodextrans, magnesium stearate, dextrose, cellulose, sugars, calcium carbonate, glycerol, alumina, starch, and equivalent carriers and diluents, or mixtures of any of these. Formulations of an immunogen of the invention can also comprise suspension agents, protectants, lubricants, buffers, preservatives, and stabilizers. To provide for the administration of such dosages for the desired therapeutic treatment, pharmaceutical compositions of the invention will advantageously comprise between about 0.1% and 45%, and especially, 1 and 15% by weight of the immunogen or immunogens based on the weight of the total composition including carrier or diluent.

The vaccine and immunogenic compositions of the subject invention can be prepared by procedures well known in the art. For example, the vaccine or immunogens are typically prepared as injectables, *e.g.*, liquid solutions or suspensions. The vaccine or immunogens are administered in a manner that is compatible with dosage formulation, and in such amount as will be therapeutically effective and immunogenic in the recipient. The optimal dosages and

administration patterns for a particular vaccine or immunogens formulation can be readily determined by a person skilled in the art.

Peptides and/or polypeptides of the present invention can also be provided in the form of a multiple antigenic peptide (MAP) construct. The preparation of MAP constructs has been described in Tam (1988). MAP constructs utilize a core matrix of lysine residues onto which multiple copies of an immunogen are synthesized (Posnett *et al.*, 1988). Multiple MAP constructs, each containing the same or different immunogens, can be prepared and administered in a vaccine composition in accordance with methods of the present invention. In one embodiment, a MAP construct is provided with and/or administered with one or more adjuvants. Influenza polypeptides of the invention can also be produced and administered as macromolecular protein structures comprising one or more polypeptides. Published U.S. Patent Application US2005/0009008 describes methods for producing virus-like particles as a vaccine for influenza virus.

According to the methods of the subject invention, the vaccine and immunogenic compositions described herein are administered to susceptible hosts, typically canids, and more typically domesticated dogs, in an effective amount and manner to induce protective immunity against subsequent challenge or infection of the host by virus. In one embodiment, the host animal is a canid. Canines include wild, zoo, and domestic canines, such as wolves, coyotes, and foxes. Canines also include dogs, particularly domestic dogs, such as, for example, pure-bred and/or mongrel companion dogs, show dogs, working dogs, herding dogs, hunting dogs, guard dogs, police dogs, racing dogs, and/or laboratory dogs. In a specific embodiment, the host animal is a domesticated dog, such as a greyhound. The vaccines or immunogens are typically administered parenterally, by injection, for example, either subcutaneously, intraperitoneally, or intramuscularly. Other suitable modes of administration include oral or nasal administration. Usually, the vaccines or immunogens are administered to an animal at least two times, with an interval of one or more weeks between each administration. However, other regimens for the initial and booster administrations of the vaccine or immunogens are contemplated, and may depend on the judgment of the practitioner and the particular host animal being treated.

Virus and virus-infected cells in a vaccine formulation may be inactivated or attenuated using methods known in the art. For example, whole virus and infected cells can be inactivated or attenuated by exposure to paraformaldehyde, formalin, phenol, UV light, elevated temperature and the like. The amount of cell-free whole virus in a vaccine dose will

usually be in the range from about 0.1 mg to about 5 mg, and more usually being from about 0.2 mg to about 2 mg. The dosage for vaccine formulations comprising virus-infected cell lines will usually contain from about 10^6 to about 10^8 cells per dose, and more usually from about 5×10^6 to about 7.5×10^7 cells per dose. The amount of protein or peptide immunogen
5 in a dose for an animal can vary from about 0.1 μg to 10000 μg , or about 1 μg to 5000 μg , or about 10 μg to 1000 μg , or about 25 μg to 750 μg , or about 50 μg to 500 μg , or 100 μg to 250 μg , depending upon the size, age, *etc.*, of the animal receiving the dose.

An immunogenic or vaccine composition of the invention, such as virus or virus-infected cells or viral proteins or peptides, can be combined with an adjuvant, typically just
10 prior to administration. Adjuvants contemplated for use in the vaccine formulations include thionyl muramyl dipeptide (MDP) (Byars *et al.*, 1987), saponin, *Cornebacterium parvum*, Freund's complete and Freund's incomplete adjuvants, aluminum, or a mixture of any of these. A variety of other adjuvants suitable for use with the methods and vaccines of the subject invention, such as alum, are well known in the art and are contemplated for use with
15 the subject invention.

The subject invention also concerns antibodies that bind specifically to a protein or a peptide of the present invention. Antibodies of the subject invention include monoclonal and polyclonal antibody compositions. Preferably, the antibodies of the subject invention are monoclonal antibodies. Whole antibodies and antigen binding fragments thereof are
20 contemplated in the present invention. Thus, for example, suitable antigen binding fragments include Fab_2 , Fab and Fv antibody fragments. Antibodies of the invention can be labeled with a detectable moiety, such as a fluorescent molecule (*e.g.*, fluorescein or an enzyme).

The subject invention also concerns methods and compositions for detection and identification of an influenza virus of the invention and for diagnosis of infection of an
25 animal with an influenza virus of the present invention. The methods of the invention include detection of the presence of canine influenza, in a biological sample from an animal. The detection of canine influenza in a sample, is useful to diagnose canine influenza in an animal. In turn, this information can provide the ability to determine the prognosis of an animal based on distinguishing levels of canine influenza present over time, and can assist in selection of
30 therapeutic agents and treatments for the animal, and assist in monitoring therapy. The method also provides the ability to establish the absence of canine influenza in an animal tested.

The ability to detect canine influenza in an animal permits assessment of outbreaks of canine influenza in different geographical locations. This information also permits early detection so that infected animals can be isolated, to limit the spread of disease, and allows early intervention for treatment options. In addition, having this information available can
5 provide direction to medical personnel for preparing to treat large numbers of ill animals, including assembling medical supplies, and, if available, vaccines.

In one embodiment, a method of the present invention involves the collection of a biological sample from a test animal, such as a canine. The biological sample may be any biological material, including, cells, tissue, hair, whole blood, serum, plasma, nipple aspirate,
10 lung lavage, cerebrospinal fluid, saliva, sweat and tears.

The animal test sample may come from an animal suspected of having canine influenza virus, whether or not the animal exhibits symptoms of the disease. Control samples can also be provided or collected from animals known to be free of canine influenza. Additional controls may be provided, *e.g.*, to reduce false positive and false negative results,
15 and verify that the reagents in the assay are actively detecting canine influenza A virus.

In addition to detecting the presence or absence of canine influenza in a biological sample, the methods of detection used in the invention can detect mutations in canine influenza virus, such as changes in nucleic acid sequence, that may result from the environment, drug treatment, genetic manipulations or mutations, injury, change in diet,
20 aging, or any other characteristic(s) of an animal. Mutations may also cause canine influenza A to become resistant to a drug that was formerly effective, or to enable the virus to infect and propagate in a different species of animal, or human. For example, avian influenza A virus has been shown to infect other animals and humans.

In one embodiment for detecting an influenza virus in an animal, diagnosis is
25 facilitated by the collection of high-quality specimens, their rapid transport to a testing facility, and appropriate storage, before laboratory testing. Virus is best detected in specimens containing infected cells and secretions. In one embodiment, specimens for the direct detection of viral antigens and/or for nucleic acids and/or virus isolation in cell cultures are taken during the first 3 days after onset of clinical symptoms. A number of types of
30 specimens are suitable to diagnose virus infections of the upper respiratory tract, including, but not limited to, nasal swab, nasopharyngeal swab, nasopharyngeal aspirate, nasal wash and throat swabs. In addition to swabs, samples of tissue or serum may be taken, and invasive procedures can also be performed.

In one embodiment, respiratory specimens are collected and transported in 1-5 ml of virus transport media. A number of media that are satisfactory for the recovery of a wide variety of viruses are commercially available. Clinical specimens are added to transport medium. Nasal or nasopharyngeal swabs can also be transported in the virus transport medium. One example of a transport medium is 10 gm of veal infusion broth and 2 gm of bovine albumin fraction V, added to sterile distilled water to 400 ml. Antibiotics such as 0.8 ml gentamicin sulfate solution (50 mg/ml) and 3.2 ml amphotericin B (250 µg/ml) can also be added. The medium is preferably sterilized by filtration. Nasal washes, such as sterile saline (0.85% NaCl), can also be used to collect specimens of respiratory viruses.

In one embodiment, sera is collected in an amount of from 1-5 ml of whole blood from an acute-phase animal, soon after the onset of clinical symptoms, and preferably not later than 7 days. A convalescent-phase serum specimen can also be collected, for example at about 14 days after onset of symptoms. Serum specimens can be useful for detecting antibodies against respiratory viruses in a neutralization test.

In some instances, samples may be collected from individual animals over a period of time (*e.g.*, once a day, once a week, once a month, biannually or annually). Obtaining numerous samples from an individual animal, over a period of time, can be used to verify results from earlier detections, and/or to identify response or resistance to a specific treatment, *e.g.*, a selected therapeutic drug.

The methods of the present invention can be used to detect the presence of one or more pathological agents in a test sample from an animal, and the level of each pathological agent. Any method for detecting the pathological agent can be used, including, but not limited to, antibody assays including enzyme-linked immunosorbent assays (ELISAs), indirect fluorescent antibody (IFA) tests, hemagglutinating, and inhibition of hemagglutination (HI) assays, and Western Blot. Known cell-culture methods can also be used. Positive cultures can be further identified using immunofluorescence of cell cultures or HI assay of the cell culture medium (supernatant).

In addition, methods for detecting nucleic acid (DNA or RNA) or protein can be used. Such methods include, but are not limited to, polymerase chain reaction (PCR), and reverse transcriptase (RT) PCR tests and real time tests, and quantitative nuclease protection assays. There are commercially available test kits available to perform these assays. For example, QIAGEN (Valencia, CA) sells a one step RT-PCR kit, and viral RNA extraction kit.

In one embodiment, the method utilizes an antibody specific for a virus or viral protein of the invention. In a specific embodiment, an antibody specific for an HA protein of a virus of the invention is utilized. In another embodiment, an antibody specific for an NP protein of a virus of the invention is used. A suitable sample, such as from the nasal or nasopharyngeal region, is obtained from an animal and virus or viral protein is isolated therefrom. The viral components are then screened for binding of an antibody specific to a protein, such as HA or NP, of a virus of the invention. In another embodiment, a serum sample (or other antibody containing sample) is obtained from an animal and the serum screened for the presence of antibody that binds to a protein of a virus of the invention. For example, an ELISA assay can be performed where the plate walls have HA and/or NP protein, or a peptide fragment thereof, bound to the wall. The plate wall is then contacted with serum or antibody from a test animal. The presence of antibody in the animal that binds specifically to the HA and/or NP protein is indicative that the test animal is infected or has been infected with an influenza virus of the present invention.

In one embodiment, the presence of a pathological agent is detected by determining the presence or absence of antibodies against the agent, in a biological sample. It can take some time (*e.g.* months) after an animal is infected before antibodies can be detected in a blood test. Once formed, antibodies usually persist for many years, even after successful treatment of the disease. Finding antibodies to canine influenza A may not indicate whether the infection was recent, or sometime in the past.

Antibody testing can also be done on fluid(s). Antibody assays include enzyme-linked immunosorbent assays (ELISAs), indirect fluorescent antibody (IFA) assays, and Western Blot. Preferably, antibody testing is done using multiple assays, for example ELISA or IFA followed by Western blot. Antibody assays can be done in a two-step process, using either an ELISA or IFA assay, followed by a Western blot assay. ELISA is considered a more reliable and accurate assay than IFA, but IFA may be used if ELISA is not available. The Western blot test (which is a more specific test) can also be done in all animals, particularly those that have tested positive or borderline positive (equivocal) in an ELISA or IFA assay.

Other antibody-based tests that can be used for detection of influenza virus include hemagglutination inhibition assays. Hemagglutination activity can be detected in a biological sample from an animal, using chicken or turkey red blood cells as described (Burleson *et al.*, 1992) and Kendal *et al.*, 1982). In one embodiment, an influenza or an HA protein or peptide

of the invention is contacted with a test sample containing serum or antibody. Red blood cells (RBC) from an animal, such as a bird, are then added. If antibody to HA is present, then the RBC will not agglutinate. If antibody to HA is not present, the RBC will agglutinate in the presence of HA. Variations and modifications to standard hemagglutination inhibition assays are known in the art and contemplated within the scope of the present invention.

Infection of an animal can also be determined by isolation of the virus from a sample, such as a nasal or nasopharyngeal swab. Viral isolation can be performed using standard methods, including cell culture and egg inoculation.

In a further embodiment, a nucleic acid-based assay can be used for detection of a virus of the present invention. In one embodiment, a nucleic acid sample is obtained from an animal and the nucleic acid subjected to PCR using primers that will generate an amplification product if the nucleic acid contains a sequence specific to an influenza virus of the present invention. In a specific embodiment, RT-PCR is used in an assay for the subject virus. In an exemplified embodiment, real-time RT-PCR is used to assay for an influenza virus of the invention. PCR, RT-PCR and real-time PCR methods are known in the art and have been described in U.S. Patent Nos. 4,683,202; 4,683,195; 4,800,159; 4,965,188; 5,994,056; 6,814,934; and in Saiki *et al.* (1985); Sambrook *et al.* (1989); Lee *et al.* (1993); and Livak *et al.* (1995). In one embodiment, the PCR assay uses oligonucleotides specific for an influenza matrix (MA) gene and/or HA gene. The amplification product can also be sequenced to determine if the product has a sequence of an influenza virus of the present invention. Other nucleic acid-based assays can be used for detection and diagnosis of viral infection by a virus of the invention and such assays are contemplated within the scope of the present invention. In one embodiment, a sample containing a nucleic acid is subjected to a PCR-based amplification using forward and reverse primers where the primers are specific for a viral polynucleotide or gene sequence. If the nucleic acid in the sample is RNA, then RT-PCR can be performed. For real-time PCR, a detectable probe is utilized with the primers.

Primer sets specific for the hemagglutinin (HA) gene of many of the circulating influenza viruses are known, and are continually being developed. The influenza virus genome is single-stranded RNA, and a DNA copy (cDNA) must be made using a reverse transcriptase (RT) polymerase. The amplification of the RNA genome, for example using RT-PCR, requires a pair of oligonucleotide primers, typically designed on the basis of the known HA sequence of influenza A subtypes and of neuraminidase (NM)-1. The primers

can be selected such that they will specifically amplify RNA of only one virus subtype. DNAs generated by using subtype-specific primers can be further analyzed by molecular genetic techniques such as sequencing. The test is preferably run with a positive control, or products are confirmed by sequencing and comparison with known sequences. The absence
5 of the target PCR products (*i.e.*, a “negative” result) may not rule out the presence of the virus. Results can then be made available within a few hours from either clinical swabs or infected cell cultures. PCR and RT-PCR tests for influenza A virus are described by Fouchier *et al.*, 2000 and Maertzdorf *et al.*, 2004.

The subject invention also concerns methods for screening for compounds or drugs
10 that have antiviral activity against a virus of the present invention. In one embodiment, cells infected with a virus of the invention are contacted with a test compound or drug. The amount of virus or viral activity following contact is then determined. Those compounds or drugs that exhibit antiviral activity can be selected for further evaluation.

The subject invention also concerns isolated cells infected with an influenza virus of
15 the present invention. In one embodiment, the cell is a canine cell, such as canine kidney epithelial cells.

The subject invention also concerns cells transformed with a polynucleotide of the present invention encoding a polypeptide of the invention. Preferably, the polynucleotide sequence is provided in an expression construct of the invention. More preferably, the
20 expression construct provides for overexpression in the cell of an operably linked polynucleotide of the invention. In one embodiment, the cell is transformed with a polynucleotide sequence comprising a sequence encoding the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional fragment or variant
25 thereof. In a specific embodiment, the cell is transformed with a polynucleotide encoding the amino acid sequence shown in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78 comprises the nucleotide sequence shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, respectively, or a
30 sequence encoding a functional fragment or variant of any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78. Thus, the subject invention concerns cells transformed with a polynucleotide sequence comprising the nucleotide sequence shown in any of SEQ ID NOs: 1, 3, 5, 7, 9, 11,

13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or a fragment or variant, including a degenerate variant, of any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77.

5 The transformed cell can be a eukaryotic cell, for example, a plant cell, including protoplasts, or the transformed cell can be a prokaryotic cell, for example, a bacterial cell such as *E. coli* or *B. subtilis*. Animal cells include human cells, mammalian cells, partially canine cells, avian cells, and insect cells. Plant cells include, but are not limited to, dicotyledonous, monocotyledonous, and conifer cells.

10 The subject invention also concerns plants, including transgenic plants that express and produce a viral protein or polypeptide of the present invention. Plants, plant tissues, and plant cells transformed with or bred to contain a polynucleotide of the invention are contemplated by the present invention. Preferably, the polynucleotide of the invention is overexpressed in the plant, plant tissue, or plant cell. Plants can be used to produce influenza
15 vaccine compositions of the present invention and the vaccines can be administered through consumption of the plant (see, for example, U.S. Patent Nos. 5,484,719 and 6,136,320).

The subject invention also concerns kits for detecting a virus or diagnosing an infection by a virus of the present invention. In one embodiment, a kit comprises an antibody of the invention that specifically binds to an influenza virus of the present invention, or an
20 antigenic portion thereof. In another embodiment, a kit comprises one or more polypeptides or peptides of the present invention. In a specific embodiment, the polypeptides have an amino acid sequence shown in any of SEQ ID NOs. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment or variant thereof. In a further embodiment, a kit
25 comprises one or more polynucleotides or oligonucleotides of the present invention. In a specific embodiment, the polynucleotides have a nucleotide sequence shown in any of SEQ ID NOs. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or a fragment or variant thereof. A kit may optionally
30 comprise one or more control antibody, control polypeptide or peptide, and/or control polynucleotide or oligonucleotide. The antibody, polypeptides, peptides, polynucleotides, and/or oligonucleotides of the kit can be provided in a suitable container or package.

The subject application also concerns the use of mongrel dogs as a model for infection and pathogenesis of influenza virus. In one embodiment, a mongrel dog is inoculated with an

influenza virus, such as a canine influenza virus of the present invention. Optionally, the dog can be administered therapeutic agents subsequent to inoculation. The dog can also have been administered a composition for generating an immune response against an influenza virus prior to inoculation with virus. Tissue, blood, serum, and other biological samples can be obtained before and/or after inoculation and examined for the presence of virus and pathogenesis of tissue using methods known in the art including, but not limited to, PCR, RT-PCR, nucleic acid sequencing, and immunohistochemistry.

Any element of any embodiment disclosed herein can be combined with any other element or embodiment disclosed herein and such combinations are specifically contemplated within the scope of the present invention.

All patents, patent applications, provisional applications, and publications referred to or cited herein are incorporated by reference in their entirety, including all figures and tables, to the extent they are not inconsistent with the explicit teachings of this specification.

MATERIALS AND METHODS FOR EXAMPLES 1-6

Blood and Nasal Swab Collection from Greyhounds.

Acute and convalescent blood samples were collected by jugular venipuncture from clinically diseased or normal greyhounds in racing kennels experiencing outbreaks of respiratory disease. Convalescent samples were collected 4 to 12 weeks after the acute sample. Serum was harvested and stored at -80°C. Nasal swabs were collected and placed in Amies transport medium with charcoal (Becton Dickinson Biosciences) pending submission for bacterial isolation.

Postmortem examination of greyhounds.

Complete postmortem examinations were performed by the Anatomic Pathology Service at the University of Florida College of Veterinary Medicine (UF CVM) on 5 of the 8 greyhounds that died in the January 2004 outbreak at a Florida track. Postmortem examination of another dog was performed at a private veterinary clinic with submission of tissues to the UF CVM for histopathologic diagnosis. Tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, and 5-µm sections were either stained with hematoxylin and eosin for histopathologic diagnosis or processed for immunohistochemistry

as described below. Unfixed tissues were submitted for bacterial culture and also stored at -80°C.

Serological tests for canine viral respiratory pathogens.

5 Paired acute and convalescent serum samples were submitted to the Animal Health Diagnostic Laboratory (AHDL) at the Cornell University College of Veterinary Medicine for serum neutralization assays against canine distemper virus, adenovirus type 2, and parainfluenza virus. Antibody titers were expressed as the last dilution of serum that inhibited viral infection of cell cultures. Seroconversion, defined as a ≥ 4 -fold increase in
10 antibody titer between the acute and convalescent sample, indicated viral infection. No seroconversions to these viral pathogens were detected.

Microbial tests for canine bacterial respiratory pathogens.

Paired nasal swabs and postmortem tissues were submitted to the Diagnostic Clinical
15 Microbiology/Parasitology/Serology Service at the UF CVM for bacterial isolation and identification. The samples were cultured on nonselective media as well as media selective for *Bordetella* species (Regan-Lowe; Remel) and *Mycoplasma* species (Remel). All cultures were held for 21 days before reporting no growth. Nasal swabs from some of the greyhounds were also submitted to the Department of Diagnostic Medicine/Pathobiology at the Kansas
20 State University College of Veterinary Medicine for bacterial culture. Of 70 clinically diseased dogs tested, *Bordetella bronchiseptica* was isolated from the nasal cavity of 1 dog, while *Mycoplasma spp.* were recovered from the nasal cavity of 33 dogs. *Pasteurella multocida* was commonly recovered from the nasal cavity of dogs with purulent nasal discharges. Two of the dogs that died in the January 2004 outbreak had scant growth of
25 *Escherichia coli* in the lungs postmortem, one dog had scant growth of *E. coli* and *Streptococcus canis*, and another had scant growth of *Pseudomonas aeruginosa* and a yeast. Neither *Bordetella bronchiseptica* nor *Mycoplasma* was isolated from the trachea or lungs of dogs that died.

30 Virus isolation from postmortem tissues.

Frozen tissues were thawed and homogenized in 10 volumes of minimum essential medium (MEM) supplemented with 0.5% bovine serum albumin (BSA) and antibiotics. Solid debris was removed by centrifugation and supernatants were inoculated onto cultured

cells or into 10-day old embryonated chicken eggs. Tissue homogenates from greyhounds that died were inoculated into diverse cell cultures that supported the replication of a broad range of viral pathogens. The cell cultures included Vero (African green monkey kidney epithelial cells, ATCC No. CCL-81), A-72 (canine tumor fibroblasts, CRL-1542), HRT-18
5 (human rectal epithelial cells, CRL-11663), MDCK (canine kidney epithelial cells, CCL-34), primary canine kidney epithelial cells (AHDL, Cornell University), primary canine lung epithelial cells (AHDL), and primary bovine testicular cells (AHDL). MDCK and HRT cells were cultured in MEM supplemented with 2.5 ug/mL TPCK-treated trypsin (Sigma); the remaining cell lines were cultured in MEM supplemented with 10% fetal calf serum and
10 antibiotics. Cells were grown in 25 cm² flasks at 37°C in a humidified atmosphere containing 5% CO₂. A control culture was inoculated with the supplemented MEM. The cultures were observed daily for morphologic changes and harvested at 5 days post inoculation. The harvested fluids and cells were clarified by centrifugation and inoculated onto fresh cells as described for the initial inoculation; two blind passages were performed. Hemagglutination
15 activity in the clarified supernatants was determined using chicken or turkey red blood cells as described (Burleson *et al.*, 1992; Kendal *et al.*, 1982). For virus isolation in chicken embryos, 0.1 mL of tissue homogenate was inoculated into the allantoic sac and incubated for 48 hours at 35°C. After two blind passages, the hemagglutination activity in the allantoic fluids was determined as described (Burleson *et al.*, 1992; Kendal *et al.*, 1982).

RT-PCR, nucleotide sequencing, and phylogenetic analyses.

Total RNA was extracted from tissue culture supernatant or allantoic fluid using the RNeasy kit (Qiagen, Valencia, CA) according to manufacturer's instructions. The total RNA (10 ng) was reverse transcribed to cDNA using a one-step RT-PCR Kit (Qiagen, Valencia,
25 CA) according to manufacturer's instructions. PCR amplification of the coding region of the 8 influenza viral genes in the cDNA was performed as previously described (Klimov *et al.*, 1992a), using universal gene-specific primer sets. The resulting DNA amplicons were used as templates for automated sequencing on an Applied Biosystems 3100 automated DNA sequencer using cycle sequencing dye terminator chemistry (ABI). Nucleotide sequences
30 were analyzed using the GCG Package[®], Version 10.0 (Accelrys) (Womble, 2000). The Phylogeny Inference Package[®] Version 3.5 was used to estimate phylogenies and calculate bootstrap values from the nucleotide sequences (Felsenstein, 1989). Phylogenetic trees were compared to those generated by neighbor-joining analysis with the Tamura-Nei gamma

model implemented in the MEGA[®] program (Kumar *et al.*, 2004) and confirmed by the PAUP[®] 4.0 Beta program (Sinauer Associates).

Experimental inoculation of dogs.

5 Four 6-month old specific pathogen-free beagles [(2 males and 2 females (Liberty Research)] were used. Physical examination and baseline blood tests including complete blood cell count/differential, serum chemistry panel, and urinalysis determined that the animals were healthy. They were housed together in a BSL 2-enhanced facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care. Baseline
10 rectal temperatures were recorded twice daily for 7 days. The dogs were anesthetized by intravenous injection of propofol (Diprivan®, Zeneca Pharmaceuticals, 0.4 mg/kg body weight to effect) for intubation with endotracheal tubes. Each dog was inoculated with a total dose of $10^{6.6}$ median tissue culture infectious doses (TCID₅₀) of A/Canine/Florida/43/2004 (Canine/FL/04) (H3N8) virus with half the dose administered into the distal trachea through
15 the endotracheal tube and the other half administered into the deep nasal passage through a catheter. Physical examinations and rectal temperature recordings were performed twice daily for 14 days post inoculation (p.i.). Blood samples (4 mL) were collected by jugular venipuncture on days 0, 3, 5, 7, 10, and 14 p.i. Nasal and oropharyngeal specimens were collected with polyester swabs (Fisher Scientific) from each dog on days 0 to 5, 7, 10, and 14
20 p.i. The swabs were placed in viral transport medium (Remel) and stored at -80°C. Two dogs (1 male and 1 female) were euthanatized by intravenous inoculation of Beuthanasia-D® solution (1 mL/5 kg body weight; Schering-Plough Animal Health Corp) on day 5 p.i. and the remaining 2 dogs on day 14 for postmortem examination. Tissues for histological analysis were processed as described. Tissues for virus culture were stored at -80°C. This study was
25 approved by the University of Florida Institutional Animal Care and Use Committee.

Virus shedding from experimentally inoculated dogs.

Serial dilutions of lung homogenates and swab extracts, prepared by clarification of the swab transport media by centrifugation, were set up in MEM supplemented with 0.5%
30 BSA and antibiotics. Plaque assays were performed as described (Burleson *et al.*, 1992) using monolayers of MDCK cells in 6-well tissue culture plates. Inoculated cell monolayers were overlaid with supplemented MEM containing 0.8% agarose and 1.5 ug/mL of TPCK-trypsin. Cells were cultured for 72 hours at 37°C in a humidified atmosphere containing 5%

CO₂ prior to fixation and staining with crystal violet. Virus concentration was expressed as plaque forming units (PFU) per gram of tissue or per swab.

Immunohistochemistry.

5 Deparaffinized and rehydrated 5-μm lung tissue sections from the greyhounds and beagles were mounted on Bond-Rite™ slides (Richard-Allan Scientific, Kalamazoo, MI) and subsequently treated with proteinase K (DakoCytomation, Carpinteria, CA) followed by peroxidase blocking reagent (Dako® EnVision™ Peroxidase Kit, Dako Corp.). The sections were incubated with 1:500 dilutions of monoclonal antibodies to canine distemper virus
10 (VMRD, Inc.), canine adenovirus type 2 (VMRD, Inc.), canine parainfluenza virus (VMRD, Inc.), or influenza A H3 (Chemicon International, Inc.) for 2 hours at room temperature. Controls included incubation of the same sections with mouse IgG (1 mg/mL, Serotec, Inc.), and incubation of the monoclonal antibodies with normal canine lung sections. Following treatment with the primary antibodies, the sections were incubated with secondary
15 immunoperoxidase and peroxidase substrate reagents (Dako® EnVision™ Peroxidase Kit, Dako Corp.) according to the manufacturer's instructions. The sections were counterstained with hematoxylin, treated with Clarifier #2 and Bluing Reagent (Richard-Allan Scientific, Kalamazoo, MI), dehydrated, and coverslips applied with Permount (ProSciTech).

20 Hemagglutination inhibition (HI) assay.

 Serum samples were incubated with receptor destroying enzyme (RDE, Denka) (1 part serum: 3 parts RDE) for 16 hours at 37°C prior to heat inactivation for 60 minutes at 56°C. Influenza A/Canine/FL/04 (H3N8) virus was grown in MDCK cells for 36-48 hr at 37°C. Virus culture supernatants were harvested, clarified by centrifugation, and stored at -
25 80°C. The HI assay was performed as described previously (Kendal *et al.*, 1982). Briefly, 4 hemagglutinating units of virus in 25μl were added to an equal volume of serially diluted serum in microtiter wells and incubated at room temperature for 30 minutes. An equal volume of 0.5% v/v turkey erythrocytes was added and the hemagglutination titers were estimated visually after 30 minutes. The endpoint HI titer was defined as the last dilution of
30 serum that completely inhibited hemagglutination. Seroconversion was defined as ≥ 4-fold increase in HI titer between paired acute and convalescent samples. Seropositivity of a single sample was defined as a HI antibody titer ≥1:32.

Microneutralization (MN) assay.

Neutralizing serum antibody responses to A/Canine/FL/04 (H3N8) were detected by a MN assay as described previously (Rowe *et al.*, 1999) except that canine sera were RDE-
5 treated as described above prior to the assay. The endpoint titer was defined as the highest dilution of serum that gave 50% neutralization of 100 TCID₅₀ of virus. Seroconversion was defined as ≥ 4 -fold increase in MN titer between paired acute and convalescent samples. Seropositivity of a single sample was defined as a MN titer $\geq 1:80$.

Following are examples which illustrate procedures for practicing the invention.
10 These examples should not be construed as limiting. All percentages are by weight and all solvent mixture proportions are by volume unless otherwise noted.

EXAMPLE 1

In January 2004, an outbreak of respiratory disease occurred in 22 racing greyhounds
15 housed in 2 kennels at a Florida track and the local farm that supplied dogs to these kennels. There were approximately 60 dogs in each kennel building and 300 dogs at the farm. The outbreak occurred over a 6-day period after which no new cases were identified. Fourteen of the 22 dogs had fevers of 39.5 to 41.5°C, a soft, gagging cough for 10 to 14 days, and eventual recovery. Of the remaining 8 dogs, 6 apparently healthy dogs died unexpectedly
20 with hemorrhage from the mouth and nose. Two other dogs were euthanatized within 24 hours of onset of hemorrhage from the mouth and nose due to rapid deterioration. Both of these dogs had fevers of 41°C. Four of the 8 deaths occurred in the kennel buildings and 4 occurred at the farm. Fifty percent of the deaths occurred on day 3 of the outbreak. The 22 dogs ranged in age from 17 months to 4 years, but 73% were 17 to 33 months old.

25 Two clinical syndromes were evident: a milder illness characterized by initial fever and then cough for 10-14 days (14 dogs) with subsequent recovery, or a peracute death associated with hemorrhage in the respiratory tract (8 dogs for a mortality rate of 36%). Postmortem examinations were performed on 6 of the 8 fatal cases. All dogs had extensive hemorrhage in the lungs, mediastinum, and pleural cavity. Histological examination of the
30 respiratory tract revealed that in addition to pulmonary hemorrhage, all dogs had tracheitis, bronchitis, bronchiolitis, and suppurative bronchopneumonia (Figure 3). The epithelial lining and airway lumens in these tissues were infiltrated by neutrophils and macrophages. Lung homogenates prepared from these dogs were inoculated into a variety of monkey, human,

bovine, and canine cell lines for virus culture. The lung homogenate from one dog caused cytopathic effects in Madin-Darby canine kidney epithelial cells (MDCK) cultured in the presence of trypsin, and the cell culture supernatant agglutinated chicken red blood cells. Preliminary evidence of an influenza type A virus was provided by a commercial ELISA for detection of the nucleoprotein of influenza A and B viruses, and by PCR analysis using primers specific for the matrix gene of influenza A viruses. In addition, the hemagglutinating activity was inhibited by reference antisera to the equine influenza A H3 subtype, but not by antisera specific for human influenza A subtypes H1-H11 and H13 (Table 3). To characterize the molecular properties of the virus, we determined the nucleotide sequences of the 8 RNA segments of the viral genome. Sequence comparisons with known influenza virus genes and phylogenetic analyses indicated that the 8 genes of the canine isolate were most similar to those from contemporary equine influenza A (H3N8) viruses, with which they shared ≥ 96 -97% sequence identity (Figure 1A, Table 4). In contrast, representative genes from avian, swine, and human influenza A isolates had ≤ 94 % identity with the canine isolate (Table 4). These data identified the canine isolate A/Canine/Florida/43/04 (Canine/FL/04) as an influenza A H3N8 virus closely related to contemporary lineages of equine influenza viruses. Since all genes of the canine isolate were of equine influenza virus origin, we concluded that the entire genome of an equine influenza virus had been transmitted to the dog.

EXAMPLE 2

To investigate the role of the Canine/FL/04 virus in the clinical and pathological observations in the greyhounds, we performed immunohistochemical staining (IHC) on lung tissues using a monoclonal antibody to influenza A H3. Viral H3 antigen was consistently detected in the cytoplasm of bronchial and bronchiolar epithelial cells, bronchial gland epithelial cells, and macrophages in airway lumens and alveolar spaces (Figure 2A). These data support a diagnosis of pulmonary infection with influenza virus of the H3 subtype in multiple dogs.

EXAMPLE 3

To determine involvement of a Canine/FL/04-like virus in the etiology of the respiratory disease outbreak, we analyzed paired acute and convalescent sera from 11 sick dogs and 16 asymptomatic contacts by hemagglutination inhibition (HI) and

microneutralization (MN). Seroconversion, defined as a ≥ 4 -fold rise in antibody titer to Canine/FL/04 from the acute to convalescent phase, occurred in 8 of 11 (73%) sick dogs in both assays (Table 1). Seroconversion occurred in 6 of 16 (38%) asymptomatic contacts in the HI assay, while 8 of 16 (50%) seroconverted in the MN assay (Table 1). The seroconversion data demonstrated infection of the dogs with a Canine/FL/04-like virus which coincided temporally with the onset of respiratory disease in most animals.

Single serum samples were collected 3 months after the outbreak from an additional 46 asymptomatic dogs housed with the sick dogs. Of these, 43 (93%) were seropositive in both assays. For the total population of 73 dogs tested, 93% were seropositive in both assays, including 82% (9/11) of the sick dogs and 95% (59/62) of the healthy contacts. The high seroprevalence in dogs with no history of respiratory disease indicates that most infections with canine influenza virus are subclinical and suggest efficient spread of the virus among dogs. It is not known if subclinical infections contribute to the spread of the virus.

EXAMPLE 4

To better understand the capacity of the Canine/FL/04 virus to infect dogs, four 6-month old purpose-bred beagles were each inoculated with $10^{6.6}$ median tissue culture infectious doses (TCID₅₀) by the intratracheal and intranasal routes. All dogs developed a fever (rectal temperature $\geq 39^\circ\text{C}$) for the first 2 days postinoculation (p.i.), but none exhibited respiratory symptoms such as cough or nasal discharge over a 14 day observation period. Virus shedding was examined by quantification of virus in nasal and oropharyngeal swabs. Only 2 of the 4 dogs shed detectable amounts of virus. One dog shed virus on days 1 and 2 p.i. (1.0 - $2.5 \log_{10}$ PFU per swab), whereas the other dog shed virus for 4 consecutive days after inoculation (1.4 - $4.5 \log_{10}$ PFU per swab). Postmortem examination of 2 dogs on day 5 p.i. revealed necrotizing and hyperplastic tracheitis, bronchitis, and bronchiolitis similar to that found in the spontaneous disease in greyhounds, but there was no pulmonary hemorrhage or bronchopneumonia. Viral H3 antigen was detected in the cytoplasm of epithelial cells of bronchi, bronchioles, and bronchial glands by IHC (Figure 2B). Infectious virus was recovered from the lung tissue of one of the dogs. Postmortem examination of the remaining 2 dogs on day 14 p.i. showed minimal histological changes in respiratory tissues, no viral H3 antigen by IHC, and no recovery of virus from lung homogenates. Seroconversion in these latter 2 dogs was detected in MN assays by day 7 p.i., with a further 2-to 3-fold increase in antibody titers by day 14. These results established the susceptibility of dogs to infection

with Canine/FL/04, as evidenced by the febrile response, presence of viral antigen and infectious virus in the lung parenchyma, histopathological findings typical for influenza, and seroconversion. The failure to reproduce severe disease and death in the experimentally inoculated beagles is not surprising since a large proportion of the naturally infected greyhounds were asymptomatic.

EXAMPLE 5

To investigate whether a Canine/FL/04-like influenza virus had circulated among greyhound populations in Florida prior to the January 2004 outbreak, archival sera from 65 racing greyhounds were tested for the presence of antibodies to Canine/FL/04 using the HI and MN assays. There were no detectable antibodies in 33 dogs sampled from 1996 to 1999. Of 32 dogs sampled between 2000 and 2003, 9 were seropositive in both assays - 1 in 2000, 2 in 2002, and 6 in 2003 (Table 5). The seropositive dogs were located at Florida tracks involved in outbreaks of respiratory disease of unknown etiology from 1999 to 2003, suggesting that a Canine/FL/04-like virus may have been the causative agent of those outbreaks. To investigate this possibility further, we examined archival tissues from greyhounds that died from hemorrhagic bronchopneumonia in March 2003. Lung homogenates inoculated into MDCK cells and chicken embryos from one dog yielded H3N8 influenza virus, termed A/Canine/Florida/242/2003 (Canine/FL/03). Sequence analysis of the complete genome of Canine/FL/03 revealed >99% identity to Canine/FL/04 (Table 4), indicating that Canine/FL/04-like viruses had infected greyhounds prior to 2004.

EXAMPLE 6

From June to August 2004, respiratory disease outbreaks occurred in thousands of racing greyhounds at 14 tracks in Florida, Texas, Alabama, Arkansas, West Virginia, and Kansas.

Officials at some of these tracks estimated that at least 80% of their dog population had clinical disease. Most of the dogs had clinical signs of fever ($\geq 39^{\circ}\text{C}$) and cough similar to the dogs in the January 2004 outbreak, but many dogs also had a mucopurulent nasal discharge. Multiple deaths were reported but an accurate mortality rate could not be determined.

We collected paired acute and convalescent sera from 94 dogs located at 4 Florida tracks: 56% of these dogs had ≥ 4 -fold rises in antibody titers to Canine/FL/04, and 100%

were seropositive (Table 6). Convalescent sera from 29 dogs in West Virginia and Kansas also had antibodies to Canine/FL/04. We isolated influenza A (H3N8) virus from the lungs of a greyhound that died of hemorrhagic bronchopneumonia at a track in Texas. Sequence analysis of the entire genome of this isolate, named A/Canine/Texas/1/2004 (Canine/TX/04), revealed $\geq 99\%$ identity to Canine/FL/04 (Table 4). The isolation of three closely related influenza viruses from fatal canine cases over a 13-month period and from different geographic locations, together with the substantial serological evidence of widespread infection among racing greyhounds, suggested sustained circulation of a Canine/FL/04-like virus in the dog population.

Phylogenetic analysis of the HA genes of Canine/FL/03, Canine/FL/04, and Canine/TX/04 showed that they constitute a monophyletic group with robust bootstrap support that was clearly distinct from contemporary H3 genes of equine viruses isolated in 2002 and 2003 (Figure 1B). Phylogenetic analysis and pairwise nucleotide sequence comparisons of the other 7 genomic segments supported the segregation of the canine genes as a distinct sub-lineage most closely related to the equine virus lineage (data not shown, and Table 4). The clustering of the canine influenza genes as a monophyletic group separate from equine influenza is also supported by the presence of 4 signature amino acid changes in the HA (Table 2). Together with the serological results from 2003 and 2004, these data are consistent with a single virus transmission event from horses to dogs with subsequent horizontal spread of the virus in the greyhound population. However, repeated introductions of this unique lineage of influenza virus from an unidentified reservoir species can not be formally excluded, unlikely as it may be.

The viral HA is a critical determinant of host species specificity of influenza virus (Suzuki *et al.*, 2000). To identify residues within HA that may be associated with adaptation to the canine host, we compared the deduced amino acid sequence of canine HAs to those of contemporary equine viruses. Four amino acid changes differentiate the equine and canine mature HA consensus amino acid sequences: N83S, W222L, I328T, and N483T (see Table 2). The canine viruses have an amino acid deletion when compared to the consensus equine sequences. Therefore, amino acid position 7 in the HA equine sequence is position 6 in the HA canine sequence, amino acid position 29 in the HA equine sequence is position 28 in the HA canine sequence, amino acid position 83 in the HA equine sequence is position 82 in the HA canine sequence, *etc.* Thus, the four substituted amino acids are at position 82, 221, 327, and 482 of the amino acid sequence shown in SEQ ID NO: 33 and SEQ ID NO: 34. The

substitution of serine for asparagine at consensus sequence position 83 is a change of unknown functional significance since various polar residues are found in H3 molecules from other species. The strictly conserved isoleucine at consensus sequence position 328 near the cleavage site of the H3 HA has been replaced by threonine. The pivotal role of HA cleavage by host proteases in pathogenesis suggests that this change merits further study. The substitution of leucine for tryptophan at consensus sequence position 222 is quite remarkable because it represents a non-conservative change adjacent to the sialic acid binding pocket which could modulate receptor function (Weis *et al.*, 1988). Interestingly, leucine at position 222 is not unique to canine H3 HA since it is typically found in the H4, H8, H9, and H12 HA subtypes (Nobusawa *et al.*, 1991; Kovacova *et al.*, 2002). The leucine substitution may be more compatible with virus specificity for mammalian hosts since infections of swine with subtype H4 (Karasin *et al.*, 2000) and humans and swine with subtype H9 (Peiris *et al.*, 1999) viruses have been reported. The substitution of asparagine with threonine at consensus sequence position 483 resulted in the loss of a glycosylation site in the HA2 subunit that is conserved in all HA subtypes (Wagner *et al.*, 2002). Although the importance of these amino acid changes in the HA for adaptation of an equine virus to dogs remains to be determined, similar amino acid changes have been observed previously in association with interspecies transfer (Vines *et al.*, 1998; Matrosovich *et al.*, 2000). Amino acid differences between other influenza viral proteins of the invention and equine consensus sequence are shown in Tables 19 to 25.

The source of the equine influenza virus that initially infected racing greyhounds remains speculative. Kennels at greyhound racetracks are not located near horses or horse racetracks, suggesting that contact between greyhounds and shedding horses is not a sufficient explanation for the multiple outbreaks in different states in 2004. A potential source of exposure to the equine virus is the feeding of horsemeat to greyhounds, whose diet is supplemented with raw meat supplied by packing houses that render carcasses, including horses which could carry influenza. Precedents for this mode of infection include reports of interspecies transmission of H5N1 avian influenza virus to pigs and zoo felids fed infected chicken carcasses (Webster, 1998; Keawcharoen *et al.*, 2004; Kuiken *et al.*, 2004). Although this is a plausible route for the initial introduction of equine influenza into dogs, it does not explain the recent multiple influenza outbreaks in thousands of dogs in different states. Our experimental inoculation study demonstrated the presence of virus in the nasal passages and oropharynx of dogs, albeit at modest titers. Nevertheless, these results indicate that shedding

is possible, and that dog-to-dog transmission of virus by large droplet aerosols, fomites, or direct mucosal contact could play a role in the epizootiology of the disease.

The interspecies transfer of a whole mammalian influenza virus to an unrelated mammal species is a rare event. Previous studies have provided limited serological or virological evidence, but not both, of transient infection of dogs with human influenza A (H3N2) viruses (Nikitin *et al.*, 1972, Kilbourne, *et al.*, 1975; Chang *et al.*, 1976; Houser *et al.*, 1980). However, there was no evidence of sustained circulation in the canine host. Although direct transfer of swine influenza viruses from pigs to people is well-documented (Dacso *et al.*, 1984; Kimura *et al.*, 1998; Patriarca *et al.*, 1984; Top *et al.*, 1977), there is no evidence for adaptation of the swine viruses in human hosts. In this report, we provide virological, serological, and molecular evidence for interspecies transmission of an entire equine influenza A (H3N8) virus to another mammalian species, the dog. Unique amino acid substitutions in the canine virus HA, coupled with serological confirmation of infection of dogs in multiple states in the U.S., suggest adaptation of the virus to the canine host. Since dogs are a primary companion animal for humans, these findings have implications for public health; dogs may provide a new source for transmission of novel influenza A viruses to humans.

Table 1. Antibody response to A/Canine/Florida/43/04 (H3N8).

	Sick Dogs (11) ^a		Healthy Contacts (16) ^b	
Response	HI ^c	SN ^d	HI	SN
Seroconversion (%) ^e	73	73	38	50
Seropositive (%) ^f	82	82	100	100
Geometric mean titer ^g	329	424	268	431

^a Number of dogs with clinical signs of disease.

^b Number of asymptomatic dogs housed in contact with clinically diseased dogs.

^c Hemagglutination-inhibition (HI) assay using A/Canine/Florida/43/04 virus.

^d Microneutralization (MN) assay using A/Canine/Florida/43/04 virus.

^e Percentage of dogs with at least a 4-fold increase in antibody titer in paired acute and convalescent sera.

^f Percentage of dogs with a positive antibody titer (HI titer ≥ 32 ; MN titer ≥ 80) in the convalescent sera.

^g Geometric mean antibody titer for the convalescent sera.

Table 2. Amino acid differences between the canine and equine H3 hemagglutinins.				
Equine H3 consensus	Can/FL/03	Can/FL/04	Can/TX/04	Potential functional significance
G7*	D	- [†]	-	D also found in duck and human H3 HA
I29	-	M	M	I is conserved in H3 HAs from all species
N83	S	S	S	Various polar amino acids present at this position in H3 HAs of other species
S92	-	N	-	N is present in some duck H3 HAs
L118	-	-	V	L is conserved in all H3 HAs
W222	L	L	L	W is conserved in most H3 HAs of all species; located near the receptor binding site
A272	V	A	V	V is present in some recent equine isolates
I328	T	T	T	T is strictly conserved in all avian, swine or humans H3 HAs
N483	T	T	T	N occurs in all H3 and other HA subtypes. Replacement results in loss of a glycosylation site.
K541	-	R	-	Basic amino acid conservative change

* Amino acid residue (single letter code) and position in the mature H3 HA. The amino acid code is: A=alanine, D=aspartic acid, G=glycine, I=isoleucine, K=lysine, L=leucine, M=methionine, N=asparagine, R=arginine, S=serine, T=threonine, V=valine, W=tryptophan.

[†] Denotes no change from the consensus equine H3 HAs.

Table 3. Hemagglutination inhibition of a virus isolate by reference antisera to different HA subtypes.		
Reference Antisera	HA Specificity	HI titer^a
Puerto Rico/8/34	H1	5
Swine/Iowa15/30	H1	5
Singapore/01/57	H2	5
Shanghai/11/87	H3 ^b	5
Equine/Miami/1/63	H3	160
Duck/Czechoslovakia/56	H4	5
Tern/South Africa/61	H5	5
Turkey/Massachusetts/65	H6	5
Fowl Plague/Dutch/27	H7	5
Fowl Plague/Rostock/34	H7	5
Equine/Prague/1/56	H7	5
Turkey/Ontario/6118/68	H8	5
Quail/Hong Kong/G1/97	H9 ^b	5
Chicken/Hong Kong/G9/97	H9 ^b	5
Chicken/Germany/49	H10	5
Duck/England/56	H11	5
Gull/Maryland/704/77	H13	5
Normal sheep serum	-	5
Normal ferret serum	-	5

^a Hemagglutination inhibition titer to virus isolate from dog # 43.

5 ^b Polyclonal antisera were produced in ferrets, whereas all other antisera were produced in sheep or goats.

Table 4. Sequence homology of A/Canine/Florida/43/04 (H3N8) genes to equine, avian, swine, and human strains of influenza A.				
Gene	Equine	Avian	Swine	Human
PB2 DQ124147	96.9 (98.7) ^a Eq/Kentucky/2/8 M73526	88.6 (96.8) Mall/Alberta/98/85 AY633315	87.9 (96.8) Sw/Ontario/ 01911-1/99 AF285892	86.2 (96.4) PR/8/34 (HK/213/03) AF389115 (AY576381)
PB1 DQ124148	97.1 (98.8) Eq/Tennessee/5/86 M25929	83.9 (97.1) Ck/BritishColumbia/04 (Gull/Md/704/77) AY61675 (M25933)	83.9 (97.1) Sw/Korea/S109/04 (Sw/Saskatch/ 18789/02) AY790287 (AY619955)	83.9 (97.1) WSN/33 (Sing/1/57) J02178 (M25924)
PA DQ124149	96.3 (97.5) M26082 Eq/Tennessee/5/86	87.0 (94.3) Ck/Chile/4591/02 (Ostrich/SA/08103/95) AY303660(AF508662)	84.3 (94.6) Sw/Hong Kong/ 126/02 M26081	83.8 (93.4) Taiwan/2/70 (Viet Nam/ 1203/04) AY210199 (AY818132)
HA (H3) DQ124190	97.4 (97.1) Eq/FL/1/93 L39916	80.7 (89.0) Dk/Norway/1/03 AJ841293	80.0 (87.7) Sw/Ontario/42729a/01 AY619977	81.8 (87.9) HK/1/68 AF348176
NP DQ124150	96.6 (97.9) Eq/Tennessee/5/86 M30758	87.9 (95.1) Ck/Chile/176822/02 AY303658	85.4 (93.5) Sw/Ontario/42729a/01 (Sw/Fujian/1/2003) AY619974 (AY747611)	84.7 (93.0) HK/1073/99 (Hong Kong /538/97) AF255742 (AF255751)
NA (N8) DQ124151	96.8 (97.0) Eq/Tennessee/5/86 L06583	84.0 (85.2) Dk/NJ/2000 L06583	na ^b	na ^b
M DQ124152	97.9 (95.7) Eq/Tennessee/5/86 (Eq/Kentucky/92) M63529 (AF001683)	94.1 (94.0) Tky/Mn/833/80 AF001683	93.7 (93.5) Sw/Saskatchewan/ 18789/02 M63527	91.2 (95.4) WSN/33 (Hong Kong/ 1073/99) J02177 (AJ278646)
NS DQ124153	97.5 (95.7) Eq/Tn/5/86 (Eq/Kentucky/92) M80973 (AF001671)	92.0 (90.4) Mal/NY/6750/78 M80945	91.1 (89.1) Sw/China/8/78 (Sw/Korea/s452/04) M80968 (AY790309)	91.4 (90.0) Brevig Mission/1/18 AF333238

^a Percent nucleotide and amino acid (in parentheses) sequence identity of A/Canine/Florida/43/04 (H3N8) genes to the most homologous gene of influenza virus virus isolates from the species, followed by their Genbank sequence database accession numbers.

^b Not applicable: N8 neuraminidase was never reported in human or swine viruses.

Table 5. Antibody titers to A/canine/Florida/43/04 (H3N8) in greyhound serum collected from 1996 to 2003.						
	Year ^a					
	1996	1997	1998	2000	2002	2003
No. of dogs tested	8	6	19	4	6	22
No. of seropositive dogs	0	0	0	1	2	6
Antibody titers ^b				512	232, 524	280-2242

^a The year of serum sample collection from racing greyhounds in Florida.

^b Microneutralization assay antibody titers for seropositive dogs, including the range for the six 2003 seropositive dogs.

Table 6. Antibody response to A/canine/Florida/43/04 (H3N8) in racing greyhounds at 4 Florida tracks in June 2004.				
Response	Track A	Track B	Track C	Track D
Number of dogs tested ^a	37	10	22	25
Seroconversion (%) ^b	46	90	100	64
Seropositive (%) ^c	100	100	100	100
Geometric mean titer ^d	401	512	290	446

^a Number of clinically diseased dogs tested by HI using A/canine/Florida/43/04 (H3N8).

^b Percentage of dogs with ≥ 4 -fold increase in antibody titer between acute and convalescent sera.

^c Percentage of dogs with a positive antibody titer (HI titer > 16) in the convalescent sera.

^d Geometric mean antibody titer for the convalescent sera.

MATERIALS AND METHODS FOR EXAMPLES 7–11

Canine tissues

Postmortem examinations were performed by the Anatomic Pathology Service at the University of Florida College of Veterinary Medicine on 6 mixed breed dogs that died in April/May 2005 during an influenza outbreak in a shelter facility in northeast Florida, and on a pet Yorkshire Terrier dog that died in May 2005 during an influenza outbreak in a veterinary clinic in southeast Florida. Tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, and 5- μ m sections were stained with hematoxylin and eosin for histopathologic diagnosis. Unfixed tissues were stored at -80°C pending virological analyses.

RNA extraction from canine tissue samples

Frozen lung tissues from each of the 7 dogs were thawed and homogenized in minimum essential medium (MEM) supplemented with 0.5% bovine serum albumin (BSA) and antibiotics (gentamycin and ciprofloxacin) using a disposable tissue grinder (Kendall, Lifeline Medical Inc., Danbury, CT). Total RNA was extracted using a commercial kit (RNeasy® Mini Kit, QIAGEN Inc., Valencia, CA) according to manufacturer's instructions and eluted in a final volume of 60 μ L of buffer. Total RNA was also extracted from lung tissue collected from dogs without respiratory disease.

Real-time RT-PCR

A single-step quantitative real-time RT-PCR was performed on total RNA extracted from the canine tissue samples using the QuantiTect® Probe RT-PCR Kit containing ROX as a passive reference dye (QIAGEN Inc., Valencia, CA). Briefly, 2 primer-probe sets were used for detection of influenza A sequences in each sample (**Table 7**). One primer-probe set was selective for canine hemagglutinin (H3) gene sequences. The other primer-probe set targeted a highly conserved region of the matrix (M) gene of type A influenza virus. For each real-time RT-PCR reaction, 5 μ L of extracted total RNA were added to a reaction mixture containing 12.5 μ L of 2X QuantiTect® Probe RT-PCR Master Mix, 0.25 μ L of QuantiTect® RT Mix, forward and reverse primers (0.4 μ M final concentration for each), probe (0.1 μ M final concentration) and RNase-free water in a final volume of 25 μ L. The TaqMan® Ribosomal RNA Control Reagents (Applied Biosystems, Foster City, CA) were

used according to manufacturer's instructions for detection of 18S rRNA as an endogenous internal control for the presence of RNA extracted from the canine tissue samples.

Quantitative one-step real-time RT-PCR was performed on the reaction mixtures in a Mx3000P[®] QPCR System (Stratagene, La Jolla, CA). Cycling conditions included a reverse transcription step at 50°C for 30 minutes, an initial denaturation step at 95°C for 15 minutes to activate the HotStarTaq[®] DNA polymerase, and amplification for 40 cycles. Each amplification cycle included denaturation at 94°C for 15 seconds followed by annealing/extension at 60°C for 1 minute. The FAM (emission wavelength 518 nm) and VIC (emission wavelength 554 nm) fluorescent signals were recorded at the end of each cycle. The threshold cycle (Ct) was determined by setting the threshold fluorescence (dR) at 1000 in each individual experiment. The Mx3000P[®] version 2.0 software program (Stratagene, La Jolla, CA) was used for data acquisition and analysis. Samples were considered positive for influenza A virus when the threshold cycle (Ct) for the H3 or M gene was 3 units smaller than the Ct for lung tissues from dogs without respiratory disease. The positive control consisted of amplification of RNA extracted from A/canine/FL/242/03 (H3N8) virus.

Virus isolation in MDCK cells

Frozen lung tissues from each of the 7 dogs were thawed and homogenized in 10 volumes of Dulbecco's Modified Eagle Medium (DMEM) supplemented with 0.5% (BSA) and antibiotics (gentamycin and ciprofloxacin). Solid debris was removed by centrifugation and supernatants were inoculated onto Madin-Darby canine kidney (MDCK) cells cultured in DMEM supplemented with 1 µg/mL TPCK-treated trypsin (Sigma-Aldrich Corp., St. Louis, MO) and antibiotics (gentamycin and ciprofloxacin). Cells were grown in 25 cm² flasks at 37°C in a humidified atmosphere containing 5% CO₂. The cultures were observed daily for morphologic changes and harvested at 5 days post inoculation. The harvested cultures were clarified by centrifugation and the supernatants inoculated onto fresh MDCK cells as described for the initial inoculation; two additional passages were performed for samples that did not show evidence of influenza virus by hemagglutination or RT-PCR. Hemagglutination activity in the clarified supernatants was determined using 0.5% turkey red blood cells as previously described (Burleson, F. *et al.*, 1992; Kendal, P. *et al.*, 1982). RT-PCR was performed as described below.

Virus isolation in embryonated chicken eggs

Homogenates were prepared from frozen lung tissues as described above for inoculation of MDCK cells. The homogenates (0.2 mL) were inoculated into the allantoic sac of 10-day old embryonated chicken eggs. After 48 hours of incubation at 35°C, the eggs were chilled at 4°C overnight before harvesting the allantoic fluid. Hemagglutination activity in the clarified supernatants was determined using 0.5% turkey red blood cells as previously described (Burleson, F. *et al.*, 1992; Kendal, P. *et al.*, 1982). RT-PCR was performed as described below. Two additional passages in embryonated eggs were performed for samples that did not show evidence of influenza virus after the initial inoculation.

RT-PCR, nucleotide sequencing, and phylogenetic analyses

Viral RNA was extracted from MDCK supernatant or allantoic fluid using the QIAamp® Viral RNA Mini Kit (QIAGEN Inc., Valencia, CA) according to manufacturer's instructions. The viral RNA was reverse transcribed to cDNA using the QIAGEN® OneStep RT-PCR Kit (QIAGEN Inc., Valencia, CA) according to manufacturer's instructions. PCR amplification of the coding region of the 8 influenza viral genes in the cDNA was performed as previously described (Klimov, A. *et al.*, 1992b), using universal gene-specific primer sets (primer sequences available on request). The resulting DNA amplicons were used as templates for automated sequencing in the ABI PRISM® 3100 automated DNA sequencer using cycle sequencing dye terminator chemistry (Applied Biosystems, Foster City, CA). Nucleotide sequences were analyzed using the Lasergene 6 Package® (DNASTAR, Inc., Madison, WI). The PHYLIP Version 3.5® software program was used to estimate phylogenies and calculate bootstrap values from the nucleotide sequences (Felsenstein, J., 1989). Phylogenetic trees were compared to those generated by neighbor-joining analysis with the Tamura-Nei model implemented in the MEGA® program (Kumar, S. *et al.*, 2004) and confirmed by the PAUP® 4.0 Beta program (Sinauer Associates, Inc., Sunderland, MA).

Hemagglutination inhibition (HI) assay

Serum samples were incubated with receptor destroying enzyme (RDE, DENKA SEIKEN Co., Ltd., Tokyo, Japan) (1 part serum: 3 parts RDE) for 16 hours at 37°C prior to heat inactivation for 30 minutes at 56°C. Influenza A/Canine/Jacksonville/05 (H3N8) virus was grown in MDCK cells for 72 hrs at 37°C in 5% CO₂. Virus culture supernatants were harvested, clarified by centrifugation, and stored at -80°C. All other viruses used in the HI

assay were grown in 10-day old embryonated chicken eggs from which allantoic fluid was collected and stored at -80°C. The HI assay was performed as described previously (Kendal, P. *et al.*, 1982). Briefly, 4 hemagglutinating units of virus in 25µl were added to an equal volume of serially diluted serum in 96-well plastic plates and incubated at room temperature for 30 minutes. An equal volume of 0.5% turkey erythrocytes was added and the hemagglutination titers were estimated visually after 30 minutes. The endpoint HI titer was defined as the last dilution of serum that completely inhibited hemagglutination.

EXAMPLE 7—CLINICAL CASES

In April and May 2005, a previously described (Crawford, P.C. *et al.*, 2005) respiratory disease outbreak occurred in dogs housed in a shelter facility in northeast Florida. The outbreak involved at least 58 dogs ranging in age from 3 months to 9 years, and included purebred dogs as well as mixed breeds. The most common clinical signs were purulent nasal discharge and a cough for 7 to 21 days. Of the 43 dogs that had clinical disease for ≥ 7 days, 41 had HI antibody titers to canine/FL/04 (H3N8) ranging from 32 to >1024. At least 10 dogs progressed to pneumonia, of which 6 were euthanized. These 6 mixed breed dogs included 3 males and 3 females ranging in age from 4 months to 3 years. The duration of clinical signs ranged from 2 to 10 days at the time of euthanasia. On postmortem examination, these dogs had pulmonary congestion and edema. Histological examination of the respiratory tract revealed rhinitis, tracheitis, bronchitis, bronchiolitis, and suppurative bronchopneumonia. There was epithelial cell necrosis and erosion in the trachea, bronchi, bronchioles, and bronchial glands. The respiratory tissues were infiltrated by neutrophils and macrophages.

In May 2005, a respiratory disease outbreak occurred in 40 pet dogs at a veterinary clinic in southeast Florida. The most common clinical signs were purulent nasal discharge and a cough for 10 to 30 days. Of the 40 dogs, 17 were seropositive for canine/FL/04 (H3N8) with HI antibody tiers ranging from 32 to >1024. Seroconversion occurred in 10 dogs for which paired acute and convalescent sera were available. Three dogs progressed to pneumonia. One of these dogs, a 9-year old male Yorkshire Terrier, died 3 days after onset of clinical signs. This dog had tracheobronchitis, pulmonary edema and congestion, and severe bronchopneumonia. Similar to the 6 shelter dogs, there was epithelial cell necrosis and erosion of the airways and neutrophilic infiltrates in the tissues.

EXAMPLE 8—REAL-TIME RT-PCR AND VIRAL ISOLATION

Lung tissues from the 7 dogs were analyzed by quantitative real-time RT-PCR assays that detect the M gene of influenza type A and the H3 gene of canine H3N8 influenza A virus. The lungs from all 7 dogs were positive for both the influenza A M gene and the canine influenza H3 gene (**Table 8**). After 3 passages in MDCK cells, influenza A subtype H3N8 virus was isolated from the lungs of a shelter dog that died after 3 days of pneumonia. This virus was named A/canine/Jacksonville/05 (H3N8) (canine/Jax/05). After 2 passages in embryonated chicken eggs, influenza A subtype H3N8 virus was recovered from the lungs of the pet dog that also died after 3 days of pneumonia. This virus was named A/canine/Miami//05 (H3N8) (canine/Miami/05).

EXAMPLE 9—GENETIC ANALYSES OF THE CANINE INFLUENZA A H3N8 ISOLATES

Sequence analyses of canine/Jax/05 and canine/Miami/05 revealed that their hemagglutinin (HA) genes were 98% identical to the canine/FL/04, canine/TX/04, and canine/Iowa/05 isolates recovered from the lungs of racing greyhounds that died of pneumonia during influenza outbreaks at tracks in 2004 and 2005 (Crawford, P.C. *et al.*, 2005; Yoon K-Y. *et al.*, 2005). In addition, the HA genes of canine/Jax/05 and canine/Miami/05 were 98% identical to contemporary equine influenza viruses isolated after the year 2000. Phylogenetic comparisons of the HA genes showed that the canine/Jax/05 and canine/Miami/05 viruses were clustered with the canine/FL/04, canine/TX/04, and canine/Iowa/05 greyhound isolates and contemporary equine isolates, forming a distinct group from the older equine viruses isolated in the early 1990's (**Figure 4**). Furthermore, the canine/Jax/05, canine/Miami/05, and canine/Iowa/05 isolates were more closely related to canine/Tx/04 than to either canine/FL/04 or canine/FL/03. The 2005 isolates formed a subgroup that appears to branch off from the earlier 2003 and 2004 canine viruses with differences at approximately 10 parsimony-informative sites. These differences support the hypothesis that canine influenza virus is being transmitted horizontally from dog-to-dog as opposed to being reintroduced periodically from an outside source. The accumulation of mutations from 2003 to 2005 illustrates the ongoing process of adaptation that the virus must undergo after being transmitted to a new host, as is expected to have happened for the canine influenza viruses.

EXAMPLE 10—AMINO ACID ANALYSES OF THE CANINE INFLUENZA A H3N8 ISOLATES.

There were conserved amino acid substitutions in all 6 canine isolates that differentiated them from contemporary equine influenza viruses (**Table 9**). These conserved
5 substitutions were I15M, N83S, W222L, I328T, and N483T. Phylogenetic comparisons of the mature HA protein showed that the canine/Jax/05, canine/Miami/05, and canine/Iowa/05 viruses formed a subgroup with the canine/TX/04 isolate (**Figure 4**). There were 3 amino acid changes (L118V, K261N, and G479E) that differentiated this subgroup from the other canine viruses (**Table 9**). There were 2 amino acid changes (F79L and G218E) that
10 differentiated the 2005 isolates from their canine/TX/04 root. Furthermore, the 2005 isolates from non-greyhound dogs, canine/Jax/05 and canine/Miami/05, differed from the canine/Iowa/05 greyhound isolate by one amino acid change, R492K. Finally, canine/Jax/05 differed from canine/Miami/05 at a single amino acid, S107P. In all other H3N8 equine and canine viruses, S is conserved at position 107 except for A/Equine/Jilin/1/89 which has a T
15 (Guo Y. *et al.*, 1992).

EXAMPLE 11—ANTIGENIC ANALYSES OF THE CANINE INFLUENZA A H3N8 ISOLATES

Hemagglutination inhibition (HI) tests were performed using an antigen panel of older
20 and contemporary equine influenza viruses and the canine influenza viruses, and serum collected in 2005 from horses and dogs that had been infected with influenza virus (**Table 10**). Serum from ferrets immunized against canine/FL/04 was also included in the analyses. The HI antibody titers in equine serum were 8 to 16-fold higher when tested with contemporary equine viruses compared to older isolates, but decreased by at least 4-fold
25 when tested with the canine viruses. The canine serum was nonreactive with the older equine viruses, but the antibody titers increased 4-fold when tested with contemporary equine isolates and canine isolates. This was also observed for the serum from ferrets immunized against canine influenza virus. These seroreactivity patterns demonstrated the antigenic similarity between the canine influenza viruses and contemporary equine influenza viruses
30 and were consistent with the phylogenetic analyses. The antibody titers in equine, canine, and ferret sera to the canine/Miami/05 isolate were similar to those for the 2003 and 2004 canine isolates. However, the titers were 2 to 4-fold lower for the canine/Jax/05 isolate. This

Table 7. Primers and probes for quantitative real-time RT-PCR analysis for the matrix gene of influenza A virus and the H3 gene of canine influenza A (H3N8).			
Primer	Target	Sequence	Application
Ca-H3-F387	H3 (nt 387-406)	5'-tatgcatcgcctccgatccat-3' (SEQ ID NO: 79)	Forward primer for H3
Ca-H3-R487	H3 (nt 487-467)	5'-gctccactcttcctgtttga-3' (SEQ ID NO: 80)	Reverse primer for H3
Ca-H3-P430	H3 (nt 430-459)	FAM-aattcacagcagagggaftcacatggacag-BHQ1 (SEQ ID NO: 81)	TaqMan® probe
FluA-M-F151	M (nt 151-174)	5'-catggartggctaaagacaagacc-3' ^a (SEQ ID NO: 82)	Forward primer for M
FluA-M-R276	M (nt 276-253)	5'-agggcatttggacaakcgtcta-3' (SEQ ID NO: 83)	Reverse primer for M
FluA-M-P218	M (nt 218-235)	FAM-acgcTcacgTgccccAgt-BHQ1 ^b (SEQ ID NO: 84)	TaqMan® probe

^a Underlined letter r represents nucleotide a or g and underlined letter k represents nucleotide g or t.

^b Uppercase letters represent locked nucleic acid residues.

Table 8. Quantitative real-time RT-PCR and viral isolation performed on lung tissues from dogs that died from pneumonia during respiratory disease outbreaks in a shelter and veterinary clinic in Florida.

Dog ID	Location	Duration of clinical disease	Real-time RT-PCR		Virus Isolation
			M (Ct)	HA (Ct)	
A/canine/FL/242/03 positive control			28.15	27.36	
1079	Shelter (NE FL)	2 days	29.81	28.84	none
1078	Shelter (NE FL)	3 days	30.37	29.71	MDCK 3 rd passage
318	Shelter (NE FL)	9 days	33.89	32.97	none
320	Shelter (NE FL)	10 days	39.44	37.09	none
319	Shelter (NE FL)	6 days	33.87	32.23	none
1080	Shelter (NE FL)	6 days	38.87	38.23	none
374	Veterinary clinic (SE FL)	3 days	24.05	22.65	Egg 2 nd passage

Table 9. Amino acid comparison of the mature HA for canine influenza viruses and contemporary equine influenza viruses.

	Amino Acid																	
	7	15	54	78	79	83	92	107	118	159	218	222	261	328	479	483	492	541
A/equine/KY/5/02	G	I	N	V	F	N	S	S	L	N	G	W	K	I	G	N	R	K
A/equine/MA/213/03	.	.	.	A	.	.	.	.	.	S	.	.	.	.	.	.	.	.
A/equine/OH/1/03	D	.	K	A	.	.	.	.	.	S	.	.	.	.	.	.	.	.
A/canine/FL/242/03	.	M	K	A	.	S	.	.	.	S	.	L	.	T	.	T	.	.
A/canine/FL/43/04	.	M	K	A	.	S	N	.	.	S	.	L	.	T	.	T	.	R
A/canine/TX/1/04	.	M	K	A	.	S	.	.	V	S	.	L	N	T	E	T	.	.
A/canine/Iowa/05	.	M	K	A	L	S	.	.	V	S	E	L	N	T	E	T	.	.
A/canine/Miami/05	.	M	K	A	L	S	.	.	V	S	E	L	N	T	E	T	K	.
A/canine/Jacksonville/05	.	M	K	A	L	S	.	P	V	S	E	L	N	T	E	T	K	.

Table 10. Antibody titers in equine, canine, and ferret serum to older and contemporary equine influenza viruses and canine influenza viruses.

	Serum antibody titers ^a		
Antigens	Equine	Canine	Ferret ^b
equine/Miami/63	40	<10	16
equine/Ky/86	40	40	32
equine/KY/92	40	<10	32
equine/NY/99	320	40	128
equine/KY/05/02	320	160	256
equine/MA/213/03	640	160	512
equine/OH/01/03	640	160	512
canine/FL/03	160	160	512
canine/FL/04	160	80	512
canine/Tx/04	160	160	512
canine/Miami/05	160	80	256
canine/Jax/05	40	40	128

^a Antibody titers were determined in a hemagglutination inhibition assay performed with serial dilutions of equine, canine, or ferret serum and the viruses listed in the antigen column.

^b Serum from ferrets immunized with canine/FL/04 virus.

MATERIALS AND EXAMPLES METHODS FOR EXAMPLES 12-15

Canine influenza virus inoculum.

The virus inoculum was prepared by inoculation of Madin-Darby canine kidney (MDCK) epithelial cells with a stock of A/canine/FL/43/04 (H3N8) representing passage 3 of the original isolate previously described (Crawford *et al.*, 2005). The inoculated MDCK cells in Dulbecco's Minimal Essential Media (DMEM) supplemented with 1 µg/mL TPCK-treated trypsin (Sigma-Aldrich Corp., St. Louis, MO) and antibiotics (gentamycin and ciprofloxacin) were grown in 250 cm² flasks at 37°C in a humidified atmosphere containing 5% CO₂. The cultures were observed daily for morphologic changes and harvested at 5 days post inoculation. The harvested cultures were clarified by centrifugation and the supernatants were stored at -80°C pending inoculation of dogs. An aliquot of supernatant was used for determination of virus titer by the Reed and Muench method. The titer was 10⁷ median tissue culture infectious doses (TCID₅₀) of A/canine/Florida/43/04 (canine/FL/04) per mL.

Experimental inoculation.

Eight 4-month old colony bred mongrel dogs (Marshall BioResources, North Rose, NY) (4 males and 4 females) were used for the experimental inoculation study approved by the University of Florida Institutional Animal Care and Use Committee. The dogs' body weights ranged from 13 to 17 kg. The dogs were healthy based on physical examinations, baseline blood tests, and recording of body temperatures for 2 weeks prior to inoculation. All dogs were free from prior exposure to canine influenza virus based on serology tests performed on paired serum samples collected at the time of arrival into the facility and 2 weeks later. The dogs were anesthetized by intravenous injection of propofol (Diprivan®, Zeneca Pharmaceuticals, 0.4 mg/kg body weight to effect) for intubation with endotracheal tubes. Six dogs (3 males and 3 females) were each inoculated with 10⁷ TCID₅₀ of canine/FL/04 virus in 5 mL of sterile saline administered into the distal trachea through a small diameter rubber catheter inserted into the endotracheal tube. Two dogs (1 male and 1 female) were sham-inoculated with an equal volume of sterile saline. The sham-inoculated control dogs were housed in a different room from the virus-inoculated dogs and cared for by different personnel. Physical examinations and rectal temperature recordings were performed twice daily for 6 days post inoculation (p.i.).

Pharyngeal and rectal swab collection.

To monitor for virus shedding, oropharyngeal specimens were collected twice daily from each dog on days 0 to 6 p.i. using polyester swabs (Fisher Scientific International Inc., Pittsburgh, PA). The swabs were placed in 1 mL of sterile phosphate-buffered saline (PBS) containing 0.5% bovine serum albumin (BSA). Rectal swabs were collected from each dog daily from days 0 to 6. Swab extracts were prepared by clarification of the swab transport media by centrifugation. An aliquot of swab extract was tested immediately for influenza A virus nucleoprotein using the Directigen™ commercial immunoassay kit (BD, Franklin Lakes, NJ) according to the manufacturer's instructions. The remaining extract was stored at -80°C pending other virological assays.

Postmortem examinations.

On day 1 p.i., one sham-inoculated dog and one virus-inoculated dog were euthanatized by intravenous inoculation of Beuthanasia-D® solution (1 mL/5 kg body weight; Schering-Plough Animal Health Corp). One virus-inoculated dog was similarly euthanatized each day from days 2 to 5 p.i. On day 6 p.i., the remaining sham-inoculated and virus-inoculated dog were euthanatized. Complete postmortem examinations were performed by one of the investigators (WLC). Tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, and 5-µm sections were either stained with hematoxylin and eosin for histopathologic diagnosis or processed for immunohistochemistry as described below. Unfixed lung tissues were submitted to the Diagnostic Clinical Microbiology/Parasitology/Serology Service at the University of Florida College of Veterinary Medicine for bacterial isolation and identification. The samples were cultured on nonselective media as well as media selective for *Bordetella* species (Regan-Lowe; Remel, Lenexa, KS) and *Mycoplasma* species (Remel). All cultures were held for 21 days before reporting no growth. Unfixed tissues were also stored at -80°C pending virological analyses.

Immunohistochemistry.

Deparaffinized and rehydrated 5-µm trachea and lung tissue sections were mounted on Bond-Rite™ slides (Richard-Allan Scientific, Kalamazoo, MI) and subsequently treated with proteinase K (DAKO Cytomation Inc., Carpinteria, CA) followed by peroxidase blocking reagent (DAKO® EnVision™ Peroxidase Kit, DAKO Corp., Carpinteria, CA). The sections were incubated with a 1:500 dilution of monoclonal antibody to influenza A H3

(Chemicon International, Inc., Temecula, CA) for 2 hours at room temperature. Controls included incubation of the same sections with mouse IgG (1 mg/mL, Serotec, Inc. Raleigh, NC), and incubation of the monoclonal antibody with normal canine lung sections. Following treatment with the primary antibody, the sections were incubated with secondary immunoperoxidase and peroxidase substrate reagents (Dako® EnVision™ Peroxidase Kit, 5 Dako Corp.) according to the manufacturer's instructions. The sections were counterstained with hematoxylin, treated with Clarifier #2 and Bluing Reagent (Richard-Allan Scientific, Kalamazoo, MI), dehydrated, and coverslips applied with Permount (ProSciTech, Queensland, Australia).

RNA extraction from swabs and tissues.

Lung and tracheal tissues from each dog were thawed and homogenized in minimum essential medium (MEM) supplemented with 0.5% bovine serum albumin (BSA) and antibiotics (gentamycin and ciprofloxacin) using a disposable tissue grinder (Kendall, 15 Lifeline Medical Inc., Danbury, CT). Total RNA was extracted from the tissue homogenates as well as oropharyngeal and rectal swab extracts using a commercial kit (RNeasy® Mini Kit, QIAGEN Inc., Valencia, CA) according to manufacturer's instructions and eluted in a final volume of 60 µL of buffer.

Real-time RT-PCR.

A single-step quantitative real-time RT-PCR was performed on the total RNA using the QuantiTect® Probe RT-PCR Kit containing ROX as a passive reference dye (QIAGEN Inc., Valencia, CA) and a primer-probe set that targeted a highly conserved region of the matrix (M) gene of type A influenza virus (Payungporn S. *et al.*, 2006a; Payungporn S. *et al.*, 25 2006b). For each real-time RT-PCR reaction, 5 µL of extracted total RNA were added to a reaction mixture containing 12.5 µL of 2X QuantiTect® Probe RT-PCR Master Mix, 0.25 µL of QuantiTect® RT Mix, forward and reverse primers (0.4 µM final concentration for each), probe (0.1 µM final concentration) and RNase-free water in a final volume of 25 µL. The TaqMan® GAPDH Control Reagents (Applied Biosystems, Foster City, CA) were used 30 according to manufacturer's instructions for detection of GAPDH as an endogenous internal control for the presence of RNA extracted from the swab and tissue samples and as a normalization control.

Quantitative one-step real-time RT-PCR was performed on the reaction mixtures in a Mx3000P[®] QPCR System (Stratagene, La Jolla, CA). Cycling conditions included a reverse transcription step at 50°C for 30 minutes, an initial denaturation step at 95°C for 15 minutes to activate the HotStarTaq[®] DNA polymerase, and amplification for 40 cycles. Each amplification cycle included denaturation at 94°C for 15 seconds followed by annealing/extension at 60°C for 1 minute. The FAM (emission wavelength 518 nm) and VIC (emission wavelength 554 nm) fluorescent signals were recorded at the end of each cycle. The threshold cycle (Ct) was determined by setting the threshold fluorescence (dR) at 1000 in each individual experiment. The Mx3000P[®] version 2.0 software program (Stratagene, La Jolla, CA) was used for data acquisition and analysis. The positive control consisted of amplification of RNA extracted from A/canine/FL/242/03 (H3N8) virus. The results were normalized by dividing the M Ct value by the corresponding GAPDH Ct value for each sample.

Virus re-isolation from tissues.

Frozen lung and trachea tissues from virus-inoculated dogs were thawed and homogenized in 10 volumes of DMEM supplemented with 0.5% BSA and antibiotics. Solid debris was removed by centrifugation and supernatants were inoculated onto MDCK cells cultured in DMEM supplemented with 1 µg/mL TPCK-treated trypsin (Sigma-Aldrich Corp., St. Louis, MO) and antibiotics as described above. Cells were grown in 25 cm² flasks at 37°C in a humidified atmosphere containing 5% CO₂. The cultures were observed daily for morphologic changes and harvested at 5 days post inoculation. The harvested cultures were clarified by centrifugation and the supernatants inoculated onto fresh MDCK cells as described for the initial inoculation; two additional passages were performed for samples that did not show evidence of influenza virus by hemagglutination or RT-PCR. Hemagglutination activity in the clarified supernatants was determined using 0.5% turkey red blood cells as previously described (Crawford *et al.*, 2005). RT-PCR was performed as described below.

RT-PCR, nucleotide sequencing, and phylogenetic analyses.

Viral RNA was extracted from MDCK supernatant using the QIAamp[®] Viral RNA Mini Kit (QIAGEN Inc., Valencia, CA) according to manufacturer's instructions. The viral RNA was reverse transcribed to cDNA using the QIAGEN[®] OneStep RT-PCR Kit (QIAGEN

Inc., Valencia, CA) according to manufacturer's instructions. PCR amplification of the coding region of the 8 influenza viral genes in the cDNA was performed as previously described (Crawford *et al.*, 2005), using universal gene-specific primer sets (primer sequences available on request). The resulting DNA amplicons were used as templates for automated sequencing in the ABI PRISM[®] 3100 automated DNA sequencer using cycle sequencing dye terminator chemistry (Applied Biosystems, Foster City, CA). Nucleotide sequences were analyzed using the Lasergene 6 Package[®] (DNASTAR, Inc., Madison, WI). The nucleotide sequences for viruses recovered from infected dogs were compared to the sequences of the virus in the inoculum to determine if any changes had occurred during replication in the respiratory tract.

EXAMPLE 12—CLINICAL DISEASE

All 6 virus-inoculated dogs developed a transient fever (rectal temperature $\geq 39^{\circ}\text{C}$) for the first 2 days p.i., but none exhibited respiratory signs such as cough or nasal discharge over the 6-day observation period. The sham-inoculated dogs remained clinically healthy.

EXAMPLE 13—VIRUS SHEDDING

Influenza A nucleoprotein was detected in the oropharyngeal swab collected from one of the virus-inoculated dogs at 24 hours p.i. The oropharyngeal swabs collected from one dog at 72, 84, and 120 hours p.i., and another dog at 108, 120, and 132 hours p.i., were positive for virus by quantitative real-time RT-PCR (Table 11). The absolute number of influenza M gene copies per μL of swab extract increased with time from 3 to 6 days p.i. No virus was detected in the rectal swabs.

EXAMPLE 14—POSTMORTEM EXAMINATIONS

In contrast to the previous experimental infection using specific pathogen-free Beagles (Crawford *et al.*, 2005), the virus-inoculated mongrel dogs had pneumonia as evidenced by gross and histological analyses of the lungs from days 1 to 6 p.i. In addition to pneumonia, the dogs had rhinitis, tracheitis, bronchitis, and bronchiolitis similar to that described in naturally infected dogs (Crawford *et al.*, 2005). There was epithelial necrosis and erosion of the lining of the airways and bronchial glands with neutrophil and macrophage infiltration of the submucosal tissues (Figure 5, upper panels). Immunohistochemistry detected viral H3 antigen in the epithelial cells of bronchi, bronchioles, and bronchial glands

(Figure 5, lower panels). No bacterial superinfection was present. The respiratory tissues from the 2 sham-inoculated dogs were normal.

EXAMPLE 15—VIRUS REPLICATION IN TRACHEA AND LUNGS

The trachea and lungs were positive for virus by quantitative real-time RT-PCR in all dogs from 1 to 6 days p.i. (Table 12). The absolute number of influenza M gene copies per μL of trachea homogenate increased from 1 to 5 days p.i., then decreased on day 6. The absolute number of M gene copies per μL of lung homogenate decreased from 1 to 6 days p.i. In general, the trachea contained $\geq$ one $\log_{10}$ more virus than the lung on each of the 6 days p.i.

Table 11. Detection of virus shedding in the oropharynx of mongrel dogs inoculated with canine influenza virus by quantitative real-time RT-PCR.

Dog ID	Time p.i. (hours) ^a	M/GAPDH ratio ^b	Matrix gene (copies / μL) ^c
860	72	1.20	1.57E+02
	84	1.30	8.25E+02
	120	1.23	1.47E+03
894	108	1.17	1.17E+02
	120	1.41	1.37E+02
	132	1.27	3.74E+02

^aTime that oropharyngeal swabs were collected from the dogs following inoculation with A/canine/FL/43/04 (H3N8) virus.

^bNormalization ratios were calculated by dividing the M (Ct) by the GAPDH (Ct) for each swab extract.

^cThe absolute number of matrix gene copies per μL of swab extract.

Table 12. Detection of virus replication in the trachea and lung of mongrel dogs inoculated with canine influenza virus by quantitative real-time RT-PCR.					
Dog ID	Time p.i. (hours)^a	M/GAPDH ratio^b		Matrix gene (copies / uL)^c	
		Lung	Trachea	Lung	Trachea
797	24	1.20	1.43	8.22E+05	3.11E+04
801	48	1.33	0.99	1.15E+05	6.52E+06
789	72	1.44	1.12	2.39E+04	1.56E+05
819	96	1.40	1.27	3.19E+04	1.43E+05
860	120	1.59	1.04	3.48E+03	1.17E+06
894	144	1.70	1.15	4.78E+02	1.50E+03

^a Time that tissues were collected from the dogs following inoculation with A/canine/FL/43/04 (H3N8) virus.

^b Normalization ratios were calculated by dividing the M (Ct) by the GAPDH (Ct) for each tissue homogenate.

^c The absolute number of matrix gene copies per uL of tissue homogenate.

MATERIALS AND EXAMPLES METHODS FOR EXAMPLE 16

10 Virus strains

Canine influenza virus strains as well as those of avian, equine and human origin (listed in **Table 15**) were propagated in embryonated eggs or MDCK cells and their infectivity was titrated by endpoint dilution in chicken embryos, or plaque assay. Rapid virus quantification was performed by hemagglutination assay using turkey red blood cell erythrocytes.

Diagnostic specimens

A Total of 60 canine's lung tissues collected from suspect cases of viral respiratory disease during the year of 2005 were tested for the presence of canine influenza virus.

RNA extraction from canine tissue samples

Blocks of lung tissue weighing between 20 and 30 mg were homogenized in a disposable tissue grinder (Kendal). Total RNA was extracted using a commercial kit (RNeasy Mini Kit, Qiagen, Valencia, CA) and eluted in a final volume of 60 μ L, following the manufacturer's recommendations.

Primers and probes design

Multiple sequence alignments of the H3 and M genes from various subtypes and from diverse species were performed using the CLUSTAL X program (Version 1.8). Matrix (M) primers and probe were selected from the conserved regions of over the known sequences corresponding to different subtypes of influenza A virus, whereas the H3 hemagglutinin gene-specific primers and probe set were selected to specifically match equine and canine influenza A virus genes and mismatch the homologous avian and human genes (Table 13). Primer design software (OLIGOS Version 9.1) and the web based analysis tools provided by EXIQON (<http://lnatools.com>) was used for T_m calculation and prediction of secondary structure as well as self hybridization. A conserved region of an 18S rRNA gene was used as endogenous internal control for the presence of RNA extracted from canine tissue sample. The Pre-Developed TaqMan® Assay Reagents for Eukaryotic 18S rRNA (VIC/TAMRA) (Applied Biosystems) was used for the real-time detection of 18S rRNA in tissue samples.

Real-time RT-PCR condition

A single-step real-time RT-PCR was performed by using the Quantitect Probe RT-PCR Kit containing ROX as a passive reference dye (Qiagen, Valencia, CA). In each real-time RT-PCR reaction, 5 μ L of RNA sample were used as a template to combine with a reaction mixture containing 10 μ L of 2X QuantiTech Probe RT-PCR Master Mix, 0.2 μ L of QuantiTech RT Mix, primers (0.4 μ M final conc. for H3 gene or 0.6 μ M final conc. for M gene), probe (0.1 μ M final conc. for H3 gene or 0.2 μ M final conc. for M gene) and RNase-free water in a final volume of 20 μ L. One-step real-time RT-PCR was performed in the Mx3005P Real-Time QPCR System (Stratagene). Cycling conditions included a reverse transcription step at 50°C for 30 minutes. After an initial denaturation step at 95°C for 15 minutes in order to activate the HotStarTaq DNA polymerase, amplification was performed during 40 cycles including denaturation (94°C for 15 seconds) and annealing/extension (60°C

for 30 seconds). The FAM (emission wavelength 516 nm for H3 and M detection) and VIC (emission wavelength 555 nm for 18S rRNA detection) fluorescent signals were obtained once per cycle at the end of the extension step. Data acquisition and analysis of the real-time PCR assay were performed using the Mx3005P software version 2.02 (Stratagene).

Specificity of H3 primers/ probe set for canine influenza (H3N8) and universality of M primers/probe set for type A influenza virus

In order to test the specificity of each primers/probe set, RNA extracted from several known subtypes of influenza A viruses were used as a template in the real-time RT-PCR assay (**Table 15**).

RNA standard for determination of the real-time RT-PCR performance

The genes of canine influenza A virus (A/canine/Florida/242/2003(H3N8)) were used to generate the PCR amplicons for H3 (nt 1-487) and M (nt 1-276) by using primers linked with T7 promoter (**Table 13**). Then the purified PCR amplicons of H3 and M genes were used as templates for *in vitro* transcription by using Riboprobe *in vitro* Transcription System-T7 (Promega) following the manufacturer's recommendations. The concentration of the transcribed RNAs was calculated by measuring absorbance at 260 nm. The RNAs were then serially diluted 10-fold, ranging from 10^8 to 10 copies/ μL to perform sensitivity tests. Moreover, a standard curve was generated by plotting the log of initial RNA template concentrations (copies/ μL) against the threshold cycle (Ct) obtained from each dilution in order to determine the overall performance of real-time RT-PCR.

Comparative sensitivity tests between real-time RT-PCR and Directigen Flu A test kit

Stock viruses of two viral strains including A/Wyoming/3/2003 (H3N2) at $10^{6.67}$ EID₅₀/mL (HA=64) and A/canine/Florida/242/2003(H3N8) at $10^{7.17}$ EID₅₀/mL (HA=16) were used for the detection threshold assay. Logarithmic dilution of specimens in phosphate-buffered saline (PBS) (125 μL) were used in a rapid influenza A antigen detection kit, Directigen Flu A, (Becton, Dickinson and Company) following the manufacturer's instructions. Each Directigen Flu A test device has an H1N1 influenza antigen spot in the center of the membrane which develops as a purple dot and indicates the integrity of the test, which is based on a monoclonal antibody to the nucleoprotein (NP). The development of a

purple triangle surrounding the dot is indicative of the presence of influenza NP in the tested specimen. The intensity of the purple signal from the triangle was scored as + (outline of triangle), ++ (lightly colored triangle), +++ (dark-purple triangle) and ++++ (very dark-purple triangle). Viral RNA was extracted 125 µL aliquots of each virus dilution by using
5 QIAamp Viral RNA Mini Kit (Qiagen, Valencia, CA) and eluting in a final volume of 50 µL. A volume of 5 uL of the extracted viral RNAs were tested by real-time RT-PCR for comparative sensitivity test with Directigen Flu A kit.

EXAMPLE 16

10 The real-time RT-PCR assay for canine influenza relies on information from three molecular probes which target 18S rRNA from host cell as well as M and H3 from the influenza A virus genome (**Table 14**). Amplification of the host gene is a reporter of specimen quality and integrity. Clinical, necropsy or laboratory samples containing canine influenza (H3N8) virus are expected to yield amplification signal with the three probes.
15 Specimens yielding amplification signal with M and 18S rRNA probes but negative for H3 would be indicative of an influenza virus subtype H3 from human, swine or avian origin or from non-H3 subtypes. These rare cases could be resolved by RT-PCR using HA universal primers to generate amplicon cDNA that can be analyzed by sequencing. Properly collected and handled specimens lacking influenza A virus yield 18S rRNA amplification signal only.
20 Situations in which only the 18S rRNA probe and the H3 probes yield amplification signal are indicative of faulty technique, unless proven otherwise; either a false negative with M probes or false positive for H3 need to be demonstrated. Finally, specimens failing to yield amplification signals with the three probes are indicative of defective sample collection, degradation, faulty RNA extraction or the presence of inhibitors the polymerases used in
25 PCR.

In order to test the specificity of the H3 primers/probe set for canine influenza A virus (H3N8) and the universality of M primers/probe set for type A influenza, several subtypes of influenza A viruses were tested by real-time RT-PCR. The results show that H3 primers/probe set yielded a positive amplification signal only with canine influenza (H3N8).
30 No significant false positive or non-specific amplification signals were observed in other subtypes or human H3 strains. The M primers/probe set yielded positive amplification signal with all of the strains tested (**Table 15**). These results indicated that H3 primers/probe

specifically detects canine influenza A virus (H3N8) whereas M primers/probe detect multiple subtypes of type A influenza viruses.

The performance of real-time RT-PCR assays was evaluated by endpoint dilution of M and H3 *in vitro* transcribed RNAs. As expected, the threshold cycle (Ct) increased in
5 direct correlation with the dilution of the RNA standards. The fluorescent signals can be detected at RNA standard dilutions of M and H3 as low as 10^3 and 10^2 copies/ μ L, respectively (**Figure 6A and 6B**). The standard curves of M and H3 genes were constructed by plotting the log of starting RNA concentrations against the threshold cycle (Ct) obtained from each dilution (**Figure 6C and 6D**). The slope of the standard curve is used to determine
10 the PCR reaction efficiency, which is theoretically exponential; 100% amplification efficiency would imply doubling of amplicon concentration each cycle. The standard curves with a slope between approximately -3.1 and -3.6 are typically acceptable for most applications requiring accurate quantification (90-110 % reaction efficiency). An Rsq value is the fit of all data to the standard curve plot. If all the data lie perfectly on the line, the Rsq
15 will be 1.00. As the data fall further from the line, the Rsq decreases. An Rsq value ≥ 0.985 is acceptable for most assays. The M standard curve revealed a slope of -3.576 (efficiency= 90.4 %) and Rsq= 1.00 whereas H3 standard curve yielded a slope of -3.423 (efficiency= 95.9%) and Rsq= 0.999. These values indicate satisfactory amplification efficiency and overall performance of the real-time RT-PCR assays. We attribute the lower efficiency and
20 sensitivity of M primers/probe set as compared to H3 primers/probe set to the N-fold degeneracy of M primer sequences required to ensure broad coverage of M gene sequences variability across viruses of multiple subtypes, hosts and lineages.

The sensitivity of real-time RT-PCR assay was also compared with the commercial rapid antigen detection assay (Directigen Flu A). Logarithmic dilutions of
25 A/Wyoming/3/2003 (H3N2) and A/canine/Florida/242/2003(H3N8) were analyzed with Directigen Flu A and by real-time RT-PCR. The results of Directigen Flu A showed that the sensitivities against both viral strains are approximately 100-fold dilution from the stock viruses used in these experiments (**Figure 7**). The signals (purple color) generated by the canine virus (A/canine/Florida/242/2003: $10^{6 \times}$ PFU/ml) samples were much weaker than
30 those found in human virus (A/Wyoming/3/2003: $10^{7 \times}$ PFU/ml), in agreement with the lower virus concentration in these samples. Alternatively, lower signal for canine influenza could

be attributed to the molecular specificity of monoclonal antibodies against the NP; *i.e.* poor conservation of the amino acids within the NP epitope of canine influenza A viruses.

Real-time RT-PCR of the M gene yielded Ct values above threshold with virus 10 and 30 PFU equivalents per reaction of A/canine/Florida/242/2003 and A/Wyoming/3/2003, respectively (**Table 16**). The differences between the sensitivity value of 2 viral strains because the differences in the original viral titers. The H3 gene detection comparison between canine and human influenza viruses was not performed because the H3 primers/probe in our realtime RT-PCR assay amplifies exclusively canine influenza A virus. RT-PCR was 10^5 times more sensitive than the rapid antigen detection kit.

To evaluate the performance of the RT-PCR test in necropsy specimens from dogs with acute respiratory disease, sixty canine lung tissue samples submitted during the year of 2005 were tested for the presence of canine influenza A virus by real-time RT-PCR. A total of 12 out of 60 samples (20%) were positive with both M and H3 genes whereas the remaining 48 samples yielded negative result for both M and H3 gene. Virus isolation attempts were conducted by egg and MDCK cell inoculation, to evaluate the specificity of the realtime assay; 2 out 12 samples that were positive for canine influenza by RT-PCR yielded canine influenza virus (data not shown, manuscript in preparation). Although all of the tissues were collected from dogs with a history of severe respiratory disease, most of the samples yielded no canine influenza virus by either realtime PCR or conventional isolation, suggesting a high incidence of other respiratory pathogens such as *Bordetella bronchiseptica*, canine distemper or parainfluenza virus. The single step real-time RT-PCR assay herein provides a rapid, sensitive and cost-effective approach for canine influenza A virus (H3N8) detection. Rapid laboratory diagnosis of canine influenza A virus (H3N8) infections in the early stage of the disease can yield information relevant to clinical patient and facility management.

Table 13: Primers and probes used for real-time RT-PCR detection and in vitro transcription				
Oligo name	Type	Target	Sequence *	Application
Ca-H3-F387	Forward primer	H3 (nt 387-406)	5'-tatgcatcgctccgatccat-3' (SEQ ID NO: 79)	Real-time PCR
Ca-H3-R487	Reverse primer	H3 (nt 487-467)	5'-gctccactcttccgttttga-3' (SEQ ID NO: 80)	
Ca-H3-P430	TaqMan probe	H3 (nt 430-459)	FAM-aattcacagcagagggattcacatggacag-BHQ1 (SEQ ID NO: 81)	
FluA-M-F151	Forward primer	M (nt 151-174)	5'-catggartggctaaagacaagacc-3' (SEQ ID NO: 82)	Real-time PCR
FluA-M-R276	Reverse primer	M (nt 276-253)	5'-agggcattttggacaacaakcgtcta-3' (SEQ ID NO: 83)	
FluA-M-P218	LNA TaqMan probe	M (nt 218-235)	FAM-acgcTcaccgTgccAgt-BHQ1 (SEQ ID NO: 84)	
H3-F1	Forward primer	H3 (nt 1-14)	5'-tattcgtctcaggaggagcaaaagcagggg-3' (SEQ ID NO: 85)	<i>In vitro</i> transcription
T7/H3-R490	Reverse primer	T7 / H3 (nt 487-467)	5'-tgtaatacgcactcactatagggctccacttcttccgtttga-3' (SEQ ID NO: 86)	
M-F1	Forward primer	M (nt 1-15)	5'-gatcgcctcttcaggaggagcaaaagcaggtag-3' (SEQ ID NO: 87)	
T7 / M-R276	Reverse primer	M (nt 276-253)	5'-tgtaatacgcactcactatagggcatttttggacaagcgtc-3' (SEQ ID NO: 88)	<i>In vitro</i> transcription

* Note: Uppercases = LNA (Locked Nucleic Acid) residues, r = a or g, k = g or t, underline = T7 promoter sequence

Table 14: Interpretation of the real-time RT-PCR assay			
Interpretation	Results		
	M	H3	18S rRNA
Positive for canine influenza A virus (H3N8)	+	+	+
Positive for influenza A virus (unknown subtype)	+	-	+
Negative for influenza A virus	-	-	+
Error in RNA extraction or presence of PCR inhibitor	-	-	-

Table 15: Specificity test of canine H3 primers/probe set and universality test of M primers/probe set with several subtypes of influenza A viruses				
Subtypes	Strain Name	Host	Real-time RT-PCR detection	
			H3 gene (Ct)	M gene (Ct)
H1	A/Ohio/1983	Human	No Ct	15.40
	A/WSN/1933	Human	No Ct	20.09
H3	A/Wyoming/3/2003	Human	No Ct	28.85
	A/Victoria/3/1975	Human	No Ct	16.62
	A/canine/FL/242/2003	Canine	28.43	29.25
H4	Turkey/MN/1066/1980	Avian	No Ct	17.49
	Clinical sample*	Avian	No Ct	20.87
H5	AChicken/Thailand/CUK2/2004	Avian	No Ct	20.13
	A/Pheasant/NJ/1335/1998	Avian	No Ct	16.64
H6	Clinical sample*	Avian	No Ct	19.52
H10	Clinical sample*	Avian	No Ct	25.64
	Clinical sample*	Avian	No Ct	19.59
H11	Clinical sample*	Avian	No Ct	15.72
	Clinical sample*	Avian	No Ct	24.55

* Note that subtypes of clinical samples were confirmed by nucleotide sequencing.

Virus	Directigen Flu A	Real-time RT-PCR of M (Ct)
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dilutions				
	A/canine/242/03	A/Wyoming/3/03	A/canine/242/03	A/Wyoming/3/2003
10 ⁻¹	++	++++	22.42	19.48
10 ⁻²	+	+++	25.85	22.66
10 ⁻³	-	-	29.27	25.76
10 ⁻⁴	Not done	Not done	32.66	28.66
10 ⁻⁵	Not done	Not done	35.48	33.14
10 ⁻⁶	Not done	Not done	37.51	35.06
10 ⁻⁷	Not done	Not done	39.09	36.44
10 ⁻⁸	Not done	Not done	No Ct	38.93

Class of Amino Acid	Examples of Amino Acids
Nonpolar	Ala, Val, Leu, Ile, Pro, Met, Phe, Trp
Uncharged Polar	Gly, Ser, Thr, Cys, Tyr, Asn, Gln
Acidic	Asp, Glu
Basic	Lys, Arg, His

Table 18.			
Letter Symbol	Amino Acid	Letter Symbol	Amino Acid
A	Alanine	M	Methionine
B	Asparagine or aspartic acid	N	Asparagine
C	Cysteine	P	Proline
D	Aspartic Acid	Q	Glutamine
E	Glutamic Acid	R	Arginine
F	Phenylalanine	S	Serine
G	Glycine	T	Threonine
H	Histidine	V	Valine
I	Isoleucine	W	Tryptophan
K	Lysine	Y	Tyrosine
L	Leucine	Z	Glutamine or glutamic acid

Table 19. Amino acid differences between PB2 proteins of H3N8 equine and canine influenza viruses

Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
5	K	K	E
12	S	L	L
37	G	G	E
175	R	R	I
374	L	I	I
375	R	R	K
447	Q	Q	H

5

Table 20. Amino acid differences between PB1 proteins of H3N8 equine and canine influenza viruses

Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
114	V	I	I
154	D	G	G
221	A	T	T
317	M	I	I
459	I	I	V
682	I	I	V

Table 21. Amino acid differences between PA proteins of H3N8 equine and canine influenza viruses			
Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
27	D	N	N
62	I	V	V
213	R	K	K
337	A	T	T
343	A	E	E
345	L	I	I
353	K	R	R
400	T	T	A
450	V	I	I
460	M	M	I
673	R	R	K
675	N	D	D

*Based on available genes of viruses isolated between 1963 and 1998.

5

Table 22. Amino acid differences between NP proteins of H3N8 equine and canine influenza viruses			
Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
16	G	D	D
157	A	T	T
214	R	R	K
285	V	V	I
286	A	T	T
359	A	T	T
375	D	D	N
384	R	K	K
452	R	K	K

10

Table 23. Amino acid differences between NA proteins of H3N8 equine and canine influenza viruses

Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
9	A/T	T	A
12	S	F	F
20	L	I	I
40	G	R	R
42	G	D	D
46	N	K	K
52	E	E	K
61	R	K	K
69	N	S	S
72	E	K	K
201	V	I	I
261	I	V	V
301	I	I	V
396	N	D	D
397	L	P	P

5

Table 24. Amino acid differences between M1 proteins of H3N8 equine and canine influenza viruses

Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
M1 161	S	S	A
M1 208	K/Q	R	R

*Based on available genes of viruses isolated between 1963 and 1998.

10

Table 25. Amino acid differences between NS1 proteins of H3N8 equine and canine influenza viruses

Position	Equine Consensus *	Canine/FL/03	Canine/FL/04
44	K	R	R
59	R	H	H
71	E	K	K
86	A	T	T
88	R	R	L
140	R	G	G
216	P	S	S

* Based on available genes of viruses isolated between 1963 and 1998.

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of
5 this application.

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CLAIMS

We claim:

1. An isolated canine influenza virus that is capable of infecting a canid animal, wherein said influenza virus is a type A influenza virus.

2. The influenza virus according to claim 1, wherein said influenza virus has an HA serotype of H3 or H5.

3. The influenza virus according to claim 1, wherein said influenza virus has the serotype H3N8.

4. The influenza virus according to claim 1, wherein said influenza virus comprises a polynucleotide which encodes a polypeptide having the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78.

5. The influenza virus according to claim 1, wherein said influenza virus comprises a polynucleotide having the nucleotide sequence shown in any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or said polynucleotide has 98% or greater sequence identity with the nucleotide sequence shown in any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77.

6. An isolated polynucleotide that comprises all or part of a genomic segment or gene of an influenza virus of any of claims 1 to 5.

7. The polynucleotide according to claim 6, wherein said polynucleotide comprises all or part of an influenza gene selected from the group consisting of a neuraminidase gene, a

nucleoprotein gene, a matrix protein gene, a polymerase basic protein gene, a polymerase acidic protein gene, a non-structural protein gene, and a hemagglutinin gene.

8. The polynucleotide according to claim 6, wherein said influenza virus comprises a polynucleotide which encodes a polypeptide having the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78.

9. The polynucleotide according to claim 6, wherein said influenza virus comprises a polynucleotide having the nucleotide sequence shown in any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77, or said polynucleotide has 98% or greater sequence identity with the nucleotide sequence shown in any of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, or 77.

10. A polynucleotide expression construct comprising a polynucleotide of any of claims 6 to 9.

11. An oligonucleotide that can hybridize to a coding or a non-coding sequence of a polynucleotide of any of claims 6 to 9.

12. The oligonucleotide according to claim 11, wherein said oligonucleotide hybridizes to said sequence under high stringency conditions.

13. The oligonucleotide according to claim 11, wherein said oligonucleotide is 10 to 500 nucleotides, 10 to 20 nucleotides, 21 to 30 nucleotides, 31 to 40 nucleotides, 41 to 50 nucleotides, 51 to 60 nucleotides, 61 to 70 nucleotides, 71 to 80 nucleotides, 81 to 90 nucleotides, or 91 to 100 nucleotides in length.

14. The oligonucleotide according to claim 11, wherein said oligonucleotide comprises a detectable label or a reporter molecule.

15. The oligonucleotide according to claim 11, wherein said oligonucleotide has from about 90 percent to 100 percent nucleotide sequence identity with a polynucleotide of claim 6.

16. The oligonucleotide according to claim 11, wherein said oligonucleotide comprises a nucleotide sequence shown in any of SEQ ID NOs: 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 79, 80, 81, 82, 83, 84, 85, 86, 87, or 88.

17. An isolated polypeptide encoded by a polynucleotide of any of claims 6 to 9.

18. The polypeptide according to claim 17, wherein said polypeptide is selected from the group consisting of a hemagglutinin protein, a neuraminidase protein, a nucleoprotein, a matrix protein, a polymerase basic protein, a polymerase acidic protein, and a non-structural protein.

19. A composition comprising an immunogen of an influenza virus of any of claims 1 to 5, wherein said immunogen is capable of inducing an immune response against an influenza virus that is capable of infecting a canid animal.

20. The composition according to claim 19, wherein said immunogen comprises cell-free whole virus, or a portion thereof; a viral polynucleotide; a viral protein; a viral polypeptide or peptide; a virus infected cell; a recombinant viral vector based construct; a reassortant virus; or naked nucleic acid of said virus.

21. The composition according to claim 20, wherein said viral protein, polypeptide, or peptide comprises an amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78.

22. The composition according to claim 20, wherein said viral polynucleotide encodes a polypeptide comprising an amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment thereof.

23. A method for inducing an immune response in an animal against an influenza virus of any of claims 1 to 5, said method comprising administering to said animal an effective amount of a composition according to any of claims 19, 20, 21, or 22.

24. The method according to claim 23, wherein said composition comprises a viral protein, polypeptide, or peptide comprising an amino acid sequence shown in any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 33, 34, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, or 78, or a functional and/or immunogenic fragment thereof.

25. The method according to claim 23, wherein said immune response is a protective immune response that prevents or inhibits infection of said animal by an influenza virus.

26. The method according to claim 23, wherein said influenza virus has an HA serotype selected from H3 and H5.

27. The method according to claim 23, wherein said influenza virus has the serotype H3N8.

28. The method according to claim 23, wherein said composition further comprises an adjuvant.

29. The method according to claim 23, wherein said animal is a canid.

30. The method according to claim 29, wherein said canid animal is a domesticated dog.

31. The method according to claim 23, wherein said composition is administered parenterally.

32. The method according to claim 31, wherein said composition is administered subcutaneously, intraperitoneally, or intramuscularly.

33. The method according to claim 23, wherein said composition is administered nasally or orally.

34. An isolated antibody that binds specifically to an epitope of a polypeptide of any of claims 17 or 18.

35. The antibody according to claim 34, wherein said antibody is a monoclonal antibody.

36. The antibody according to claim 34, wherein said antibody binds to a hemagglutinin protein.

37. The antibody according to claim 36, wherein said hemagglutinin protein is an H3 or an H5 hemagglutinin protein.

38. The antibody according to claim 36, wherein said hemagglutinin protein comprises an amino acid sequence shown in SEQ ID NO: 16, SEQ ID NO: 32, SEQ ID NO: 62, or SEQ ID NO: 78.

39. A cell comprising an influenza virus of any of claims 1 to 5 or a polynucleotide of claim 6.

40. The cell according to claim 39, wherein said cell is a canid animal cell.

41. A method for detection of an influenza virus of that is capable of infecting a canid animal, said method comprising obtaining a biological sample from an animal and screening said sample for the presence of an antibody or a ligand that binds to a protein, polypeptide, or peptide of an influenza virus of any of claims 1 to 5.

42. A method for detection of an influenza virus that is capable of infecting a canid animal, said method comprising obtaining a nucleic acid sample from an animal, and contacting said nucleic acid sample with an oligonucleotide according to any of claims 11 to 16, and determining if said oligonucleotide hybridizes under stringent conditions to said nucleic acid.

43. A method for screening for a compound that possesses antiviral activity against an influenza virus that is capable of infecting a canid animal, said method comprising contacting a cell infected with or comprising a virus of any of claims 1 to 5 with a test compound and determining whether said test compound inhibits activity of said virus in said cell.

44. A reassortant virus comprising at least one gene, genomic segment, or a polynucleotide of an influenza virus of claim 1.

45. An isolated virus that comprises one or more polynucleotides wherein said one or more polynucleotides encode a canine influenza virus protein selected from the group consisting of HA, NA, NP, MA, PBI, PB2, PA, and NS, or a functional or immunogenic fragment thereof.

46. The virus according to claim 45, wherein said one or more polynucleotides comprise a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, and 77.

47. The virus according to claim 45, wherein said HA protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 16, 32, 62, and 78.

48. The virus according to claim 45, wherein said NA protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 12, 28, 58, and 74.

49. The virus according to claim 45, wherein said NP protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 10, 26, 56, and 72.

50. The virus according to claim 45, wherein said MA protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 30, 60, and 76.

51. The virus according to claim 45, wherein said PBI protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 20, 50, and 66.

52. The virus according to claim 45, wherein said PB2 protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 18, 48, and 64.

53. The virus according to claim 45, wherein said PA protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 6, 22, 52, and 68.

54. The virus according to claim 45, wherein said NS protein has an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 24, 54, and 70.

55. The influenza virus according to claim 1, wherein said influenza virus comprises a polynucleotide which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:33, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence of SEQ ID NO:33.

56. The influenza virus according to claim 1, wherein said influenza virus comprises a polynucleotide encoding a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

57. The influenza virus according to claim 1, wherein said influenza virus comprises a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

58. The influenza virus according to claim 56, wherein said polynucleotide encodes a hemagglutinin (HA) that comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

59. The influenza virus according to claim 57, wherein said hemagglutinin (HA) comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

60. The polynucleotide according to claim 6, wherein said polynucleotide encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:33, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence of SEQ ID NO:33.

61. The polynucleotide according to claim 6, wherein said polynucleotide encodes a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

62. The polynucleotide according to claim 61, wherein said polynucleotide encodes a hemagglutinin (HA) that comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

63. The polynucleotide expression construct according to claim 10, wherein said polynucleotide encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:33, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence of SEQ ID NO:33.

64. The polynucleotide expression construct according to claim 10, wherein said polynucleotide encodes a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at

position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

65. The polynucleotide expression construct according to claim 64, wherein said polynucleotide encodes a hemagglutinin (HA) that comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

66. The oligonucleotide according to claim 11, wherein said polynucleotide encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:33, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence of SEQ ID NO:33.

67. The oligonucleotide according to claim 11, wherein said polynucleotide encodes a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

68. The oligonucleotide according to claim 67, wherein said polynucleotide encodes a hemagglutinin (HA) that comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

69. The polypeptide according to claim 17, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:33, or a functional and/or immunogenic fragment thereof, or said polypeptide has 99% or greater sequence identity with the amino acid sequence of SEQ ID NO:33.

70. The polypeptide according to claim 17, wherein said polypeptide is a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

71. The polypeptide according to claim 70, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

72. The composition according to claim 19, wherein said influenza virus comprises a polynucleotide which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:33, or a functional and/or immunogenic fragment thereof, or said polynucleotide encodes a polypeptide having 99% or greater sequence identity with the amino acid sequence of SEQ ID NO:33.

73. The composition according to claim 19, wherein said influenza virus comprises a polynucleotide encoding a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

74. The composition according to claim 19, wherein said influenza virus comprises a hemagglutinin (HA) comprising the amino acid sequence of SEQ ID NO:33, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:33, wherein said HA protein comprises a serine at position 82, a leucine at position 221, a threonine at position 327, and a threonine at position 482 of the amino acid sequence.

75. The composition according to claim 73, wherein said polynucleotide encodes a hemagglutinin (HA) that comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

76. The composition according to claim 74, wherein said hemagglutinin (HA) comprises the amino acid sequence of SEQ ID NO:16, or an amino acid sequence having greater than 95% amino acid sequence identity to SEQ ID NO:16.

77. The method according to claim 23, wherein said method comprises administering to said animal an effective amount of a composition of any of claims 72 to 76.

78. The antibody according to claim 34, wherein said antibody binds specifically to an epitope of a polypeptide of any of claims 69, 70, or 71.

79. The cell according to claim 39, wherein said cell comprises an influenza virus of any of claims 57 to 61 or a polynucleotide of any of claims 60 to 62.

80. The reassortant virus according to claim 44, wherein said reassortant virus comprises at least one gene, genomic segment, or a polynucleotide of an influenza virus of any of claims 55 to 59.

81. The virus according to claim 45, wherein said virus comprises one or more polynucleotides of any of claims 60 to 62.

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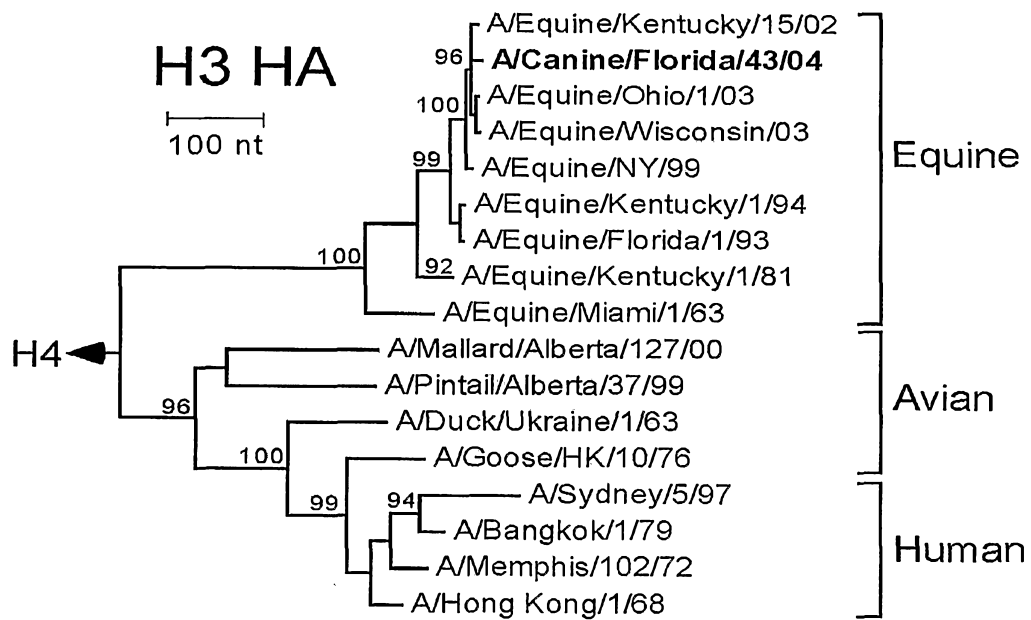


FIG. 1A

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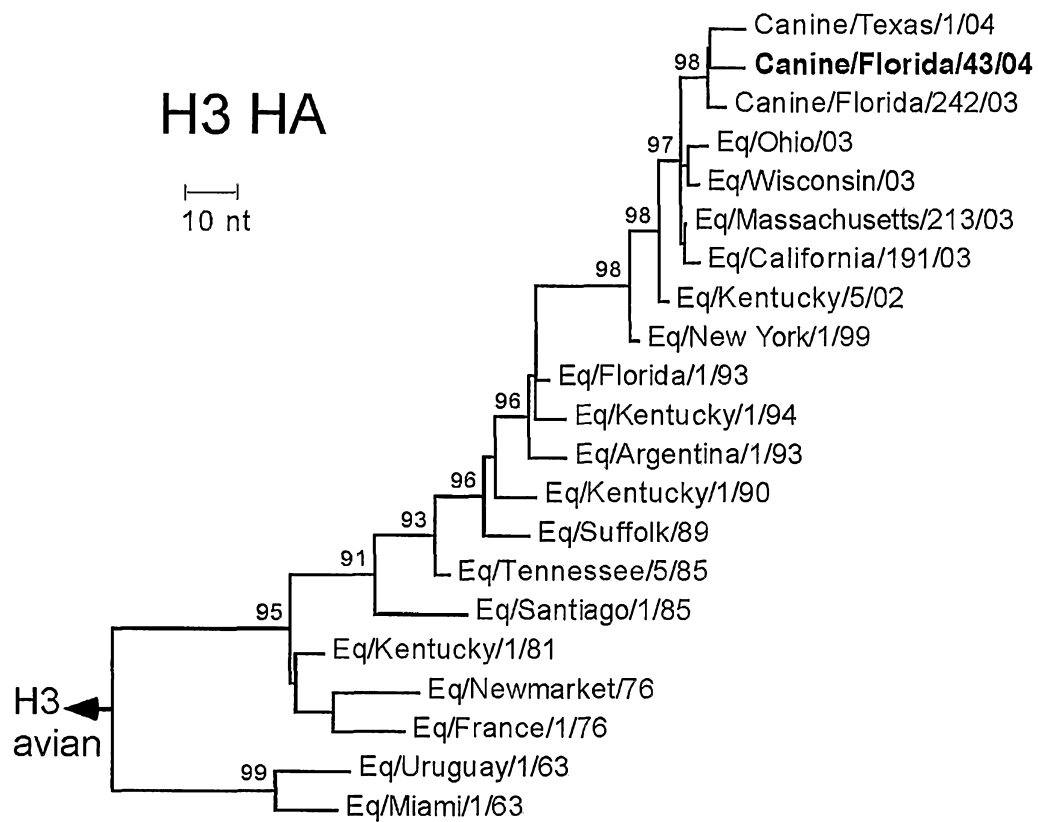


FIG. 1B

FIG. 2A

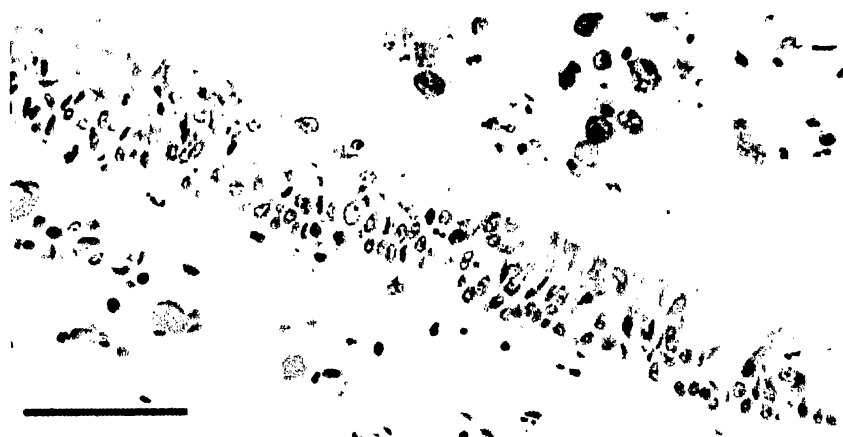
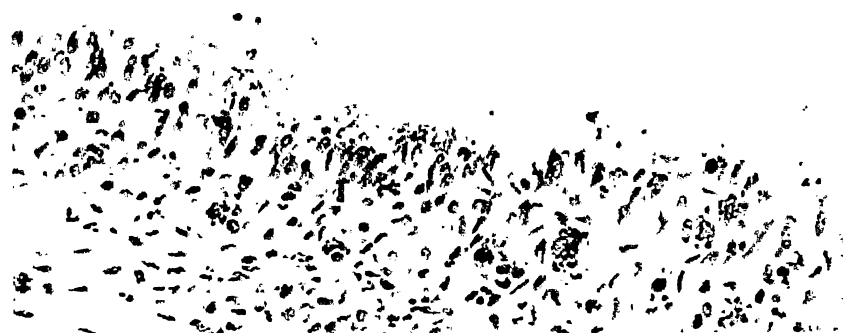


FIG. 2B



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FIG. 3A



FIG. 3B

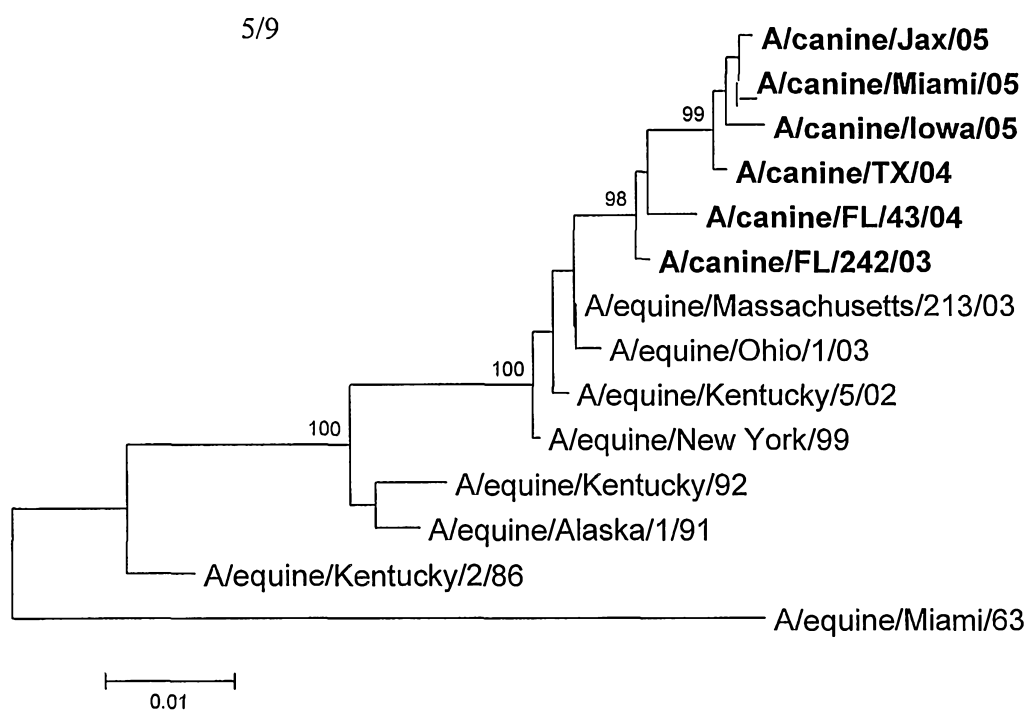


FIG. 4A

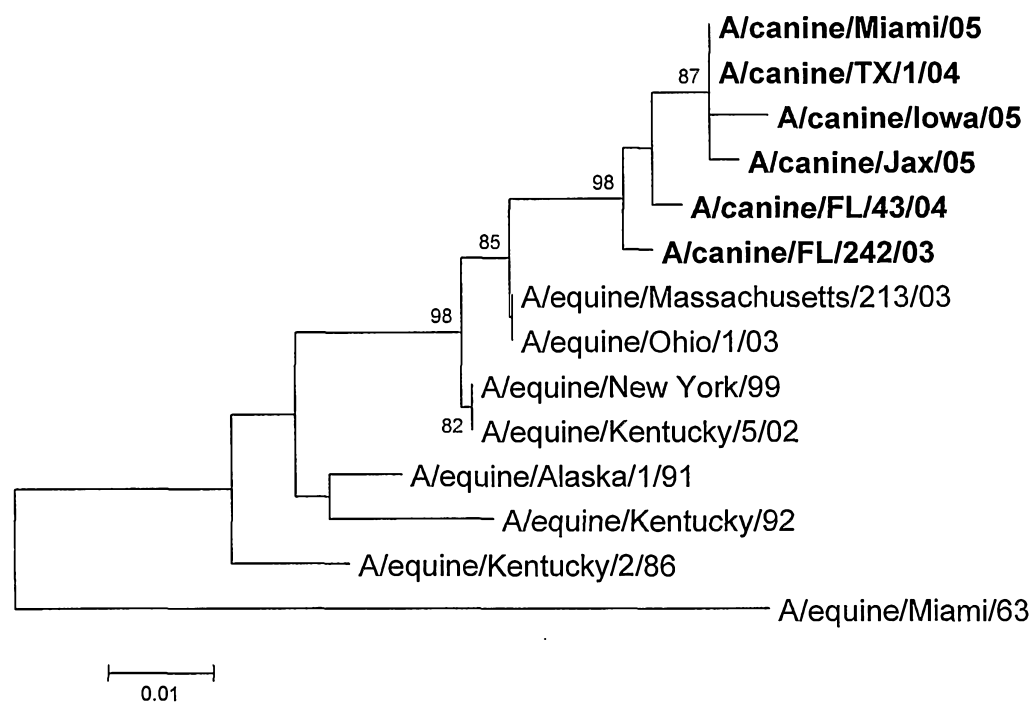


FIG. 4B

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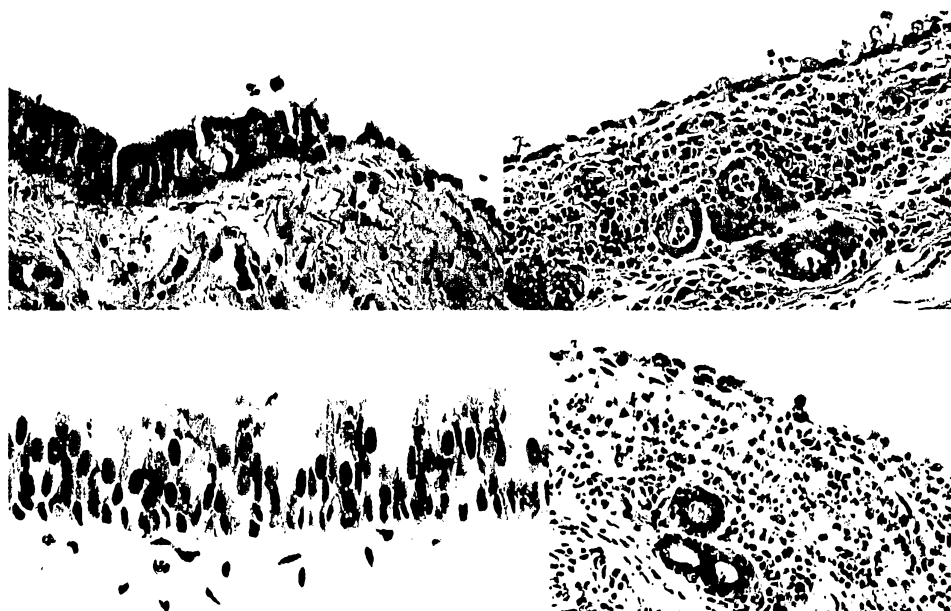


FIG. 5

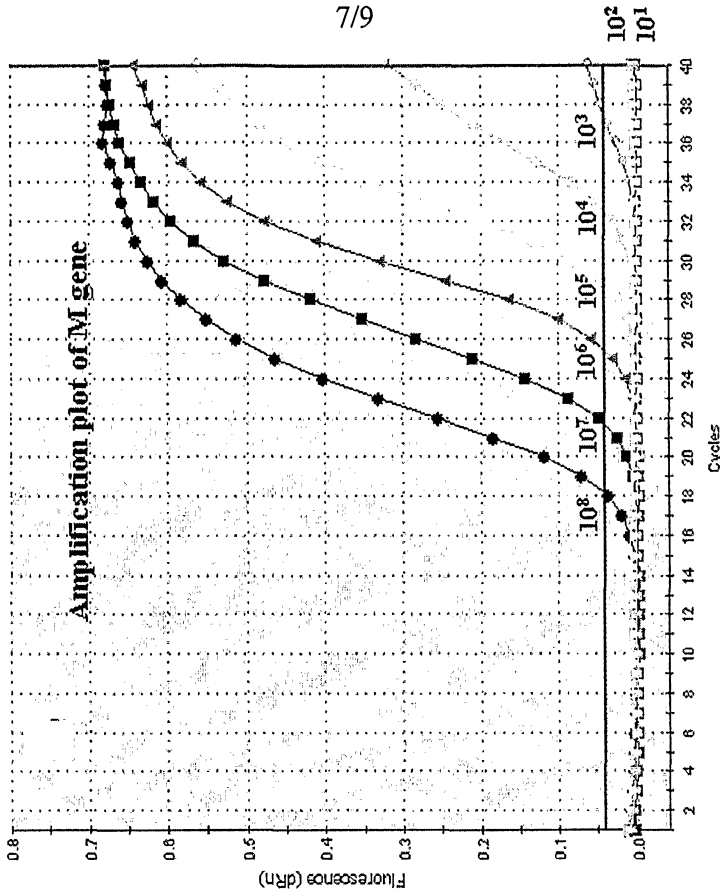


FIG. 6B

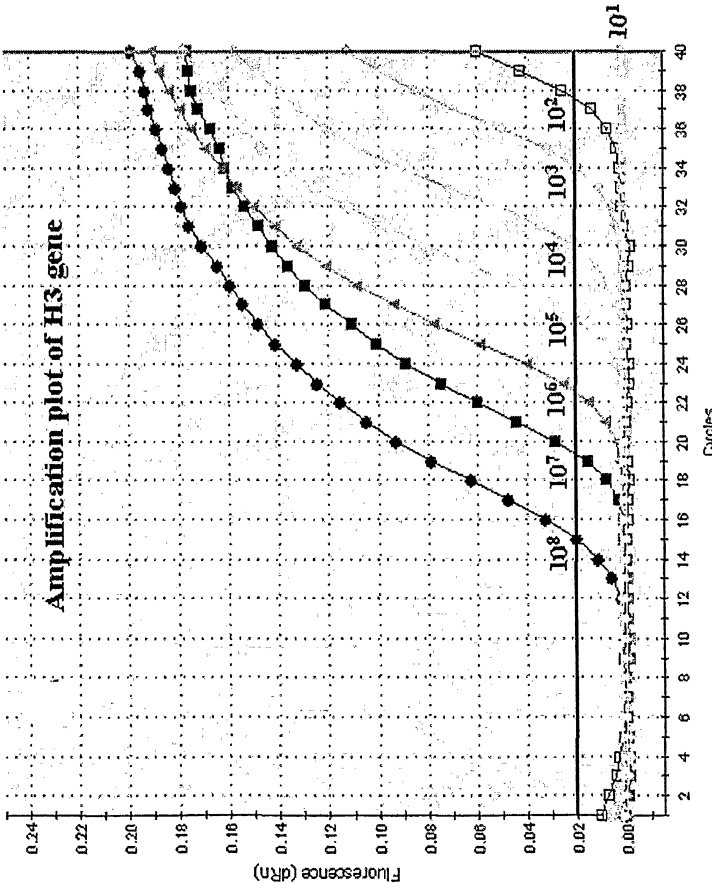


FIG. 6A

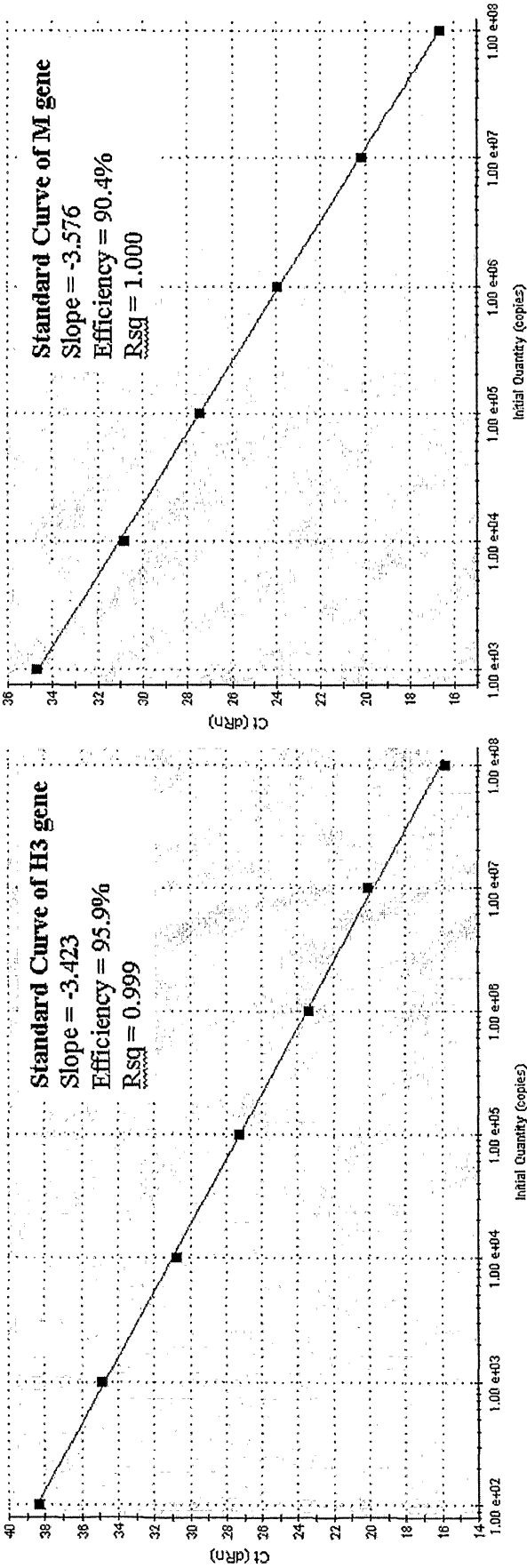


FIG. 6D

FIG. 6C

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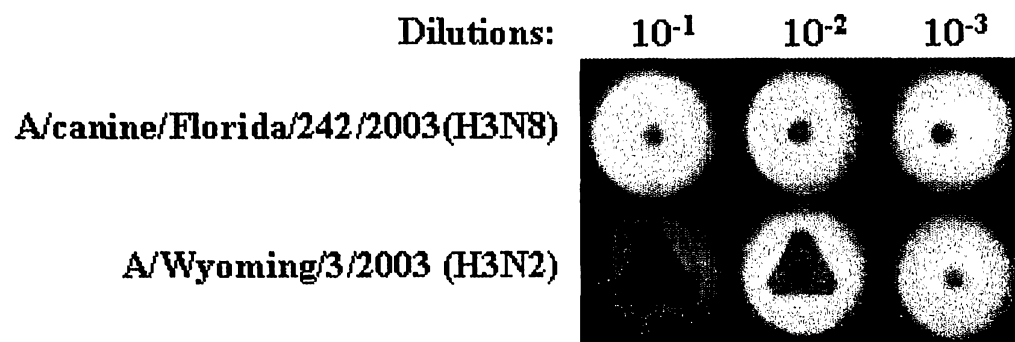


FIG. 7

SEQUENCE LISTING

<110> Crawford, Patti Cynthia
 Gibbs, E. Paul J.
 Dubovi, Edward J.
 Donis, Ruben Omar
 Katz, Jacqueline M.
 Klimov, Alexander I.

<120> Materials and Methods for Respiratory Disease Control in Canines

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<150> US 60/673,443

<151> 2005-04-21

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420 425 430	
caa ctc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc cac aat	1344
Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe His Asn	
435 440 445	
tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg	1392
Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu	
450 455 460	
cct gac atg acc cca agc acc gag atg tca ttg aga gga gtg aga gtc	1440
Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val	
465 470 475 480	
agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg	1488
Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val	
485 490 495	
agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta	1536
Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu	
500 505 510	
ctg tcc cct gaa gaa gtc agt gaa aca caa gga acg gaa aag ctg aca	1584
Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr	
515 520 525	
ata att tat tcg tca tca atg atg tgg gag att aat ggt ccc gaa tca	1632
Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser	

530	535	540	
gtg ttg gtc aat act tat caa tgg atc atc agg aac tgg gaa att gta Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val 545 550 555 560			1680
aaa att cag tgg tca cag gac ccc aca atg tta tac aat aag ata gaa Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu 565 570 575			1728
ttt gag cca ttc caa tcc ctg gtc cct agg gcc acc aga agc caa tac Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr 580 585 590			1776
agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ctt gga Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly 595 600 605			1824
aca ttt gat act gct caa ata ata aaa ctc ctc cct ttt gcc gct gct Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala 610 615 620			1872
cct ccg gaa cag agt agg atg cag ttc tct tct ttg act gtt aat gta Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val 625 630 635 640			1920
aga ggt tcg gga atg agg ata ctt gta aga ggc aat tcc cca gtg ttc Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe 645 650 655			1968
aac tac aat aaa gcc act aaa agg ctc aca gtc ctc gga aag gat gca Asn Tyr Asn Lys Ala Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala 660 665 670			2016
ggg gcg ctt act gag gac cca gat gaa ggt acg gct gga gta gaa tct Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser 675 680 685			2064
gct gtt cta aga ggg ttt ctc att tta ggt aaa gag aac aag aga tat Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr 690 695 700			2112
ggc cca gca cta agc atc aat gaa cta agc aaa ctt gca aaa ggg gag Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu 705 710 715 720			2160
aaa gcc aat gta cta att ggg caa ggg gac gta gtg ttg gta atg aaa Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys 725 730 735			2208
cgg aaa cgt gac tct agc ata ctt act gac agc cag aca gcg acc aaa Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys 740 745 750			2256
agg att cgg atg gcc atc aat			2277

Arg Ile Arg Met Ala Ile Asn
755

<210> 2
<211> 759
<212> PRT
<213> Influenza virus

<400> 2

Met Glu Arg Ile Glu 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 Glu 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 Ser 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

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 Ile 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 Ala 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 Ile 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 Lys 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 His 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
 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
625 630 635 640

Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe
645 650 655

Asn Tyr Asn Lys Ala 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
705 710 715 720

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

<210> 3
<211> 2274
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(2274)

<400> 3
atg gat gtc aat ccg act cta ctc ttc tta aag gtg cca gcg cag aat 48
Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn
1 5 10 15
gct ata agc aca aca ttc cct tat act gga gat cct ccc tac agt cat 96
Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His

20	25	30	
gga aca ggg aca gga tac acc atg gat act gtc aac aga aca cac caa Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln 35 40 45			144
tat tca gaa aaa ggg aaa tgg aca aca aac act gag att gga gca cca Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro 50 55 60			192
caa ctt aat cca atc gat gga cca ctt cct gaa gac aat gaa cca agc Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser 65 70 75 80			240
ggg tac gcc caa aca gat tgt gta ttg gaa gca atg gct ttc ctt gaa Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu 85 90 95			288
gaa tcc cat cca gga atc ttt gaa aat tcg tgt ctt gaa acg atg gag Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu 100 105 110			336
gtg att cag cag aca aga gtg gac aaa cta aca caa ggc cga caa act Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr 115 120 125			384
tat gat tgg acc ttg aat agg aat caa cct gcc gca aca gca ctt gct Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala 130 135 140			432
aat acg att gaa gta ttc aga tca aat ggt ctg act tcc aat gaa tcg Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser 145 150 155 160			480
ggg aga ttg atg gac ttc ctc aaa gat gtc atg gag tcc atg aac aag Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys 165 170 175			528
gaa gaa atg gaa ata aca aca cac ttc caa cgg aag aga aga gta aga Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg 180 185 190			576
gac aac atg aca aag aga atg gta aca cag aga acc ata ggg aag aaa Asp Asn Met Thr Lys Arg Met Val Thr Gln Arg Thr Ile Gly Lys Lys 195 200 205			624
aaa caa cga tta aac aga aag agc tat cta atc aga aca tta acc cta Lys Gln Arg Leu Asn Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu 210 215 220			672
aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gca Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala 225 230 235 240			720
atc gct acc cca ggg atg cag ata aga ggg ttt gta tat ttt gtt gaa			768

Ile	Ala	Thr	Pro	Gly	Met	Gln	Ile	Arg	Gly	Phe	Val	Tyr	Phe	Val	Glu	
				245					250					255		
aca	cta	gct	cga	aga	ata	tgt	gaa	aag	ctt	gaa	caa	tca	gga	ttg	cca	816
Thr	Leu	Ala	Arg	Arg	Ile	Cys	Glu	Lys	Leu	Glu	Gln	Ser	Gly	Leu	Pro	
			260					265					270			
ggt	ggc	ggt	aat	gag	aaa	aag	gcc	aaa	ctg	gct	aat	gtc	gtc	aga	aaa	864
Val	Gly	Gly	Asn	Glu	Lys	Lys	Ala	Lys	Leu	Ala	Asn	Val	Val	Arg	Lys	
		275					280					285				
atg	atg	act	aat	tcc	caa	gac	act	gaa	ctc	tcc	ttc	acc	atc	act	ggg	912
Met	Met	Thr	Asn	Ser	Gln	Asp	Thr	Glu	Leu	Ser	Phe	Thr	Ile	Thr	Gly	
	290					295					300					
gac	aat	acc	aaa	tgg	aat	gaa	aat	cag	aac	cca	cgc	ata	ttc	ctg	gca	960
Asp	Asn	Thr	Lys	Trp	Asn	Glu	Asn	Gln	Asn	Pro	Arg	Ile	Phe	Leu	Ala	
305					310					315				320		
atg	atc	aca	tac	ata	act	aga	aac	cag	cca	gaa	tgg	ttc	aga	aat	gtt	1008
Met	Ile	Thr	Tyr	Ile	Thr	Arg	Asn	Gln	Pro	Glu	Trp	Phe	Arg	Asn	Val	
			325						330					335		
cta	agc	att	gca	ccg	att	atg	ttc	tca	aat	aaa	atg	gca	aga	ctg	ggg	1056
Leu	Ser	Ile	Ala	Pro	Ile	Met	Phe	Ser	Asn	Lys	Met	Ala	Arg	Leu	Gly	
			340					345					350			
aaa	gga	tat	atg	ttt	gaa	agc	aaa	agt	atg	aaa	ttg	aga	act	caa	ata	1104
Lys	Gly	Tyr	Met	Phe	Glu	Ser	Lys	Ser	Met	Lys	Leu	Arg	Thr	Gln	Ile	
		355					360					365				
cca	gca	gaa	atg	cta	gca	agc	att	gac	cta	aaa	tat	ttc	aat	gat	tca	1152
Pro	Ala	Glu	Met	Leu	Ala	Ser	Ile	Asp	Leu	Lys	Tyr	Phe	Asn	Asp	Ser	
	370					375					380					
aca	aaa	aag	aaa	att	gag	aag	ata	cga	cca	ctt	ctg	gtt	gac	ggg	act	1200
Thr	Lys	Lys	Lys	Ile	Glu	Lys	Ile	Arg	Pro	Leu	Leu	Val	Asp	Gly	Thr	
385					390					395				400		
gct	tca	ctg	agt	cct	ggc	atg	atg	atg	gga	atg	ttc	aac	atg	ttg	agc	1248
Ala	Ser	Leu	Ser	Pro	Gly	Met	Met	Met	Gly	Met	Phe	Asn	Met	Leu	Ser	
				405					410					415		
act	gtg	ctg	ggt	gta	tcc	ata	tta	aac	ctg	ggc	cag	agg	aaa	tac	aca	1296
Thr	Val	Leu	Gly	Val	Ser	Ile	Leu	Asn	Leu	Gly	Gln	Arg	Lys	Tyr	Thr	
			420					425					430			
aag	acc	aca	tac	tgg	tgg	gat	ggt	ctg	caa	tca	tcc	gat	gac	ttt	gct	1344
Lys	Thr	Thr	Tyr	Trp	Trp	Asp	Gly	Leu	Gln	Ser	Ser	Asp	Asp	Phe	Ala	
		435					440					445				
ttg	ata	gtg	aat	gcg	cct	aat	cat	gaa	gga	gta	caa	gct	gga	gta	gac	1392
Leu	Ile	Val	Asn	Ala	Pro	Asn	His	Glu	Gly	Val	Gln	Ala	Gly	Val	Asp	
	450					455					460					

aga ttc tat aga act tgc aaa ctg gtc ggg atc aac atg agc aaa aag	1440
Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys	
465 470 475 480	
aag tcc tac ata aat aga act gga aca ttc gaa ttc aca agc ttt ttc	1488
Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe	
485 490 495	
tac cgg tat ggt ttt gta gcc aat ttc agc atg gaa cta ccc agt ttt	1536
Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe	
500 505 510	
ggg gtt tcc gga ata aat gaa tct gca gac atg agc att gga gtg aca	1584
Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	
515 520 525	
gtc atc aaa aac aac atg ata aat aat gat ctc ggt cct gcc acg gca	1632
Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala	
530 535 540	
caa atg gca ctc caa ctc ttc att aag gat tat cgg tac aca tac cgg	1680
Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg	
545 550 555 560	
tgc cat aga ggt gat acc cag ata caa acc aga aga tct ttt gag ttg	1728
Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu	
565 570 575	
aag aaa ctg tgg gaa cag act cga tca aag act ggt cta ctg gta tca	1776
Lys Lys Leu Trp Glu Gln Thr Arg Ser Lys Thr Gly Leu Leu Val Ser	
580 585 590	
gat ggg ggt cca aac cta tat aac atc aga aac cta cac atc ccg gaa	1824
Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu	
595 600 605	
gtc tgt tta aaa tgg gag cta atg gat gaa gat tat aag ggg agg cta	1872
Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Lys Gly Arg Leu	
610 615 620	
tgc aat cca ttg aat cct ttc gtt agt cac aaa gaa att gaa tca gtc	1920
Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val	
625 630 635 640	
aac agt gca gta gta atg cct gcg cat ggc cct gcc aaa agc atg gag	1968
Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu	
645 650 655	
tat gat gct gtt gca aca aca cat tct tgg atc ccc aag agg aac cgg	2016
Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg	
660 665 670	
tcc ata ttg aac aca agc caa agg gga gta ctc gaa gat gag cag atg	2064
Ser Ile Leu Asn Thr Ser Gln Arg Gly Val Leu Glu Asp Glu Gln Met	
675 680 685	

tat cag aaa tgc tgc aac ctg ttt gaa aaa ttc ttc ccc agc agc tca 2112
 Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser
 690 695 700

tac aga aga cca gtc gga att tct agt atg gtt gag gcc atg gtg tcc 2160
 Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser
 705 710 715 720

agg gcc cgc att gat gca cga att gac ttc gaa tct gga cgg ata aag 2208
 Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
 725 730 735

aag gat gag ttc gct gag atc atg aag atc tgt tcc acc att gaa gag 2256
 Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu
 740 745 750

ctc aga cgg caa aaa tag 2274
 Leu Arg Arg Gln Lys
 755

<210> 4
 <211> 757
 <212> PRT
 <213> Influenza virus

<400> 4

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 Val Thr Gln Arg Thr Ile Gly Lys Lys
 195 200 205

Lys Gln Arg Leu Asn 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	Val	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 Ala 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 Val 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 Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu
740 745 750

Leu Arg Arg Gln Lys
755

<210> 5
 <211> 2151
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(2151)

<400> 5
 atg gaa gac ttt gtg cga cag tgc ttc aat cca atg atc gtc gag ctt 48
 Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu
 1 5 10 15

 gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca 96
 Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr
 20 25 30

 aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac 144
 Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr
 35 40 45

 tcg gat ttt cac ttt att aat gaa ctg ggt gag tca gtg gtc ata gag 192
 Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu
 50 55 60

 tct ggt gac cca aat gct ctt ttg aaa cac aga ttt gaa atc att gag 240
 Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
 65 70 75 80

 ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac 288
 Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn
 85 90 95

 acc aca aga gct gaa aaa cct aaa ttt ctt cca gat tta tac gac tat 336
 Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
 100 105 110

 aag gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt cac 384
 Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His
 115 120 125

 ata tac tac ctg gag aag gcc aac aaa ata aag tct gag aaa aca cat 432
 Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His
 130 135 140

 atc cac att ttc tca ttt aca gga gag gaa atg gct aca aaa gcg gac 480
 Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp
 145 150 155 160

 tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc 528
 Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe
 165 170 175

acc ata aga caa gaa atg gcc agt aga ggc ctc tgg gat tcc ttt cgt	576
Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg	
180 185 190	
cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa ata aca	624
Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr	
195 200 205	
ggg acg atg cgc aag ctt gcc aat tac agt ctc cca ccg aac ttc tcc	672
Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser	
210 215 220	
agc ctt gaa aat ttt aga gtc tat gtg gat gga ttc gaa ccg aac ggc	720
Ser Leu Glu Asn Phe Arg Val Tyr Val Asp Gly Phe Glu Pro Asn Gly	
225 230 235 240	
tgc att gag agt aag ctt tct caa atg tcc aaa gaa gta aat gcc aga	768
Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Arg	
245 250 255	
atc gaa cca ttt tca aag aca aca ccc cga cca ctc aaa atg cca ggt	816
Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
260 265 270	
ggg cca ccc tgc cat cag cga tct aaa ttc ttg cta atg gat gct ctg	864
Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
275 280 285	
aaa ctg agc att gag gac cca agt cac gag gga gag gga ata cca cta	912
Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
290 295 300	
tat gat gca atc aaa tgc atg aaa act ttc ttt gga tgg aaa gag ccc	960
Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
305 310 315 320	
agt att gtt aaa cca cat gaa aag ggt ata aac ccg aac tat ctc caa	1008
Ser Ile Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Gln	
325 330 335	
act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa	1056
Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu	
340 345 350	
agg acc ccc aag acc aag aat atg aaa aaa aca agc caa ttg aaa tgg	1104
Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
355 360 365	
gca cta ggt gaa aat atg gca cca gag aaa gtg gat ttt gag gat tgt	1152
Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
370 375 380	
aaa gac atc aat gat tta aaa caa tat gac agt gat gag cca gaa gca	1200
Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala	

385	390	395	400	
agg tct ctt gca agt tgg att caa agt gag ttc aac aaa gct tgt gag				1248
Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu				
	405	410	415	
ctg aca gat tca agc tgg ata gag ctc gat gaa att ggg gag gat gtc				1296
Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val				
	420	425	430	
gcc cca ata gaa tac att gcg agc atg agg aga aat tat ttt act gct				1344
Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala				
	435	440	445	
gag att tcc cat tgt aga gca aca gaa tat ata ata aaa gga gtg tac				1392
Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Ile Lys Gly Val Tyr				
	450	455	460	
atc aac act gct cta ctc aat gca tcc tgt gct gcg atg gat gaa ttt				1440
Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe				
	465	470	475	480
caa tta att ccg atg ata agt aaa tgc agg acc aaa gaa ggg aga agg				1488
Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg				
	485	490	495	
aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga				1536
Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg				
	500	505	510	
aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct ctc act				1584
Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr				
	515	520	525	
gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa				1632
Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu				
	530	535	540	
att gga gac atg ctt cta aga act gct gta ggt caa gtg tca aga ccc				1680
Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro				
	545	550	555	560
atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa				1728
Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys				
	565	570	575	
tgg gga atg gaa atg agg cgc tgc ctc ctt cag tct ctg caa cag att				1776
Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile				
	580	585	590	
gaa agc atg atc gaa gct gag tcc tca gtc aaa gaa aag gac atg acc				1824
Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr				
	595	600	605	
aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc				1872

Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser
 610 615 620
 ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta 1920
 Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu
 625 630 635 640
 tta gca aaa tct gtg ttt aac agt tta tat gca tct cca caa ctg gaa 1968
 Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu
 645 650 655
 ggg ttt tca gct gaa tct agg aaa tta ctt ctc att gtt cag gct ctt 2016
 Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu
 660 665 670
 aag gat gac ctg gaa cct gga acc ttt gat att ggg ggg tta tat gaa 2064
 Lys Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu
 675 680 685
 tca att gag gag tgc ctg att aat gat ccc tgg gtt ttg ctt aat gca 2112
 Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala
 690 695 700
 tct tgg ttc aac tcc ttc ctt aca cat gca ctg aag tag 2151
 Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys
 705 710 715

<210> 6
 <211> 716
 <212> PRT
 <213> Influenza virus

<400> 6

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
 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
 145 150 155 160

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 Val Asp Gly Phe Glu Pro Asn Gly
 225 230 235 240

Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Arg
 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
 305 310 315 320

Ser Ile Val Lys Pro His Glu 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
 385 390 395 400

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 Ile Lys Gly Val Tyr
 450 455 460

Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe
 465 470 475 480

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

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

Met 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

Lys 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> 7
<211> 838
<212> DNA
<213> Influenza virus

<220>

<221> CDS

<222> (1)..(657)

<400> 7

atg gat tcc aac act gtg tca agc ttt cag gta gac tgt ttt ctt tgg	48
Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp	
1 5 10 15	
cat gtc cgc aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc	96
His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe	
20 25 30	
ctt gac cgg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc	144
Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser	
35 40 45	
act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata	192
Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile	
50 55 60	
gtg gag cag att ctg gaa aag gaa tca gat gag gca ctt aaa atg acc	240
Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr	
65 70 75 80	
att gcc tct gtt cct act tca ctc tac tta act gac atg act ctt gat	288
Ile Ala Ser Val Thr Ser Leu Tyr Leu Thr Asp Met Thr Leu Asp	
85 90 95	
gag atg tca aga gac tgg ttc atg ctc atg ccc aag caa aaa gta aca	336
Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr	
100 105 110	
ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc	384
Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile	
115 120 125	
ata ctt aaa gca aac ttt agt gtg att ttc gaa ggg ctg gaa aca cta	432
Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Gly Leu Glu Thr Leu	
130 135 140	
ata cta ctt aga gcc ttc acc gaa gaa gga gca gtc gtt ggc gaa att	480
Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile	
145 150 155 160	
tca cca tta cct tct ctt cca gga cat act aat gag gat gtc aaa aat	528
Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn	
165 170 175	
gca att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt	576
Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val	
180 185 190	
aga atc tct gaa act cta cag aga ttc gct tgg aga agc agt cat gag	624

Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu
 195 200 205
 aat ggg aga cct tca ttc cct tca aag cag aaa tgaaaaatgg agagaacaat 677
 Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys
 210 215
 taagccagaa atttgaagaa ataagatggt tgattgaaga agtgcgacat agattgaaaa 737
 atacagaaaa tagttttgaa caaataacat ttatgcaagc cttacaacta ttgcttgaag 797
 tagaacaaga gataagaact ttctcgtttc agcttattta a 838

 <210> 8
 <211> 219
 <212> PRT
 <213> Influenza virus

 <400> 8
 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 Thr Ser Leu 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 Gly Leu Glu Thr Leu
 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
210 215

<210> 9
<211> 1497
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(1497)

<400> 9
atg gcg tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat 48
Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
1 5 10 15
ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
20 25 30
gtg gga gga atc ggc cga ttt tat gtt cag atg tgt act gag ctt aaa 144
Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
35 40 45
cta aac gac cat gaa ggg cgg ctg att cag aac agc ata aca ata gaa 192
Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
50 55 60
agg atg gta ctt tcg gca ttc gac gaa aga aga aac aag tat ctc gag 240
Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
65 70 75 80
gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc ccg ata 288
Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile

				85				90				95								
tac	aga	agg	aaa	gat	ggg	aaa	tgg	atg	agg	gaa	ctc	atc	ctc	cat	gat			336		
Tyr	Arg	Arg	Lys	Asp	Gly	Lys	Trp	Met	Arg	Glu	Leu	Ile	Leu	His	Asp					
100								105				110								
aaa	gaa	gaa	atc	atg	aga	atc	tgg	cgt	cag	gcc	aac	aat	ggt	gaa	gac			384		
Lys	Glu	Glu	Ile	Met	Arg	Ile	Trp	Arg	Gln	Ala	Asn	Asn	Gly	Glu	Asp					
115								120				125								
gct	act	gct	ggt	ctt	act	cat	atg	atg	atc	tgg	cac	tcc	aat	ctc	aat			432		
Ala	Thr	Ala	Gly	Leu	Thr	His	Met	Met	Ile	Trp	His	Ser	Asn	Leu	Asn					
130								135				140								
gac	acc	aca	tac	caa	aga	aca	agg	gct	ctt	gtt	cgg	act	ggg	atg	gat			480		
Asp	Thr	Thr	Tyr	Gln	Arg	Thr	Arg	Ala	Leu	Val	Arg	Thr	Gly	Met	Asp					
145				150				155				160								
ccc	aga	atg	tgc	tct	ctg	atg	caa	ggc	tca	acc	ctc	cca	cgg	aga	tct			528		
Pro	Arg	Met	Cys	Ser	Leu	Met	Gln	Gly	Ser	Thr	Leu	Pro	Arg	Arg	Ser					
				165				170				175								
gga	gcc	gct	ggt	gct	gca	gta	aaa	ggg	gtt	gga	aca	atg	gta	atg	gaa			576		
Gly	Ala	Ala	Gly	Ala	Ala	Val	Lys	Gly	Val	Gly	Thr	Met	Val	Met	Glu					
180								185				190								
ctc	atc	aga	atg	atc	aaa	cgc	gga	ata	aat	gat	cgg	aat	ttc	tgg	aga			624		
Leu	Ile	Arg	Met	Ile	Lys	Arg	Gly	Ile	Asn	Asp	Arg	Asn	Phe	Trp	Arg					
195								200				205								
ggt	gaa	aat	ggt	cga	aaa	acc	aga	att	gct	tat	gaa	aga	atg	tgc	aat			672		
Gly	Glu	Asn	Gly	Arg	Lys	Thr	Arg	Ile	Ala	Tyr	Glu	Arg	Met	Cys	Asn					
210				215				220												
atc	ctc	aaa	ggg	aaa	ttt	cag	aca	gca	gca	caa	cgg	gct	atg	atg	gac			720		
Ile	Leu	Lys	Gly	Lys	Phe	Gln	Thr	Ala	Ala	Gln	Arg	Ala	Met	Met	Asp					
225				230				235				240								
cag	gtg	agg	gaa	ggc	cgc	aat	cct	gga	aac	gct	gag	att	gag	gat	ctc			768		
Gln	Val	Arg	Glu	Gly	Arg	Asn	Pro	Gly	Asn	Ala	Glu	Ile	Glu	Asp	Leu					
				245				250				255								
att	ttc	ttg	gca	cga	tca	gca	ctt	att	ttg	aga	gga	tca	gta	gcc	cat			816		
Ile	Phe	Leu	Ala	Arg	Ser	Ala	Leu	Ile	Leu	Arg	Gly	Ser	Val	Ala	His					
260								265				270								
aaa	tca	tgc	cta	cct	gcc	tgt	gtt	tat	ggc	ctt	gca	ata	acc	agt	ggg			864		
Lys	Ser	Cys	Leu	Pro	Ala	Cys	Val	Tyr	Gly	Leu	Ala	Ile	Thr	Ser	Gly					
275								280				285								
tat	gac	ttt	gag	aag	gaa	gga	tac	tct	ctg	gtt	gga	att	gat	cct	ttc			912		
Tyr	Asp	Phe	Glu	Lys	Glu	Gly	Tyr	Ser	Leu	Val	Gly	Ile	Asp	Pro	Phe					
290				295				300												
aaa	cta	ctc	cag	aac	agt	caa	att	ttc	agt	cta	atc	aga	cca	aaa	gaa			960		

Lys	Leu	Leu	Gln	Asn	Ser	Gln	Ile	Phe	Ser	Leu	Ile	Arg	Pro	Lys	Glu		
305					310					315					320		
aac	cca	gca	cac	aag	agc	cag	ttg	gtg	tgg	atg	gca	tgc	cat	tct	gca		1008
Asn	Pro	Ala	His	Lys	Ser	Gln	Leu	Val	Trp	Met	Ala	Cys	His	Ser	Ala		
				325					330					335			
gca	ttt	gag	gac	ctg	aga	gtt	tta	aat	ttc	att	aga	gga	acc	aaa	gta		1056
Ala	Phe	Glu	Asp	Leu	Arg	Val	Leu	Asn	Phe	Ile	Arg	Gly	Thr	Lys	Val		
			340					345					350				
atc	cca	aga	gga	cag	tta	aca	acc	aga	gga	gtt	caa	att	gct	tca	aat		1104
Ile	Pro	Arg	Gly	Gln	Leu	Thr	Thr	Arg	Gly	Val	Gln	Ile	Ala	Ser	Asn		
			355					360					365				
gaa	aac	atg	gag	aca	ata	aat	tct	agc	aca	ctt	gaa	ctg	aga	agc	aaa		1152
Glu	Asn	Met	Glu	Thr	Ile	Asn	Ser	Ser	Thr	Leu	Glu	Leu	Arg	Ser	Lys		
	370					375					380						
tat	tgg	gca	ata	agg	acc	aga	agc	gga	gga	aac	acc	agt	caa	cag	aga		1200
Tyr	Trp	Ala	Ile	Arg	Thr	Arg	Ser	Gly	Gly	Asn	Thr	Ser	Gln	Gln	Arg		
385					390					395					400		
gca	tct	gca	gga	cag	ata	agt	gtg	caa	cct	act	ttc	tca	gta	cag	aga		1248
Ala	Ser	Ala	Gly	Gln	Ile	Ser	Val	Gln	Pro	Thr	Phe	Ser	Val	Gln	Arg		
				405					410					415			
aat	cta	ccc	ttt	gag	aga	gcg	acc	att	atg	gct	gca	ttc	act	ggt	aac		1296
Asn	Leu	Pro	Phe	Glu	Arg	Ala	Thr	Ile	Met	Ala	Ala	Phe	Thr	Gly	Asn		
			420					425					430				
act	gaa	ggg	agg	act	tcc	gac	atg	aga	acg	gaa	atc	ata	agg	atg	atg		1344
Thr	Glu	Gly	Arg	Thr	Ser	Asp	Met	Arg	Thr	Glu	Ile	Ile	Arg	Met	Met		
			435				440					445					
gaa	aat	gcc	aaa	tca	gaa	gat	gtg	tct	ttc	cag	ggg	cgg	gga	gtc	ttc		1392
Glu	Asn	Ala	Lys	Ser	Glu	Asp	Val	Ser	Phe	Gln	Gly	Arg	Gly	Val	Phe		
	450					455					460						
gag	ctc	tcg	gac	gaa	aag	gca	acg	aac	ccg	atc	gtg	cct	tcc	ttt	gac		1440
Glu	Leu	Ser	Asp	Glu	Lys	Ala	Thr	Asn	Pro	Ile	Val	Pro	Ser	Phe	Asp		
465					470					475					480		
atg	agc	aat	gaa	ggg	tct	tat	ttc	ttc	gga	gac	aat	gct	gag	gag	ttt		1488
Met	Ser	Asn	Glu	Gly	Ser	Tyr	Phe	Phe	Gly	Asp	Asn	Ala	Glu	Glu	Phe		
				485					490					495			
gac	agt	taa															1497
Asp	Ser																

<210> 10
 <211> 498
 <212> PRT

<213> Influenza virus

<400> 10

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
 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 Lys 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
 225 230 235 240

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 Ile 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
 305 310 315 320

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
 385 390 395 400

Ala Ser 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
 465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

Asp Ser

<210> 11
 <211> 1413
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1413)

<400> 11
 atg aat cca aat caa aag ata ata gca att gga ttt gca tca ttg ggg 48
 Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
 1 5 10 15
 ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca 96
 Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
 20 25 30
 gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144
 Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
 35 40 45
 atc ata aga aag tac aat gaa aca gta aga gta gaa aaa att act caa 192
 Ile Ile Arg Lys Tyr Asn Glu Thr Val Arg Val Glu Lys Ile Thr Gln
 50 55 60
 tgg tat aat acc agt aca att aag tac ata gag aga cct tca aat gaa 240
 Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu
 65 70 75 80
 tac tac atg aac aac act gaa cca ctt tgt gag gcc caa ggc ttt gca 288
 Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala

cca	ttt	tcc	aaa	gat	aat	gga	ata	cga	att	ggg	tcg	aga	ggc	cat	gtt	336	
Pro	Phe	Ser	Lys	Asp	Asn	Gly	Ile	Arg	Ile	Gly	Ser	Arg	Gly	His	Val		
			100						105			110					
ttt	gtg	ata	aga	gaa	cct	ttt	gta	tca	tgt	tcg	ccc	tca	gaa	tgt	aga	384	
Phe	Val	Ile	Arg	Glu	Pro	Phe	Val	Ser	Cys	Ser	Pro	Ser	Glu	Cys	Arg		
			115						120			125					
acc	ttt	ttc	ctc	aca	cag	ggc	tca	tta	ctc	aat	gac	aaa	cat	tct	aac	432	
Thr	Phe	Phe	Leu	Thr	Gln	Gly	Ser	Leu	Leu	Asn	Asp	Lys	His	Ser	Asn		
			130						135			140					
ggc	aca	gta	aag	gac	cga	agt	ccg	tat	agg	act	ttg	atg	agt	gtc	aaa	480	
Gly	Thr	Val	Lys	Asp	Arg	Ser	Pro	Tyr	Arg	Thr	Leu	Met	Ser	Val	Lys		
			145						155			160					
ata	ggg	caa	tca	cct	aat	gta	tat	caa	gct	aga	ttt	gaa	tcg	gta	gca	528	
Ile	Gly	Gln	Ser	Pro	Asn	Val	Tyr	Gln	Ala	Arg	Phe	Glu	Ser	Val	Ala		
			165						170			175					
tgg	tca	gca	aca	gca	tgc	cat	gat	gga	aaa	aaa	tgg	atg	aca	gtt	gga	576	
Trp	Ser	Ala	Thr	Ala	Cys	His	Asp	Gly	Lys	Lys	Trp	Met	Thr	Val	Gly		
			180						185			190					
gtc	aca	ggg	ccc	gac	aat	caa	gca	att	gca	gta	gtg	aac	tat	gga	ggt	624	
Val	Thr	Gly	Pro	Asp	Asn	Gln	Ala	Ile	Ala	Val	Val	Asn	Tyr	Gly	Gly		
			195						200			205					
gtt	ccg	gtt	gat	att	att	aat	tca	tgg	gca	ggg	gat	att	tta	aga	acc	672	
Val	Pro	Val	Asp	Ile	Ile	Asn	Ser	Trp	Ala	Gly	Asp	Ile	Leu	Arg	Thr		
			210						215			220					
caa	gaa	tca	tca	tgc	acc	tgc	att	aaa	gga	gac	tgt	tat	tgg	gta	atg	720	
Gln	Glu	Ser	Ser	Cys	Thr	Cys	Ile	Lys	Gly	Asp	Cys	Tyr	Trp	Val	Met		
			225						235			240					
act	gat	gga	ccg	gca	aat	agg	caa	gct	aaa	tat	agg	ata	ttc	aaa	gca	768	
Thr	Asp	Gly	Pro	Ala	Asn	Arg	Gln	Ala	Lys	Tyr	Arg	Ile	Phe	Lys	Ala		
			245						250			255					
aaa	gat	gga	aga	gta	att	gga	cag	act	gat	ata	agt	ttc	aat	ggg	gga	816	
Lys	Asp	Gly	Arg	Val	Ile	Gly	Gln	Thr	Asp	Ile	Ser	Phe	Asn	Gly	Gly		
			260						265			270					
cac	ata	gag	gag	tgt	tct	tgt	tac	ccc	aat	gaa	ggg	aag	gtg	gaa	tgc	864	
His	Ile	Glu	Glu	Cys	Ser	Cys	Tyr	Pro	Asn	Glu	Gly	Lys	Val	Glu	Cys		
			275						280			285					
ata	tgc	agg	gac	aat	tgg	act	gga	aca	aat	aga	cca	gtt	ctg	gta	ata	912	
Ile	Cys	Arg	Asp	Asn	Trp	Thr	Gly	Thr	Asn	Arg	Pro	Val	Leu	Val	Ile		
			290						295			300					
tct	tct	gat	cta	tcg	tac	aca	gtt	gga	tat	ttg	tgt	gct	ggc	att	ccc	960	

32

Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro
 305 310 315 320
 act gac act cct agg gga gag gat agt caa ttc aca ggc tca tgt aca 1008
 Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
 325 330 335
 agt cct ttg gga aat aaa gga tac ggt gta aaa ggt ttc ggg ttt cga 1056
 Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
 340 345 350
 caa gga act gac gta tgg gcc gga agg aca att agt agg act tca aga 1104
 Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
 355 360 365
 tca gga ttc gaa ata ata aaa atc agg aat ggt tgg aca cag aac agt 1152
 Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
 370 375 380
 aaa gac caa atc agg agg caa gtg att atc gat gac cca aat tgg tca 1200
 Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
 385 390 395 400
 gga tat agc ggt tct ttc aca ttg ccg gtt gaa cta aca aaa aag gga 1248
 Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
 405 410 415
 tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa 1296
 Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
 420 425 430
 gaa aca aca ata tgg acc tct agt agc tcc att gtg atg tgt gga gta 1344
 Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
 435 440 445
 gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att ctt ccc 1392
 Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460
 ttt gac atc gat aag atg taa 1413
 Phe Asp Ile Asp Lys Met
 465 470

<210> 12

<211> 470

<212> PRT

<213> Influenza virus

<400> 12

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 Lys Tyr Asn Glu Thr Val Arg Val Glu Lys Ile 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 Val 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 Ile 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 Val 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

Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
 325 330 335

Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
 340 345 350

Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
 355 360 365

Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
 370 375 380

Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
 385 390 395 400

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
 405 410 415

Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
 420 425 430

Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
 435 440 445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460

Phe Asp Ile Asp Lys Met
465 470

<210> 13
<211> 982
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(756)

<400> 13
atg agt ctt cta acc gag gtc gaa acg tac gtt ctc tct atc gta cca 48
Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro
1 5 10 15
tca ggc ccc ctc aaa gcc gag atc gcg cag aga ctt gaa gat gtc ttt 96
Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
20 25 30
gca gga aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca 144
Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr
35 40 45
aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc 192
Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe
50 55 60
acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc 240
Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val
65 70 75 80
caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gca 288
Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala
85 90 95
gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gca 336
Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala
100 105 110
aaa gag gta gca ctc agc tat tcc act ggt gca cta gcc agc tgc atg 384
Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met
115 120 125
gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gca ttt 432
Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe
130 135 140
ggc ctg gta tgc gcc aca tgt gaa cag att gct gat tcc cag cat cga 480
Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg

145	150								155				160				
gct cac agg cag atg gtg aca aca acc aac cca ttg atc aga cat gaa	528																
Ala His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu																	
	165								170				175				
aac aga atg gta tta gcc agt acc acg gct aaa gcc atg gaa cag atg	576																
Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met																	
	180								185				190				
gca gga tcg agt gag cag gca gca gag gcc atg gag gtt gct agt agg	624																
Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg																	
	195								200				205				
gct agg cag atg gta cag gca atg aga acc att ggg acc cac cct agc	672																
Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser																	
	210								215				220				
tcc agt gcc ggt ttg aaa gat gat ctc ctt gaa aat tta cag gcc tac	720																
Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr																	
225	230								235				240				
cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctctc	766																
Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys																	
	245								250								
gttattgcag caagtatcat tgggatcttg cacttgatat tgtggattct tgatcgtctt	826																
ttcttcaaatt tcatttatcg tcgccttaaa tacgggttga aaagaggggcc ttctacggaa	886																
ggagtacctg agtctatgag ggaagaatat cggcaggaac agcagaatgc tgtggatgtt	946																
gacgatggtc attttgtcaa catagagctg gaqtaa	982																

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<210> 14
<211> 252
<212> PRT
<213> Influenza virus
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<400> 14

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

37

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 Gly 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
 Ala 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> 15

<211> 1698

<212> DNA

<213> Influenza virus

<220>

<221> CDS

<222> (1)..(1698)

<400> 15

atg	aag	aca	acc	att	att	ttg	ata	cta	cta	acc	cat	tgg	gcc	tac	agt	48
Met	Lys	Thr	Thr	Ile	Ile	Leu	Ile	Leu	Leu	Thr	His	Trp	Ala	Tyr	Ser	
1				5					10					15		

caa	aac	cca	atc	agt	ggc	aac	aac	aca	gcc	aca	ctg	tgt	ctg	gga	cac	96
Gln	Asn	Pro	Ile	Ser	Gly	Asn	Asn	Thr	Ala	Thr	Leu	Cys	Leu	Gly	His	
			20					25					30			

cat	gca	gta	gca	aat	gga	aca	ttg	gta	aaa	aca	atg	agt	gat	gat	caa	144
His	Ala	Val	Ala	Asn	Gly	Thr	Leu	Val	Lys	Thr	Met	Ser	Asp	Asp	Gln	
			35				40					45				

att	gag	gtg	aca	aat	gct	aca	gaa	tta	gtt	cag	agc	att	tca	atg	ggg	192
Ile	Glu	Val	Thr	Asn	Ala	Thr	Glu	Leu	Val	Gln	Ser	Ile	Ser	Met	Gly	
	50					55					60					

aaa	ata	tgc	aac	aaa	tca	tat	aga	att	cta	gat	gga	aga	aat	tgc	aca	240
Lys	Ile	Cys	Asn	Lys	Ser	Tyr	Arg	Ile	Leu	Asp	Gly	Arg	Asn	Cys	Thr	
65					70					75				80		

tta	ata	gat	gca	atg	cta	gga	gac	ccc	cac	tgt	gac	gcc	ttt	cag	tat	288
Leu	Ile	Asp	Ala	Met	Leu	Gly	Asp	Pro	His	Cys	Asp	Ala	Phe	Gln	Tyr	
				85					90					95		

gag	agt	tgg	gac	ctc	ttc	ata	gaa	aga	agc	aac	gct	ttc	agc	aat	tgc	336
Glu	Ser	Trp	Asp	Leu	Phe	Ile	Glu	Arg	Ser	Asn	Ala	Phe	Ser	Asn	Cys	
			100					105					110			

tac	cca	tat	gac	atc	cct	gac	tat	gca	tgc	ctc	cga	tcc	att	gta	gca	384
Tyr	Pro	Tyr	Asp	Ile	Pro	Asp	Tyr	Ala	Ser	Leu	Arg	Ser	Ile	Val	Ala	
			115				120					125				

tcc	tca	gga	aca	ttg	gaa	ttc	aca	gca	gag	gga	ttc	aca	tgg	aca	ggt	432
Ser	Ser	Gly	Thr	Leu	Glu	Phe	Thr	Ala	Glu	Gly	Phe	Thr	Trp	Thr	Gly	
	130					135					140					

gtc	act	caa	aac	gga	aga	agt	gga	gcc	tgc	aaa	agg	gga	tca	gcc	gat	480
Val	Thr	Gln	Asn	Gly	Arg	Ser	Gly	Ala	Cys	Lys	Arg	Gly	Ser	Ala	Asp	
145					150					155					160	

agt	ttc	ttt	agc	cga	ctg	aat	tgg	cta	aca	aaa	tct	gga	agc	tct	tac	528
Ser	Phe	Phe	Ser	Arg	Leu	Asn	Trp	Leu	Thr	Lys	Ser	Gly	Ser	Ser	Tyr	
				165					170					175		

ccc	aca	ttg	aat	gtg	aca	atg	cct	aac	aat	aaa	aat	ttc	gac	aag	cta	576
Pro	Thr	Leu	Asn	Val	Thr	Met	Pro	Asn	Asn	Lys	Asn	Phe	Asp	Lys	Leu	
			180					185					190			

tac atc tgg ggg att cat cac ccg agc tca aat caa gag cag aca aaa Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys 195 200 205	624
ttg tac atc caa gaa tca gga cga gta aca gtc tca aca aaa aga agt Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser 210 215 220	672
caa caa aca ata atc cct aac atc gga tct aga ccg ttg gtc aga ggt Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly 225 230 235 240	720
caa tca ggc agg ata agc ata tac tgg acc att gta aaa cct gga gat Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp 245 250 255	768
atc cta atg ata aac agt aat ggc aac tta gtt gca ccg cgg gga tat Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr 260 265 270	816
ttt aaa ttg aaa aca ggg aaa agc tct gta atg aga tca gat gca ccc Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Ala Pro 275 280 285	864
ata gac att tgt gtg tct gaa tgt att aca cca aat gga agc atc tcc Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser 290 295 300	912
aac gac aag cca ttc caa aat gtg aac aaa gtt aca tat gga aaa tgc Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys 305 310 315 320	960
cct aag tat atc agg caa aac act tta aag ctg gcc act ggg atg agg Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg 325 330 335	1008
aat gta cca gaa aag caa acc aga gga atc ttt gga gca ata gcg gga Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly 340 345 350	1056
ttc atc gaa aac ggc tgg gaa gga atg gtt gat ggg tgg tat ggg ttc Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe 355 360 365	1104
cga tat caa aac tct gaa gga aca ggg caa gct gca gat cta aag agc Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser 370 375 380	1152
act caa gca gcc atc gac cag att aat gga aag tta aac aga gtg att Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile 385 390 395 400	1200
gaa aga acc aat gag aaa ttc cat caa ata gag aag gaa ttc tca gaa Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu 405 410 415	1248

gta gaa gga aga att cag gac ctg gag aaa tat gta gaa gac acc aaa 1296
 Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys
 420 425 430

ata gac cta tgg tcc tac aat gca gaa ttg ctg gtg gct cta gaa aat 1344
 Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn
 435 440 445

caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag 1392
 Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu
 450 455 460

aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga 1440
 Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly
 465 470 475 480

tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gga tca ata 1488
 Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile
 485 490 495

aga act ggg aca tat gac cat tac ata tac aga gat gaa gca tta aac 1536
 Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn
 500 505 510

aac cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat 1584
 Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
 515 520 525

tgg ata ttg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt 1632
 Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
 530 535 540

gtt cta ttg ggt ttc att atg tgg gct tgc caa aga ggc aac atc aga 1680
 Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Arg Gly Asn Ile Arg
 545 550 555 560

tgc aac att tgc att tga 1698
 Cys Asn Ile Cys Ile
 565

<210> 16

<211> 565

<212> PRT

<213> Influenza virus

<400> 16

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 Phe Gln Tyr
 85 90 95

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Asn 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 Leu 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 Gly Ser Arg Pro Leu Val Arg Gly
 225 230 235 240

Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp

Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu
450 455 460

43

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 Gly 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 Arg Gly Asn Ile Arg
 545 550 555 560

Cys Asn Ile Cys Ile
 565

<210> 17
 <211> 2277
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(2277)

<400> 17
 atg gag aga ata aaa gaa ctg aga gat ctg atg tta caa tcc cgc acc 48
 Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr
 1 5 10 15
 cgc gag ata cta aca aaa act act gtg gac cac atg gcc ata atc aag 96
 Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys
 20 25 30
 aaa tac aca tca gga aga caa gag aag aac cct gca ctt agg atg aaa 144
 Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys
 35 40 45
 tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg 192
 Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met
 50 55 60

gag atg att cct gag aga aat gaa cag gga caa acc ctt tgg agc aaa Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys 65 70 75 80	240
acg aac gat gct ggc tca gac cgc gta atg gta tca cct ctg gca gtg Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val 85 90 95	288
aca tgg tgg aat agg aat gga cca aca acg agc aca att cat tat cca Thr Trp Trp Asn Arg Asn Gly Pro Thr Thr Ser Thr Ile His Tyr Pro 100 105 110	336
aaa gtc tac aaa act tat ttt gaa aag gtt gaa aga ttg aaa cac gga Lys Val Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly 115 120 125	384
acc ttt ggc ccc gtt cat ttt agg aat caa gtc aag ata aga cga aga Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg 130 135 140	432
gtt gat gta aac cct ggt cac gcg gac ctc agt gcc aaa gaa gca caa Val Asp Val Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln 145 150 155 160	480
gat gtg atc atg gaa gtt gtt ttc cca aat gaa gtg gga gcc aga att Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile 165 170 175	528
cta aca tcg gaa tca caa cta aca ata acc aaa gag aaa aag gaa gaa Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu 180 185 190	576
ctt cag gac tgc aaa att gct ccc ttg atg gta gca tac atg cta gaa Leu Gln Asp Cys Lys Ile Ala Pro Leu Met Val Ala Tyr Met Leu Glu 195 200 205	624
aga gag ttg gtc cga aaa aca agg ttc ctc cca gta gca ggc gga aca Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Ala Gly Gly Thr 210 215 220	672
agc agt gta tac att gaa gtg ttg cat ctg act cag gga aca tgc tgg Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp 225 230 235 240	720
gag caa atg tac acc cca gga gga gaa gtt aga aac gat gat att gat Glu Gln Met Tyr Thr Pro Gly Gly Glu Val Arg Asn Asp Asp Ile Asp 245 250 255	768
caa agt tta att att gca gcc cgg aac ata gtg aga aga gcg aca gta Gln Ser Leu Ile Ile Ala Ala Arg Asn Ile Val Arg Arg Ala Thr Val 260 265 270	816
tca gca gat cca cta gca tcc cta ctg gaa atg tgc cac agt aca cag Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln 275 280 285	864

att ggt gga ata agg atg gta gac atc ctt aag cag aat cca aca gag Ile Gly Gly Ile Arg Met Val Asp Ile Leu Lys Gln Asn Pro Thr Glu 290 295 300	912
gaa caa gct gtg gat ata tgc aaa gca gca atg gga ttg aga att agc Glu Gln Ala Val Asp Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser 305 310 315 320	960
tca tca ttc agc ttt ggt gga ttc acc ttc aaa aga aca agt gga tca Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser 325 330 335	1008
tca gtc aag aga gaa gaa gaa atg ctt acg ggc aac ctt caa aca ttg Ser Val Lys Arg Glu Glu Glu Met Leu Thr Gly Asn Leu Gln Thr Leu 340 345 350	1056
aaa ata aga gtg cat gag ggc tat gaa gaa ttc aca atg gtc gga aga Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg 355 360 365	1104
aga gca aca gcc att atc aga aag gca acc aga aga ttg att caa ttg Arg Ala Thr Ala Ile Ile Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu 370 375 380	1152
ata gta agt ggg aga gat gaa caa tca att gct gaa gca ata att gta Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val 385 390 395 400	1200
gcc atg gtg ttt tcg caa gaa gat tgc atg ata aaa gca gtt cga ggc Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly 405 410 415	1248
gat ttg aac ttt gtt aat aga gca aat cag cgt ttg aac ccc atg cat Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His 420 425 430	1296
caa ctc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc caa aat Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn 435 440 445	1344
tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu 450 455 460	1392
cct gac atg acc cca agc acc gag atg tca ttg aga gga gtg aga gtc Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val 465 470 475 480	1440
agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val 485 490 495	1488
agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu	1536

500							505					510					
ctg	tcc	cct	gaa	gaa	gtc	agt	gaa	aca	caa	gga	acg	gaa	aag	ctg	aca	1584	
Leu	Ser	Pro	Glu	Glu	Val	Ser	Glu	Thr	Gln	Gly	Thr	Glu	Lys	Leu	Thr		
515							520					525					
ata	att	tat	tcg	tca	tca	atg	atg	tgg	gag	att	aat	ggt	ccc	gaa	tca	1632	
Ile	Ile	Tyr	Ser	Ser	Ser	Met	Met	Trp	Glu	Ile	Asn	Gly	Pro	Glu	Ser		
530							535					540					
gtg	ttg	gtc	aat	act	tat	caa	tgg	atc	atc	agg	aac	tgg	gaa	att	gta	1680	
Val	Leu	Val	Asn	Thr	Tyr	Gln	Trp	Ile	Ile	Arg	Asn	Trp	Glu	Ile	Val		
545							550					555					560
aaa	att	cag	tgg	tca	cag	gac	ccc	aca	atg	tta	tac	aat	aag	ata	gaa	1728	
Lys	Ile	Gln	Trp	Ser	Gln	Asp	Pro	Thr	Met	Leu	Tyr	Asn	Lys	Ile	Glu		
565							570					575					
ttt	gag	cca	ttc	caa	tcc	ctg	gtc	cct	agg	gcc	acc	aga	agc	caa	tac	1776	
Phe	Glu	Pro	Phe	Gln	Ser	Leu	Val	Pro	Arg	Ala	Thr	Arg	Ser	Gln	Tyr		
580							585					590					
agc	ggt	ttc	gta	aga	acc	ctg	ttt	cag	caa	atg	cga	gat	gta	ctt	gga	1824	
Ser	Gly	Phe	Val	Arg	Thr	Leu	Phe	Gln	Gln	Met	Arg	Asp	Val	Leu	Gly		
595							600					605					
aca	ttt	gat	act	gct	caa	ata	ata	aaa	ctc	ctc	cct	ttt	gcc	gct	gct	1872	
Thr	Phe	Asp	Thr	Ala	Gln	Ile	Ile	Lys	Leu	Leu	Pro	Phe	Ala	Ala	Ala		
610							615					620					
cct	ccg	gaa	cag	agt	agg	atg	cag	ttc	tct	tct	ttg	act	gtt	aat	gta	1920	
Pro	Pro	Glu	Gln	Ser	Arg	Met	Gln	Phe	Ser	Ser	Leu	Thr	Val	Asn	Val		
625							630					635					640
aga	ggt	tcg	gga	atg	agg	ata	ctt	gta	aga	ggc	aat	tcc	cca	gtg	ttc	1968	
Arg	Gly	Ser	Gly	Met	Arg	Ile	Leu	Val	Arg	Gly	Asn	Ser	Pro	Val	Phe		
645							650					655					
aac	tac	aat	aaa	gcc	act	aaa	agg	ctc	aca	gtc	ctc	gga	aag	gat	gca	2016	
Asn	Tyr	Asn	Lys	Ala	Thr	Lys	Arg	Leu	Thr	Val	Leu	Gly	Lys	Asp	Ala		
660							665					670					
ggt	gcg	ctt	act	gag	gac	cca	gat	gaa	ggt	acg	gct	gga	gta	gaa	tct	2064	
Gly	Ala	Leu	Thr	Glu	Asp	Pro	Asp	Glu	Gly	Thr	Ala	Gly	Val	Glu	Ser		
675							680					685					
gct	gtt	cta	aga	ggg	ttt	ctc	att	tta	ggt	aaa	gaa	aac	aag	aga	tat	2112	
Ala	Val	Leu	Arg	Gly	Phe	Leu	Ile	Leu	Gly	Lys	Glu	Asn	Lys	Arg	Tyr		
690							695					700					
ggc	cca	gca	cta	agc	atc	aat	gaa	cta	agc	aaa	ctt	gca	aaa	ggg	gag	2160	
Gly	Pro	Ala	Leu	Ser	Ile	Asn	Glu	Leu	Ser	Lys	Leu	Ala	Lys	Gly	Glu		
705							710					715					720
aaa	gcc	aat	gta	cta	att	ggg	caa	ggg	gac	rta	gtg	ttg	gta	atg	aaa	2208	

47

Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Xaa Val Leu Val Met Lys
 725 730 735

cgg aaa cgt gac tct agc ata ctt act gac agc cag aca gcg acc aaa 2256
 Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys
 740 745 750

agg att cgg atg gcc atc aat 2277
 Arg Ile Arg Met Ala Ile Asn
 755

<210> 18
 <211> 759
 <212> PRT
 <213> Influenza virus

<220>
 <221> misc_feature
 <222> (731)..(731)
 <223> The 'Xaa' at location 731 stands for Val, or Ile.

<400> 18

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 Ser 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

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 Ala 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 Ile 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

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					640

Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe
645 650 655

Asn Tyr Asn Lys Ala 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
705 710 715 720

Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Xaa 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

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<210> 19
<211> 2274
<212> DNA
<213> Influenza virus
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<220>

<221> CDS

<222> (1)..(2274)

<400> 19

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Met	Asp	Val	Asn	Pro	Thr	Leu	Leu	Phe	Leu	Lys	Val	Pro	Ala	Gln	Asn	
1				5					10					15		

gct	ata	agc	aca	aca	ttc	cct	tat	act	gga	gat	cct	ccc	tac	agt	cat	96
Ala	Ile	Ser	Thr	Thr	Phe	Pro	Tyr	Thr	Gly	Asp	Pro	Pro	Tyr	Ser	His	
			20					25					30			

gga	aca	ggg	aca	gga	tac	acc	atg	gat	act	gtc	aac	aga	aca	cac	caa	144
Gly	Thr	Gly	Thr	Gly	Tyr	Thr	Met	Asp	Thr	Val	Asn	Arg	Thr	His	Gln	
		35					40					45				

tat	tca	gaa	aaa	ggg	aaa	tgg	aca	aca	aac	act	gag	att	gga	gca	cca	192
Tyr	Ser	Glu	Lys	Gly	Lys	Trp	Thr	Thr	Asn	Thr	Glu	Ile	Gly	Ala	Pro	
	50					55					60					

caa	ctt	aat	cca	atc	gat	gga	cca	ctt	cct	gaa	gac	aat	gaa	cca	agt	240
Gln	Leu	Asn	Pro	Ile	Asp	Gly	Pro	Leu	Pro	Glu	Asp	Asn	Glu	Pro	Ser	
65					70					75					80	

ggg	tac	gcc	caa	aca	gat	tgt	gta	ttg	gaa	gca	atg	gct	ttc	ctt	gaa	288
Gly	Tyr	Ala	Gln	Thr	Asp	Cys	Val	Leu	Glu	Ala	Met	Ala	Phe	Leu	Glu	
				85				90						95		

gaa	tcc	cat	ccc	gga	atc	ttt	gaa	aat	tcg	tgt	ctt	gaa	acg	atg	gag	336
Glu	Ser	His	Pro	Gly	Ile	Phe	Glu	Asn	Ser	Cys	Leu	Glu	Thr	Met	Glu	
			100					105						110		

gtg	att	cag	cag	aca	aga	gtg	gac	aaa	cta	aca	caa	ggc	cga	caa	act	384
Val	Ile	Gln	Gln	Thr	Arg	Val	Asp	Lys	Leu	Thr	Gln	Gly	Arg	Gln	Thr	
		115					120					125				

tat	gat	tgg	acc	ttg	aat	agg	aat	caa	cct	gcc	gca	aca	gca	ctt	gct	432
Tyr	Asp	Trp	Thr	Leu	Asn	Arg	Asn	Gln	Pro	Ala	Ala	Thr	Ala	Leu	Ala	
	130					135					140					

aat	acg	att	gaa	gta	ttc	aga	tca	aat	ggt	ctg	act	tcc	aat	gaa	tcg	480
Asn	Thr	Ile	Glu	Val	Phe	Arg	Ser	Asn	Gly	Leu	Thr	Ser	Asn	Glu	Ser	
145					150					155					160	

ggg	aga	ttg	atg	gac	ttc	ctc	aaa	gat	gtc	atg	gag	tcc	atg	aac	aag	528
Gly	Arg	Leu	Met	Asp	Phe	Leu	Lys	Asp	Val	Met	Glu	Ser	Met	Asn	Lys	
				165					170					175		

gaa	gaa	atg	gaa	ata	aca	aca	cac	ttc	caa	cgg	aag	aga	aga	gta	aga	576
Glu	Glu	Met	Glu	Ile	Thr	Thr	His	Phe	Gln	Arg	Lys	Arg	Arg	Val	Arg	
			180					185						190		

gac aac atg aca aag aga atg gta aca cag aga acc ata ggg aag aaa Asp Asn Met Thr Lys Arg Met Val Thr Gln Arg Thr Ile Gly Lys Lys 195 200 205	624
aaa caa cga tta aac aga aag agc tat cta atc aga aca tta acc cta Lys Gln Arg Leu Asn Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu 210 215 220	672
aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gca Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala 225 230 235 240	720
atc gct acc cca ggg atg cag ata aga ggg ttt gta tat ttt gtt gaa Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu 245 250 255	768
aca cta gcc cga aga ata tgt gaa aag ctt gaa caa tca gga ttg cca Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro 260 265 270	816
gtt ggc ggt aat gag aaa aag gcc aaa ctg gct aat gtc gtc aga aaa Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys 275 280 285	864
atg atg act aat tcc caa gac act gaa ctc tcc ttc acc atc act ggg Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly 290 295 300	912
gac aat acc aaa tgg aat gaa aat cag aac cca cgc ata ttc ctg gca Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala 305 310 315 320	960
atg atc aca tac ata act aga aac cag cca gaa tgg ttc aga aat gtt Met Ile Thr Tyr Ile Thr Arg Asn Gln Pro Glu Trp Phe Arg Asn Val 325 330 335	1008
cta agc att gca ccg att atg ttc tca aat aaa atg gca aga ctg ggg Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly 340 345 350	1056
aaa gga tat atg ttt gaa agc aaa agt atg aaa ttg aga act caa ata Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile 355 360 365	1104
cca gca gaa atg cta gca agc att gac cta aaa tat ttc aat gat tca Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser 370 375 380	1152
aca aaa aag aaa att gaa aag ata cga cca ctt ctg gtt gac ggg act Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr 385 390 395 400	1200
gct tca ctg agt cct ggc atg atg atg gga atg ttc aac atg ttg agc Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser 405 410 415	1248

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Thr	Val	Leu	Gly	Val	Ser	Ile	Leu	Asn	Leu	Gly	Gln	Arg	Lys	Tyr	Thr	
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aag	acc	aca	tac	tgg	tgg	gat	ggt	ctg	caa	tca	tcc	gat	gac	ttt	gct	1344
Lys	Thr	Thr	Tyr	Trp	Trp	Asp	Gly	Leu	Gln	Ser	Ser	Asp	Asp	Phe	Ala	
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Leu	Ile	Val	Asn	Ala	Pro	Asn	His	Glu	Gly	Ile	Gln	Ala	Gly	Val	Asp	
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Arg	Phe	Tyr	Arg	Thr	Cys	Lys	Leu	Val	Gly	Ile	Asn	Met	Ser	Lys	Lys	
465					470				475						480	
aaa	tcc	tac	ata	aat	aga	act	gga	aca	ttc	gaa	ttc	aca	agc	ttt	ttc	1488
Lys	Ser	Tyr	Ile	Asn	Arg	Thr	Gly	Thr	Phe	Glu	Phe	Thr	Ser	Phe	Phe	
				485				490						495		
tac	cgg	tat	ggt	ttt	gta	gcc	aat	ttc	agc	atg	gaa	cta	ccc	agt	ttt	1536
Tyr	Arg	Tyr	Gly	Phe	Val	Ala	Asn	Phe	Ser	Met	Glu	Leu	Pro	Ser	Phe	
			500					505					510			
ggg	gtt	tcc	gga	ata	aat	gaa	tct	gca	gac	atg	agc	att	gga	gtg	aca	1584
Gly	Val	Ser	Gly	Ile	Asn	Glu	Ser	Ala	Asp	Met	Ser	Ile	Gly	Val	Thr	
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gtc	atc	aaa	aac	aac	atg	ata	aat	aat	gat	ctc	ggt	cct	gcc	acg	gca	1632
Val	Ile	Lys	Asn	Asn	Met	Ile	Asn	Asn	Asp	Leu	Gly	Pro	Ala	Thr	Ala	
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caa	atg	gca	ctc	caa	ctc	ttc	att	aag	gat	tat	cgg	tac	aca	tac	cgg	1680
Gln	Met	Ala	Leu	Gln	Leu	Phe	Ile	Lys	Asp	Tyr	Arg	Tyr	Thr	Tyr	Arg	
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Cys	His	Arg	Gly	Asp	Thr	Gln	Ile	Gln	Thr	Arg	Arg	Ser	Phe	Glu	Leu	
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Lys	Lys	Leu	Trp	Glu	Gln	Thr	Arg	Ser	Lys	Thr	Gly	Leu	Leu	Val	Ser	
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Asp	Gly	Gly	Pro	Asn	Leu	Tyr	Asn	Ile	Arg	Asn	Leu	His	Ile	Pro	Glu	
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Val	Cys	Leu	Lys	Trp	Glu	Leu	Met	Asp	Glu	Asp	Tyr	Lys	Gly	Arg	Leu	
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Asn Ser Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu				
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Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg				
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Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met				
	675	680	685	
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Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser				
	690	695	700	
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Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser				
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agg gcc cgc att gat gca cga att gac ttc gaa tct gga cgg ata aag				2208
Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys				
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Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu				
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Leu Arg Arg Gln Lys				
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Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln				
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Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro				

55

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				
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				95
Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu				
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				110
Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr				
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				125
Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala				
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				140
Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser				
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				155
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Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys				
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Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg				
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				190
Asp Asn Met Thr Lys Arg Met Val Thr Gln Arg Thr Ile Gly Lys Lys				
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				205
Lys Gln Arg Leu Asn Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu				
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Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala				
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				240
Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu				
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Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro				
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Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys
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Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly
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Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala
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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
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Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala
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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
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Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr
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Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala
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Gln Met Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg
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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
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Tyr Asp Ala Val Ala Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg
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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
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Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
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Leu Arg Arg Gln Lys
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 gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca 96
 Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr
 20 25 30
 aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac 144
 Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr
 35 40 45
 tcg gat ttt cac ttt att aat gaa ctg ggt gag tca gtg gtc ata gag 192
 Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu
 50 55 60
 tct ggt gac cca aat gct ctt ttg aaa cac aga ttt gaa atc att gag 240
 Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
 65 70 75 80
 ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac 288
 Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn
 85 90 95
 acc aca aga gct gaa aaa cct aaa ttt ctt cca gat tta tac gac tat 336
 Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
 100 105 110
 aag gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt cac 384
 Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His

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tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe 165 170 175			528
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agc ctt gaa aat ttt aga gtc tat gtg gat gga ttc gaa ccg aac ggc Ser Leu Glu Asn Phe Arg Val Tyr Val Asp Gly Phe Glu Pro Asn Gly 225 230 235 240			720
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ggt cca ccc tgc cat cag cga tct aaa ttc ttg cta atg gat gct ctg Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu 275 280 285			864
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agt att gtt aaa cca cat gaa aag ggt ata aac ccg aac tat ctc caa Ser Ile Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Gln 325 330 335			1008
act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa			1056

Thr	Trp	Lys	Gln	Val	Leu	Glu	Glu	Ile	Gln	Asp	Leu	Glu	Asn	Glu	Glu		
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Arg	Thr	Pro	Lys	Thr	Lys	Asn	Met	Lys	Lys	Thr	Ser	Gln	Leu	Lys	Trp		
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gca	cta	ggt	gaa	aat	atg	gca	cca	gag	aaa	gtg	gat	ttt	gag	gat	tgt	1152	
Ala	Leu	Gly	Glu	Asn	Met	Ala	Pro	Glu	Lys	Val	Asp	Phe	Glu	Asp	Cys		
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Lys	Asp	Ile	Asn	Asp	Leu	Lys	Gln	Tyr	Asp	Ser	Asp	Glu	Pro	Glu	Thr		
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agg	tct	ctt	gca	agt	tgg	att	caa	agt	gag	ttc	aac	aaa	gct	tgt	gag	1248	
Arg	Ser	Leu	Ala	Ser	Trp	Ile	Gln	Ser	Glu	Phe	Asn	Lys	Ala	Cys	Glu		
			405					410					415				
ctg	aca	gat	tca	agc	tgg	ata	gag	ctc	gat	gaa	att	ggg	gag	gat	gtc	1296	
Leu	Thr	Asp	Ser	Ser	Trp	Ile	Glu	Leu	Asp	Glu	Ile	Gly	Glu	Asp	Val		
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gcc	cca	ata	gaa	tac	att	gcg	agc	atg	agg	aga	aat	tat	ttt	act	gct	1344	
Ala	Pro	Ile	Glu	Tyr	Ile	Ala	Ser	Met	Arg	Arg	Asn	Tyr	Phe	Thr	Ala		
		435				440						445					
gag	att	tcc	cat	tgt	aga	gca	aca	gaa	tat	ata	atg	aaa	gga	gtg	tac	1392	
Glu	Ile	Ser	His	Cys	Arg	Ala	Thr	Glu	Tyr	Ile	Met	Lys	Gly	Val	Tyr		
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atc	aac	act	gct	cta	ctc	aat	gca	tcc	tgt	gct	gcg	atg	gat	gaa	ttt	1440	
Ile	Asn	Thr	Ala	Leu	Leu	Asn	Ala	Ser	Cys	Ala	Ala	Met	Asp	Glu	Phe		
465					470				475						480		
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Gln	Leu	Ile	Pro	Met	Ile	Ser	Lys	Cys	Arg	Thr	Lys	Glu	Gly	Arg	Arg		
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Lys	Thr	Asn	Leu	Tyr	Gly	Phe	Ile	Ile	Lys	Gly	Arg	Ser	His	Leu	Arg		
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Asn	Asp	Thr	Asp	Val	Val	Asn	Phe	Val	Ser	Met	Glu	Phe	Ser	Leu	Thr		
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gat	cca	aga	ttt	gag	cca	cac	aaa	tgg	gaa	aaa	tac	tgc	gtt	cta	gaa	1632	
Asp	Pro	Arg	Phe	Glu	Pro	His	Lys	Trp	Glu	Lys	Tyr	Cys	Val	Leu	Glu		
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Ile	Gly	Asp	Met	Leu	Leu	Arg	Thr	Ala	Val	Gly	Gln	Val	Ser	Arg	Pro		
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Trp	Gly	Met	Glu	Met	Arg	Arg	Cys	Leu	Leu	Gln	Ser	Leu	Gln	Gln	Ile	
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gaa	agc	atg	atc	gaa	gct	gag	tcc	tca	gtc	aaa	gaa	aag	gac	atg	acc	1824
Glu	Ser	Met	Ile	Glu	Ala	Glu	Ser	Ser	Val	Lys	Glu	Lys	Asp	Met	Thr	
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Lys	Glu	Phe	Phe	Glu	Asn	Lys	Ser	Glu	Thr	Trp	Pro	Ile	Gly	Glu	Ser	
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Gly	Phe	Ser	Ala	Glu	Ser	Arg	Lys	Leu	Leu	Leu	Ile	Val	Gln	Ala	Leu	
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agg	gat	gac	ctg	gaa	cct	gga	acc	ttt	gat	att	ggg	ggg	tta	tat	gaa	2064
Arg	Asp	Asp	Leu	Glu	Pro	Gly	Thr	Phe	Asp	Ile	Gly	Gly	Leu	Tyr	Glu	
		675					680					685				
tca	att	gag	gag	tgc	ctg	att	aat	gat	ccc	tgg	gtt	ttg	ctt	aat	gca	2112
Ser	Ile	Glu	Glu	Cys	Leu	Ile	Asn	Asp	Pro	Trp	Val	Leu	Leu	Asn	Ala	
	690					695				700						
tct	tgg	ttc	aac	tcc	ttc	ctt	aca	cat	gca	ctg	aag	tag				2151
Ser	Trp	Phe	Asn	Ser	Phe	Leu	Thr	His	Ala	Leu	Lys					
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 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
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 Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
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 Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His
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 Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe
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 Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg
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 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
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 Ser Leu Glu Asn Phe Arg Val Tyr Val Asp Gly Phe Glu Pro Asn Gly
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 Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Arg
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Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly
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Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu
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Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro
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Ser Ile Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Gln
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Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu
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Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp
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Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys
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Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Thr
 385 390 395 400

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

64

465		470		475		480
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
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
Met 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
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

65

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> 23
 <211> 838
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(657)

<400> 23
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 Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp
 1 5 10 15
 cat gtc cgc aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc 96
 His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe
 20 25 30
 ctt gac cgg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc 144
 Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser
 35 40 45
 act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata 192
 Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile
 50 55 60
 gtg gag cag att ctg gaa aag gaa tca gat gag gca ctt aaa atg acc 240
 Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr
 65 70 75 80
 att gcc tct gtt cct act tca cgc tac tta act gac atg act ctt gat 288
 Ile Ala Ser Val Pro Thr Ser Arg Tyr Leu Thr Asp Met Thr Leu Asp
 85 90 95
 gag atg tca aga gac tgg ttc atg ctc atg ccc aag caa aaa gta aca 336
 Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr
 100 105 110
 ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc 384
 Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile
 115 120 125
 ata ctt aaa gca aac ttt agt gtg att ttc gaa ggg ctg gaa aca cta 432
 Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Gly Leu Glu Thr Leu
 130 135 140

66

ata cta ctt aga gcc ttc acc gaa gaa gga gca gtc gtt ggc gaa att 480
 Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile
 145 150 155 160

tca cca tta cct tct ctt cca gga cat act aat gag gat gtc aaa aat 528
 Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn
 165 170 175

gca att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt 576
 Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val
 180 185 190

aga atc tct gaa act cta cag aga ttc gct tgg aga agc agt cat gag 624
 Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu
 195 200 205

aat ggg aga cct tca ttc cct tca aag cag aaa tgaaaaatgg agagaacaat 677
 Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys
 210 215

taagccagaa atttgaagaa ataagatggt tgattgaaga agtgcgacat agattgaaaa 737

atacagaaaa tagttttgaa caaataacat ttatgcaagc.cttacaacta ttgcttgaag 797

tagaacaaga gataagaact ttctcgtttc agcttattta a 838

<210> 24

<211> 219

<212> PRT

<213> Influenza virus

<400> 24

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 Thr 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 Gly Leu Glu Thr Leu
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
210 215

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<210> 25
<211> 1497
<212> DNA
<213> Influenza virus
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<220>
<221> CDS
<222> (1)..(1497)
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<400> 25
atg gcg tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat      48
Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
1          5          10          15
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ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
20 25 30

gtg gga gga atc ggc cgg ttt tat gtt cag atg tgt act gag ctt aaa 144

68

Val	Gly	Gly	Ile	Gly	Arg	Phe	Tyr	Val	Gln	Met	Cys	Thr	Glu	Leu	Lys	
	35						40					45				
cta	aac	gac	cat	gaa	ggg	cgg	ctg	att	cag	aac	agc	ata	aca	ata	gaa	192
Leu	Asn	Asp	His	Glu	Gly	Arg	Leu	Ile	Gln	Asn	Ser	Ile	Thr	Ile	Glu	
	50					55					60					
agg	atg	gta	ctt	tcg	gca	ttc	gac	gaa	aga	aga	aac	aag	tat	ctc	gag	240
Arg	Met	Val	Leu	Ser	Ala	Phe	Asp	Glu	Arg	Arg	Asn	Lys	Tyr	Leu	Glu	
65					70					75					80	
gag	cat	ccc	agt	gct	ggg	aaa	gac	cct	aag	aaa	acg	gga	ggc	ccg	ata	288
Glu	His	Pro	Ser	Ala	Gly	Lys	Asp	Pro	Lys	Lys	Thr	Gly	Gly	Pro	Ile	
				85					90					95		
tac	aga	agg	aaa	gat	ggg	aaa	tgg	atg	agg	gaa	ctc	atc	ctc	cat	gat	336
Tyr	Arg	Arg	Lys	Asp	Gly	Lys	Trp	Met	Arg	Glu	Leu	Ile	Leu	His	Asp	
			100					105					110			
aaa	gaa	gaa	atc	atg	aga	atc	tgg	cgt	cag	gcc	aac	aat	ggt	gaa	gac	384
Lys	Glu	Glu	Ile	Met	Arg	Ile	Trp	Arg	Gln	Ala	Asn	Asn	Gly	Glu	Asp	
		115					120					125				
gct	act	gct	ggt	ctt	act	cat	atg	atg	atc	tgg	cac	tcc	aat	ctc	aat	432
Ala	Thr	Ala	Gly	Leu	Thr	His	Met	Met	Ile	Trp	His	Ser	Asn	Leu	Asn	
		130				135					140					
gac	acc	aca	tac	caa	aga	aca	agg	gct	ctt	gtt	cgg	act	ggg	atg	gat	480
Asp	Thr	Thr	Tyr	Gln	Arg	Thr	Arg	Ala	Leu	Val	Arg	Thr	Gly	Met	Asp	
145					150					155					160	
ccc	aga	atg	tgc	tct	ctg	atg	caa	ggc	tca	acc	ctc	cca	cgg	aga	tct	528
Pro	Arg	Met	Cys	Ser	Leu	Met	Gln	Gly	Ser	Thr	Leu	Pro	Arg	Arg	Ser	
				165					170					175		
gga	gcc	gct	ggt	gct	gca	gta	aaa	ggt	gtt	gga	aca	atg	gta	atg	gaa	576
Gly	Ala	Ala	Gly	Ala	Ala	Val	Lys	Gly	Val	Gly	Thr	Met	Val	Met	Glu	
			180					185					190			
ctc	atc	aga	atg	atc	aaa	cgc	gga	ata	aat	gat	cgg	aat	ttc	tgg	aga	624
Leu	Ile	Arg	Met	Ile	Lys	Arg	Gly	Ile	Asn	Asp	Arg	Asn	Phe	Trp	Arg	
		195					200					205				
ggt	gaa	aat	ggt	cga	aga	acc	aga	att	gct	tat	gaa	aga	atg	tgc	aat	672
Gly	Glu	Asn	Gly	Arg	Arg	Thr	Arg	Ile	Ala	Tyr	Glu	Arg	Met	Cys	Asn	
	210				215						220					
atc	ctc	aaa	ggg	aaa	ttt	cag	aca	gca	gca	caa	cgg	gct	atg	atg	gac	720
Ile	Leu	Lys	Gly	Lys	Phe	Gln	Thr	Ala	Ala	Gln	Arg	Ala	Met	Met	Asp	
225					230					235					240	
cag	gtg	agg	gaa	ggc	cgc	aat	cct	gga	aac	gct	gag	att	gag	gat	ctc	768
Gln	Val	Arg	Glu	Gly	Arg	Asn	Pro	Gly	Asn	Ala	Glu	Ile	Glu	Asp	Leu	
				245					250					255		

att ttc ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat	816
Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His	
260 265 270	
aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gca gta acc agt ggg	864
Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly	
275 280 285	
tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc	912
Tyr Asp Phe Glu Lys Glu Tyr Ser Leu Val Gly Ile Asp Pro Phe	
290 295 300	
aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa	960
Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu	
305 310 315 320	
aac cca gca cac aag agc cag ttg gtg tgg atg gca tgc cat tct gca	1008
Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala	
325 330 335	
gca ttt gag gac ctg aga gtt tta aat ttc att aga gga acc aaa gta	1056
Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val	
340 345 350	
atc cca aga gga cag tta aca acc aga gga gtt caa att gct tca aat	1104
Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn	
355 360 365	
gaa aac atg gag aca ata gat tct agc aca ctt gaa ctg aga agc aaa	1152
Glu Asn Met Glu Thr Ile Asp Ser Ser Thr Leu Glu Leu Arg Ser Lys	
370 375 380	
tat tgg gca ata agg acc aga agc gga gga aac acc agt caa cag aga	1200
Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg	
385 390 395 400	
gca tct gca gga cag ata agt gtg caa cct act ttc tca gta cag aga	1248
Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg	
405 410 415	
aat ctt ccc ttt gag aga gca acc att atg gct gca ttc act ggt aac	1296
Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn	
420 425 430	
act gaa ggg agg act tcc gac atg aga acg gaa atc ata agg atg atg	1344
Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met	
435 440 445	
gaa aat gcc aaa tca gaa gat gtg tct ttc cag ggg cgg gga gtc ttc	1392
Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe	
450 455 460	
gag ctc tcg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac	1440
Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp	
465 470 475 480	

70

atg agc aat gaa ggg tct tat ttc ttc gga gac aat gct gag gag ttt 1488
 Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

gac agt taa 1497
 Asp Ser

<210> 26
 <211> 498
 <212> PRT
 <213> Influenza virus

<400> 26

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
 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
 225 230 235 240

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
 305 310 315 320

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 Asp Ser Ser Thr Leu Glu Leu Arg Ser Lys

72

370 375 380
 Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg
 385 390 395 400
 Ala Ser 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
 465 470 475 480
 Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

Asp Ser

<210> 27
 <211> 1410
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1410)

<400> 27
 atg aat cca aat caa aag ata ata aca att gga ttt gca tca ttg ggg 48
 Met Asn Pro Asn Gln Lys Ile Ile Thr Ile Gly Phe Ala Ser Leu Gly
 1 5 10 15
 ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca 96
 Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
 20 25 30
 gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144

Val	Leu	Val	Leu	Asn	Asn	Asn	Arg	Thr	Asp	Leu	Asn	Cys	Lys	Gly	Thr	
	35						40					45				
atc	ata	aga	gag	tac	aat	gaa	aca	gta	aga	gta	gaa	aaa	att	act	caa	192
Ile	Ile	Arg	Glu	Tyr	Asn	Glu	Thr	Val	Arg	Val	Glu	Lys	Ile	Thr	Gln	
	50					55					60					
tgg	tat	aat	acc	agt	aca	att	aag	tac	ata	gag	aga	cct	tca	aat	gaa	240
Trp	Tyr	Asn	Thr	Ser	Thr	Ile	Lys	Tyr	Ile	Glu	Arg	Pro	Ser	Asn	Glu	
65					70					75				80		
tac	tac	atg	aac	aac	act	gaa	cca	ctt	tgt	gag	gcc	caa	ggc	ttt	gca	288
Tyr	Tyr	Met	Asn	Asn	Thr	Glu	Pro	Leu	Cys	Glu	Ala	Gln	Gly	Phe	Ala	
				85					90					95		
cca	ttt	tcc	aaa	gat	aat	gga	ata	cga	att	ggg	tcg	aga	ggc	cat	gtt	336
Pro	Phe	Ser	Lys	Asp	Asn	Gly	Ile	Arg	Ile	Gly	Ser	Arg	Gly	His	Val	
			100					105					110			
ttt	gtg	ata	aga	gaa	cct	ttt	gta	tca	tgt	tcg	ccc	tca	gaa	tgt	aga	384
Phe	Val	Ile	Arg	Glu	Pro	Phe	Val	Ser	Cys	Ser	Pro	Ser	Glu	Cys	Arg	
		115					120					125				
acc	ttt	ttc	ctc	aca	cag	ggc	tca	tta	ctc	aat	gac	aaa	cat	tct	aac	432
Thr	Phe	Phe	Leu	Thr	Gln	Gly	Ser	Leu	Leu	Asn	Asp	Lys	His	Ser	Asn	
	130					135					140					
ggc	aca	gta	aag	gac	cga	agt	ccg	tat	agg	act	ttg	atg	agt	gtc	aaa	480
Gly	Thr	Val	Lys	Asp	Arg	Ser	Pro	Tyr	Arg	Thr	Leu	Met	Ser	Val	Lys	
145					150					155					160	
ata	ggg	caa	tca	cct	aat	gta	tat	caa	gct	agg	ttt	gaa	tcg	gtg	gca	528
Ile	Gly	Gln	Ser	Pro	Asn	Val	Tyr	Gln	Ala	Arg	Phe	Glu	Ser	Val	Ala	
				165					170					175		
tgg	tca	gca	aca	gca	tgc	cat	gat	gga	aaa	aaa	tgg	atg	aca	gtt	gga	576
Trp	Ser	Ala	Thr	Ala	Cys	His	Asp	Gly	Lys	Lys	Trp	Met	Thr	Val	Gly	
			180					185					190			
gtc	aca	ggg	ccc	gac	aat	caa	gca	att	gca	gta	gtg	aac	tat	gga	ggt	624
Val	Thr	Gly	Pro	Asp	Asn	Gln	Ala	Ile	Ala	Val	Val	Asn	Tyr	Gly	Gly	
		195					200					205				
gtt	ccg	gtt	gat	att	att	aat	tca	tgg	gca	ggg	gat	att	tta	aga	acc	672
Val	Pro	Val	Asp	Ile	Ile	Asn	Ser	Trp	Ala	Gly	Asp	Ile	Leu	Arg	Thr	
	210					215					220					
caa	gaa	tca	tca	tgc	acc	tgc	att	aaa	gga	gac	tgt	tat	tgg	gta	atg	720
Gln	Glu	Ser	Ser	Cys	Thr	Cys	Ile	Lys	Gly	Asp	Cys	Tyr	Trp	Val	Met	
225					230					235					240	
act	gat	gga	ccg	gca	aat	agg	caa	gct	aaa	tat	agg	ata	ttc	aaa	gca	768
Thr	Asp	Gly	Pro	Ala	Asn	Arg	Gln	Ala	Lys	Tyr	Arg	Ile	Phe	Lys	Ala	
				245					250					255		

aaa gat gga aga gta att gga cag act gat ata agt ttc aat ggg gga Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly 260 265 270	816
cac ata gag gag tgt tct tgt tac ccc aat gaa ggg aag gtg gaa tgc His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys 275 280 285	864
ata tgc agg gac aat tgg act gga aca aat aga cca att ctg gta ata Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile 290 295 300	912
tct tct gat cta tcg tac aca gtt gga tat ttg tgt gct ggc att ccc Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro 305 310 315 320	960
act gac act cct agg gga gag gat agt caa ttc aca ggc tca tgt aca Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr 325 330 335	1008
agt cct ttg gga aat aaa gga tac ggt gta aaa ggt ttc ggg ttt cga Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg 340 345 350	1056
caa gga act gac gta tgg gcc gga agg aca att agt agg act tca aga Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg 355 360 365	1104
tca gga ttc gaa ata ata aaa atc agg aat ggt tgg aca cag aac agt Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser 370 375 380	1152
aaa gac caa atc agg agg caa gtg att atc gat gac cca aat tgg tca Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser 385 390 395 400	1200
gga tat agc ggt tct ttc aca ttg ccg gtt gaa cta aca aaa aag gga Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly 405 410 415	1248
tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu 420 425 430	1296
gaa aca aca ata tgg acc tct agc agc tcc att gtg atg tgt gga gta Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val 435 440 445	1344
gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att ctt ccc Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro 450 455 460	1392
ttt gac atc gat aag atg Phe Asp Ile Asp Lys Met 465 470	1410

<210> 28
 <211> 470
 <212> PRT
 <213> Influenza virus

<400> 28

Met Asn Pro Asn Gln Lys Ile Ile Thr 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 Ile 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 Val 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 Ile 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

Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
 325 330 335

Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
 340 345 350

Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
 355 360 365

Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
 370 375 380

Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
 385 390 395 400

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly

405

410

415

Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
420 425 430

Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
435 440 445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
450 455 460

Phe Asp Ile Asp Lys Met
465 470

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<210> 29
<211> 982
<212> DNA
<213> Influenza virus
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<220>
<221> CDS
<222> (1)..(756)
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[illegible]

Val	Lys	Leu	Tyr	Arg	Lys	Leu	Lys	Arg	Glu	Ile	Thr	Phe	His	Gly	Ala		
			100					105					110				
aaa	gag	gtg	gca	ctc	agc	tat	tcc	act	ggg	gca	cta	gcc	agc	tgc	atg		384
Lys	Glu	Val	Ala	Leu	Ser	Tyr	Ser	Thr	Gly	Ala	Leu	Ala	Ser	Cys	Met		
		115					120					125					
gga	ctc	ata	tac	aac	aga	atg	gga	act	gtt	aca	acc	gaa	gtg	gca	ttt		432
Gly	Leu	Ile	Tyr	Asn	Arg	Met	Gly	Thr	Val	Thr	Thr	Glu	Val	Ala	Phe		
		130				135					140						
ggc	ctg	gta	tgc	gcc	aca	tgt	gaa	cag	att	gct	gat	tcc	cag	cat	cga		480
Gly	Leu	Val	Cys	Ala	Thr	Cys	Glu	Gln	Ile	Ala	Asp	Ser	Gln	His	Arg		
145					150					155					160		
tct	cac	agg	cag	atg	gtg	aca	aca	acc	aac	cca	tta	atc	aga	cat	gaa		528
Ser	His	Arg	Gln	Met	Val	Thr	Thr	Thr	Asn	Pro	Leu	Ile	Arg	His	Glu		
			165						170					175			
aac	aga	atg	gta	tta	gcc	agt	acc	acg	gct	aaa	gcc	atg	gaa	cag	atg		576
Asn	Arg	Met	Val	Leu	Ala	Ser	Thr	Thr	Ala	Lys	Ala	Met	Glu	Gln	Met		
		180						185					190				
gca	gga	tcg	agt	gag	cag	gca	gca	gag	gcc	atg	gag	gtt	gct	agt	agg		624
Ala	Gly	Ser	Ser	Glu	Gln	Ala	Ala	Glu	Ala	Met	Glu	Val	Ala	Ser	Arg		
		195				200					205						
gct	agg	cag	atg	gta	cag	gca	atg	aga	acc	att	ggg	acc	cac	cct	agc		672
Ala	Arg	Gln	Met	Val	Gln	Ala	Met	Arg	Thr	Ile	Gly	Thr	His	Pro	Ser		
	210				215						220						
tcc	agt	gcc	ggg	ttg	aaa	gat	gat	ctc	ctt	gaa	aat	tta	cag	gcc	tac		720
Ser	Ser	Ala	Gly	Leu	Lys	Asp	Asp	Leu	Leu	Glu	Asn	Leu	Gln	Ala	Tyr		
225				230						235				240			
cag	aaa	cgg	atg	gga	gtg	caa	atg	cag	cga	ttc	aag	tgatcctctc					766
Gln	Lys	Arg	Met	Gly	Val	Gln	Met	Gln	Arg	Phe	Lys						
			245					250									
gttattgcag	caagtatcat	tgggatcttg	cacttgatat	tgtggattct	tgatcgtctt												826
ttcttcaa	at	tcatttatcg	tcgccttaaa	tacgggttga	aaagagggcc	ttctacggaa											886
ggagtacctg	agtcctatgag	ggaagaatat	cggcaggaac	agcagaatgc	tgtggatggt												946
gacgatgggc	attttgtcaa	catagagctg	gagtaa														982

<210> 30
 <211> 252
 <212> PRT
 <213> Influenza virus

<400> 30

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	Gly	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	

80

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> 31
 <211> 1698
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1698)

<400> 31
 atg aag aca acc att att ttg ata cta ctg acc cat tgg gcc tac agt 48
 Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser
 1 5 10 15
 caa aac cca atc agt gac aac aac aca gcc aca ctg tgt ctg gga cac 96
 Gln Asn Pro Ile Ser Asp Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 20 25 30
 cat gca gta gca aat gga aca ttg gta aaa aca ata agt gat gat caa 144
 His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Ile Ser Asp Asp Gln
 35 40 45
 att gag gtg aca aat gct aca gaa tta gtt cag agc att tca atg ggg 192
 Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
 50 55 60
 aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca 240
 Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 65 70 75 80
 tta ata gat gca atg cta gga gac ccc cac tgt gac gcc ttt cag tat 288
 Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
 85 90 95
 gag agt tgg gac ctc ttt ata gaa aga agc agc gct ttc agc aat tgc 336
 Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
 100 105 110
 tac cca tat gac atc cct gac tat gca tcg ctc cga tcc att gta gca 384
 Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
 115 120 125
 tcc tca gga aca ttg gaa ttc aca gca gag gga ttc aca tgg aca ggt 432
 Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
 130 135 140

gtc act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat	480
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp	
145 150 155 160	
agt ttc ttt agc cga ctg aat tgg cta aca aaa tct gga agc tct tac	528
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr	
165 170 175	
ccc aca ttg aat gtg aca atg cct aac aat aaa aat ttc gac aag cta	576
Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu	
180 185 190	
tac atc tgg ggg att cat cac ccg agc tca aat caa gag cag aca aaa	624
Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys	
195 200 205	
ttg tac atc caa gaa tca gga cga gta aca gtc tca aca aaa aga agt	672
Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser	
210 215 220	
caa caa aca ata atc cct aac atc gga tct aga ccg ttg gtc aga ggt	720
Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly	
225 230 235 240	
caa tca ggc agg ata agc ata tac tgg acc att gta aaa cct gga gat	768
Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp	
245 250 255	
atc cta atg ata aac agt aat ggc aac tta gtt gca ccg cgg gga tat	816
Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr	
260 265 270	
ttt aaa ttg aaa aca ggg aaa agc tct gta atg aga tca gat gta ccc	864
Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro	
275 280 285	
ata gac att tgt gtg tct gaa tgt att aca cca aat gga agc atc tcc	912
Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser	
290 295 300	
aac gac aag cca ttc caa aat gtg aac aaa gtt aca tat gga aaa tgc	960
Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys	
305 310 315 320	
ccc aag tat atc agg caa aac act tta aag ctg gcc act ggg atg agg	1008
Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg	
325 330 335	
aat gta cca gaa aag caa acc aga gga atc ttt gga gca ata gcg gga	1056
Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly	
340 345 350	
ttc atc gaa aac ggc tgg gaa gga atg gtt gat ggg tgg tat ggg ttc	1104
Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe	

355	360	365	
cga tat caa aac tct gaa gga aca ggg caa gct gca gat cta aag agc Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser 370 375 380			1152
act caa gca gcc atc gac cag att aat gga aag tta aac aga gtg att Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile 385 390 395 400			1200
gaa aga acc aat gag aaa ttc cat caa ata gag aag gaa ttc tca gaa Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu 405 410 415			1248
gta gaa gga aga att cag gac ttg gag aaa tat gta gaa gac acc aaa Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys 420 425 430			1296
ata gac cta tgg tcc tac aat gca gaa ttg ctg gtg gct cta gaa aat Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn 435 440 445			1344
caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu 450 455 460			1392
aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly 465 470 475 480			1440
tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gga tca ata Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile 485 490 495			1488
aga act ggg aca tat gac cat tac ata tac aga gat gaa gca tta aac Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn 500 505 510			1536
aac cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp 515 520 525			1584
tgg ata ctg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val 530 535 540			1632
gtt cta ttg ggt ttc att atg tgg gct tgc caa aaa ggc aac atc aga Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg 545 550 555 560			1680
tgc aac att tgc att tga Cys Asn Ile Cys Ile 565			1698

<210> 32
 <211> 565
 <212> PRT
 <213> Influenza virus

<400> 32

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 Asp Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 20 25 30

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Ile 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 Phe 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 Leu 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

84

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 Gly Ser Arg Pro Leu Val Arg Gly
 225 230 235 240

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 Lys 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

85

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 Gly 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> 33

<211> 549

<212> PRT

<213> Influenza virus

<400> 33

Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 1 5 10 15

His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln
 20 25 30

86

Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
 35 40 45

Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 50 55 60

Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
 65 70 75 80

Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Asn Ala Phe Ser Asn Cys
 85 90 95

Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala
 100 105 110

Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
 115 120 125

Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp
 130 135 140

Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr
 145 150 155 160

Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu
 165 170 175

Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys
 180 185 190

Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser
 195 200 205

Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly
 210 215 220

Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp
 225 230 235 240

Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr
 245 250 255

Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Ala Pro
 260 265 270

Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser
 275 280 285

Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys
 290 295 300

Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg
 305 310 315 320

Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala Gly
 325 330 335

Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly Phe
 340 345 350

Arg Tyr Gln Asn Ser Glu Gly Thr Gly Gln Ala Ala Asp Leu Lys Ser
 355 360 365

Thr Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Val Ile
 370 375 380

Glu Arg Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser Glu
 385 390 395 400

Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys
 405 410 415

Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn
 420 425 430

Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu
 435 440 445

Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly
 450 455 460

Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser Ile

465 470 475 480
 Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Arg Asp Glu Ala Leu Asn
 485 490 495
 Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
 500 505 510
 Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
 515 520 525
 Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Arg Gly Asn Ile Arg
 530 535 540
 Cys Asn Ile Cys Ile
 545

 <210> 34
 <211> 549
 <212> PRT
 <213> Influenza virus

 <400> 34
 Gln Asn Pro Ile Ser Asp Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 1 5 10 15
 His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Ile Ser Asp Asp Gln
 20 25 30
 Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
 35 40 45
 Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 50 55 60
 Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
 65 70 75 80
 Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
 85 90 95
 Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala

100	105	110
Ser Ser Gly Thr Leu Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly 115 120 125		
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp 130 135 140		
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr 145 150 155 160		
Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu 165 170 175		
Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys 180 185 190		
Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser 195 200 205		
Gln Gln Thr Ile Ile Pro Asn Ile Gly Ser Arg Pro Leu Val Arg Gly 210 215 220		
Gln Ser Gly Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly Asp 225 230 235 240		
Ile Leu Met Ile Asn Ser Asn Gly Asn Leu Val Ala Pro Arg Gly Tyr 245 250 255		
Phe Lys Leu Lys Thr Gly Lys Ser Ser Val Met Arg Ser Asp Val Pro 260 265 270		
Ile Asp Ile Cys Val Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile Ser 275 280 285		
Asn Asp Lys Pro Phe Gln Asn Val Asn Lys Val Thr Tyr Gly Lys Cys 290 295 300		
Pro Lys Tyr Ile Arg Gln Asn Thr Leu Lys Leu Ala Thr Gly Met Arg 305 310 315 320		

90

Asn	Val	Pro	Glu	Lys	Gln	Thr	Arg	Gly	Ile	Phe	Gly	Ala	Ile	Ala	Gly	325	330	335	
Phe	Ile	Glu	Asn	Gly	Trp	Glu	Gly	Met	Val	Asp	Gly	Trp	Tyr	Gly	Phe	340	345	350	
Arg	Tyr	Gln	Asn	Ser	Glu	Gly	Thr	Gly	Gln	Ala	Ala	Asp	Leu	Lys	Ser	355	360	365	
Thr	Gln	Ala	Ala	Ile	Asp	Gln	Ile	Asn	Gly	Lys	Leu	Asn	Arg	Val	Ile	370	375	380	
Glu	Arg	Thr	Asn	Glu	Lys	Phe	His	Gln	Ile	Glu	Lys	Glu	Phe	Ser	Glu	385	390	395	400
Val	Glu	Gly	Arg	Ile	Gln	Asp	Leu	Glu	Lys	Tyr	Val	Glu	Asp	Thr	Lys	405	410	415	
Ile	Asp	Leu	Trp	Ser	Tyr	Asn	Ala	Glu	Leu	Leu	Val	Ala	Leu	Glu	Asn	420	425	430	
Gln	His	Thr	Ile	Asp	Leu	Thr	Asp	Ala	Glu	Met	Asn	Lys	Leu	Phe	Glu	435	440	445	
Lys	Thr	Arg	Arg	Gln	Leu	Arg	Glu	Asn	Ala	Glu	Asp	Met	Gly	Gly	Gly	450	455	460	
Cys	Phe	Lys	Ile	Tyr	His	Lys	Cys	Asp	Asn	Ala	Cys	Ile	Gly	Ser	Ile	465	470	475	480
Arg	Thr	Gly	Thr	Tyr	Asp	His	Tyr	Ile	Tyr	Arg	Asp	Glu	Ala	Leu	Asn	485	490	495	
Asn	Arg	Phe	Gln	Ile	Lys	Gly	Val	Glu	Leu	Lys	Ser	Gly	Tyr	Lys	Asp	500	505	510	
Trp	Ile	Leu	Trp	Ile	Ser	Phe	Ala	Ile	Ser	Cys	Phe	Leu	Ile	Cys	Val	515	520	525	
Val	Leu	Leu	Gly	Phe	Ile	Met	Trp	Ala	Cys	Gln	Lys	Gly	Asn	Ile	Arg	530	535	540	

Cys Asn Ile Cys Ile
545

<210> 35
<211> 9
<212> DNA
<213> Influenza virus

<400> 35
gagagttgg

9

<210> 36
<211> 9
<212> DNA
<213> Influenza virus

<400> 36
ccgttggtc

9

<210> 37
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<212> DNA
<213> Influenza virus

<400> 37
caaaccaga

9

<210> 38
<211> 9
<212> DNA
<213> Influenza virus

<400> 38
agaactggg

9

<210> 39
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<212> DNA
<213> Influenza virus

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tatgagagtt gggac

15

<210> 40
<211> 15
<212> DNA
<213> Influenza virus

<400> 40
agaccgttgg tcaga 15

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<211> 15
<212> DNA
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aagcaaacca gagga 15

<210> 42
<211> 15
<212> DNA
<213> Influenza virus

<400> 42
ataagaactg ggaca 15

<210> 43
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<212> DNA
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<400> 43
acaatgagt 9

<210> 44
<211> 15
<212> DNA
<213> Influenza virus

<400> 44
aaaacaatga gtgat 15

<210> 45
<211> 9
<212> DNA
<213> Influenza virus

<400> 45
gatgtaccc 9

<210> 46
<211> 15
<212> DNA
<213> Influenza virus

<400> 46

tcagatgtac ccata

15

<210> 47

<211> 2280

<212> DNA

<213> Influenza virus

<220>

<221> CDS

<222> (1)..(2280)

<400> 47

atg gag aga ata aaa gaa ctg aga gat ctg atg tta caa tcc cgc acc	48
Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr	
1 5 10 15	

cgc gag ata cta aca aaa act act gtg gac cac atg gcc ata atc aag	96
Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys	
20 25 30	

aaa tac aca tca gga aga caa gag aag aac cct gca ctt agg atg aaa	144
Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys	
35 40 45	

tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg	192
Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met	
50 55 60	

gag atg att cct gag aga aat gaa cag gga caa acc ctt tgg agc aaa	240
Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys	
65 70 75 80	

acg aac gat gct ggc tca gac cgc gta atg gta tca cct ctg gca gtg	288
Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val	
85 90 95	

aca tgg tgg aat agg aat gga cca aca acg aac aca att cat tat cca	336
Thr Trp Trp Asn Arg Asn Gly Pro Thr Thr Asn Thr Ile His Tyr Pro	
100 105 110	

aaa gtc tac aaa act tat ttt gaa aag gtt gaa aga ttg aaa cac gga	384
Lys Val Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly	
115 120 125	

acc ttt ggc ccc gtt cat ttt agg aat caa gtc aag ata aga cga aga	432
Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg	
130 135 140	

gtt gat gta aac cct ggt cac gcg gac ctc agt gct aaa gaa gca caa	480
Val Asp Val Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln	
145 150 155 160	

gat gtg atc atg gaa gtt gtt ttc cca aat gaa gtg gga gcc aga att	528
---	-----

Asp	Val	Ile	Met	Glu	Val	Val	Phe	Pro	Asn	Glu	Val	Gly	Ala	Arg	Ile	
				165					170					175		
cta	aca	tca	gaa	tca	caa	cta	aca	ata	acc	aaa	gag	aaa	aag	gaa	gaa	576
Leu	Thr	Ser	Glu	Ser	Gln	Leu	Thr	Ile	Thr	Lys	Glu	Lys	Lys	Glu	Glu	
			180					185					190			
ctt	cag	gac	tgc	aaa	att	gct	ccc	ttg	atg	gta	gca	tac	atg	cta	gaa	624
Leu	Gln	Asp	Cys	Lys	Ile	Ala	Pro	Leu	Met	Val	Ala	Tyr	Met	Leu	Glu	
		195					200					205				
aga	gag	ttg	gtc	cga	aaa	aca	agg	ttc	ctc	cca	gta	gta	ggc	gga	aca	672
Arg	Glu	Leu	Val	Arg	Lys	Thr	Arg	Phe	Leu	Pro	Val	Val	Gly	Gly	Thr	
	210					215					220					
agc	agt	gta	tac	att	gaa	gtg	ttg	cat	ctg	act	cag	gga	aca	tgc	tgg	720
Ser	Ser	Val	Tyr	Ile	Glu	Val	Leu	His	Leu	Thr	Gln	Gly	Thr	Cys	Trp	
225					230					235					240	
gag	caa	atg	tac	acc	cca	gga	gga	aaa	gtt	aga	aac	gat	gat	att	gat	768
Glu	Gln	Met	Tyr	Thr	Pro	Gly	Gly	Lys	Val	Arg	Asn	Asp	Asp	Ile	Asp	
				245					250					255		
caa	agt	tta	att	att	gca	gcc	cgg	aac	ata	gtg	aga	aga	gca	aca	gta	816
Gln	Ser	Leu	Ile	Ile	Ala	Ala	Arg	Asn	Ile	Val	Arg	Arg	Ala	Thr	Val	
			260					265					270			
tca	gca	gat	cca	cta	gca	tcc	cta	ctg	gaa	atg	tgc	cac	agt	aca	cag	864
Ser	Ala	Asp	Pro	Leu	Ala	Ser	Leu	Leu	Glu	Met	Cys	His	Ser	Thr	Gln	
		275					280					285				
att	ggt	gga	aca	agg	atg	gta	gac	atc	ctt	aag	cag	aac	cca	aca	gag	912
Ile	Gly	Gly	Thr	Arg	Met	Val	Asp	Ile	Leu	Lys	Gln	Asn	Pro	Thr	Glu	
	290					295					300					
gaa	caa	gct	gtg	gat	ata	tgc	aaa	gca	gca	atg	gga	ttg	aga	att	agc	960
Glu	Gln	Ala	Val	Asp	Ile	Cys	Lys	Ala	Ala	Met	Gly	Leu	Arg	Ile	Ser	
305					310					315					320	
tca	tca	ttc	agc	ttt	ggt	gga	ttc	acc	ttc	aaa	agg	aca	agt	gga	tca	1008
Ser	Ser	Phe	Ser	Phe	Gly	Gly	Phe	Thr	Phe	Lys	Arg	Thr	Ser	Gly	Ser	
				325					330					335		
tca	gtc	aag	aga	gaa	gaa	gaa	atg	ctt	acg	ggc	aac	ctt	caa	aca	ttg	1056
Ser	Val	Lys	Arg	Glu	Glu	Glu	Met	Leu	Thr	Gly	Asn	Leu	Gln	Thr	Leu	
			340					345					350			
aaa	ata	aga	gtg	cat	gag	ggc	tat	gaa	gaa	ttc	aca	atg	gtc	gga	aga	1104
Lys	Ile	Arg	Val	His	Glu	Gly	Tyr	Glu	Glu	Phe	Thr	Met	Val	Gly	Arg	
		355					360					365				
aga	gca	aca	gcc	att	atc	aga	aag	gca	acc	aga	aga	ttg	att	caa	ttg	1152
Arg	Ala	Thr	Ala	Ile	Ile	Arg	Lys	Ala	Thr	Arg	Arg	Leu	Ile	Gln	Leu	
	370					375						380				

ata gta agt ggg aga gat gaa caa tca att gct gaa gca ata att gta Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val 385 390 395 400	1200
gcc atg gtg ttt tgc caa gaa gat tgc atg ata aaa gca gtt cga ggc Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly 405 410 415	1248
gat ttg aac ttt gtt aat aga gca aat cag cgt ttg aac ccc atg cat Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His 420 425 430	1296
caa ctc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc caa aat Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn 435 440 445	1344
tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu 450 455 460	1392
cct gac atg acc cca agc acc gag atg tca ttg aga gga gtg aga gtc Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val 465 470 475 480	1440
agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val 485 490 495	1488
agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu 500 505 510	1536
ctg tcc cct gaa gaa gtc agt gaa aca caa gga acg gaa aag ctg aca Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr 515 520 525	1584
ata att tat tgc tca tca atg atg tgg gag att aat ggt ccc gaa tca Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser 530 535 540	1632
gtg ttg gtc aat act tat caa tgg atc atc aga aac tgg gaa att gta Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val 545 550 555 560	1680
aaa att cag tgg tca cag gac ccc aca atg tta tac aat aag ata gaa Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu 565 570 575	1728
ttt gaa cca ttc caa tcc ctg gtc cct agg gcc acc aga agc caa tac Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr 580 585 590	1776
agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ctt gga Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly 595 600 605	1824

aca ttt gat act gct caa ata ata aaa ctc ctc cct ttt gcc gct gct 1872
 Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala
 610 615 620
 cct ccg gaa cag agt agg atg cag ttc tct tct ttg act gtt aat gta 1920
 Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val
 625 630 635 640
 aga ggt tcg gga atg agg ata ctt gta aga ggc aat tcc cca gtg ttc 1968
 Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe
 645 650 655
 aac tac aat aaa gtc act aaa agg ctc aca gtc ctc gga aag gat gca 2016
 Asn Tyr Asn Lys Val Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala
 660 665 670
 ggt gcg ctt act gag gac cca gat gaa ggt acg gct gga gta gag tct 2064
 Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser
 675 680 685
 gct gtt cta aga ggg ttt ctc att tta ggt aaa gaa aac aag aga tat 2112
 Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr
 690 695 700
 ggc cca gca cta agc atc aat gaa ctt agc aaa ctt gca aaa ggg gag 2160
 Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu
 705 710 715 720
 aaa gcc aat gta cta att ggg caa ggg gac gta gtg ttg gta atg aaa 2208
 Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys
 725 730 735
 cgg aaa cgt gac tct agc ata ctt act gac agc cag aca gcg acc aaa 2256
 Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys
 740 745 750
 agg att cgg atg gcc atc aat tag 2280
 Arg Ile Arg Met Ala Ile Asn
 755

<210> 48
 <211> 759
 <212> PRT
 <213> Influenza virus

<400> 48

Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr
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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
 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 Lys Val Arg Asn Asp Asp Ile Asp

98

			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
 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
 625 630 635 640

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

100

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
705 710 715 720

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
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<210> 49
<211> 2274
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(2274)

<400> 49
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1 5 10 15
gct ata agc aca aca ttc cct tat act gga gat cct ccc tac agt cat 96
Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His
20 25 30
gga aca ggg aca gga tac acc atg gat act gtc aac aga aca cac caa 144
Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln
35 40 45
tat tca gaa aaa ggg aaa tgg aca aca aac act gag att gga gca cca 192
Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro
50 55 60
caa ctt aat cca atc gat gga cca ctt cct gaa gac aat gaa cca agt 240
Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser
65 70 75 80
ggg tac gcc caa aca gat tgt gta ttg gaa gca atg gct ttc ctt gaa 288
Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu
85 90 95

gaa tcc cat ccc gga atc ttt gaa aat tcg tgt ctt gaa acg atg gag	336
Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu	
100 105 110	
gtg att cag cag aca aga gtg gac aaa cta aca caa ggc cga caa act	384
Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr	
115 120 125	
tat gat tgg acc ttg aat agg aat caa cct gcc gca aca gca ctt gct	432
Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala	
130 135 140	
aat acg att gaa gta ttc aga tca aat ggt ctg acc tcc aat gaa tcg	480
Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser	
145 150 155 160	
ggg aga ttg atg gac ttc ctc aaa gat gtc atg gag tcc atg aac aag	528
Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys	
165 170 175	
gag gaa atg gaa ata aca aca cac ttc caa cgg aag aga aga gta aga	576
Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg	
180 185 190	
gac aac atg aca aag aga atg ata aca cag aga acc ata gga aag aaa	624
Asp Asn Met Thr Lys Arg Met Ile Thr Gln Arg Thr Ile Gly Lys Lys	
195 200 205	
aaa caa cga tta agc aga aag agc tat cta atc aga aca tta acc cta	672
Lys Gln Arg Leu Ser Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu	
210 215 220	
aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gca	720
Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala	
225 230 235 240	
atc gct acc cca ggg atg cag ata aga gga ttt gta tat ttt gtt gaa	768
Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu	
245 250 255	
aca cta gct cga aga ata tgt gaa aag ctt gaa caa tca gga ttg cca	816
Thr Leu Ala Arg Arg Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro	
260 265 270	
gtt ggc ggt aat gag aaa aag gcc aaa ctg gct aat gtc gtc aga aaa	864
Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys	
275 280 285	
atg atg act aat tcc caa gac act gaa ctc tcc ttc acc atc act ggg	912
Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly	
290 295 300	
gac aat acc aaa tgg aat gaa aat cag aac cca cgc ata ttc ctg gca	960
Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Ile Phe Leu Ala	

102

305	310	315	320	
atg atc aca tac ata act aga gat cag cca gaa tgg ttc aga aat gtt				1008
Met Ile Thr Tyr Ile Thr Arg Asp Gln Pro Glu Trp Phe Arg Asn Val	325	330	335	
cta agc att gca ccg att atg ttc tca aat aaa atg gca aga ctg ggg				1056
Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly	340	345	350	
aaa gga tat atg ttt gaa agc aaa agt atg aaa ttg aga act caa ata				1104
Lys Gly Tyr Met Phe Glu Ser Lys Ser Met Lys Leu Arg Thr Gln Ile	355	360	365	
cca gca gaa atg cta gca agc att gac cta aaa tat ttc aat gat tca				1152
Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Asp Ser	370	375	380	
aca aaa aag aaa att gaa aag ata cga cca ctc ctg gtt gac ggg act				1200
Thr Lys Lys Lys Ile Glu Lys Ile Arg Pro Leu Leu Val Asp Gly Thr	385	390	395	400
gct tca ctg agt cct ggc atg atg atg gga atg ttc aac atg ttg agc				1248
Ala Ser Leu Ser Pro Gly Met Met Met Gly Met Phe Asn Met Leu Ser	405	410	415	
act gtg ctg ggt gta tcc ata tta aac ctg ggc cag agg aaa tat aca				1296
Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Arg Lys Tyr Thr	420	425	430	
aag acc aca tac tgg tgg gat ggt ctg caa tca tcc gat gac ttt gct				1344
Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala	435	440	445	
ttg ata gtg aat gcg cct aat cat gaa gga ata caa gct gga gta gac				1392
Leu Ile Val Asn Ala Pro Asn His Glu Gly Ile Gln Ala Gly Val Asp	450	455	460	
aga ttc tat aga act tgc aaa ctg gtc ggg atc aac atg agc aaa aag				1440
Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys	465	470	475	480
aag tcc tac ata aat aga act gga aca ttc gaa ttc aca agc ttt ttc				1488
Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe	485	490	495	
tac cgg tat ggt ttt gta gcc aat ttc agc atg gaa cta ccc agt ttt				1536
Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe	500	505	510	
ggg gtt tcc gga ata aat gaa tct gca gac atg agc att gga gtg aca				1584
Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr	515	520	525	
gtc atc aaa aac aac atg ata aat aat gat ctc ggt cct gcc acg gca				1632

Val	Ile	Lys	Asn	Asn	Met	Ile	Asn	Asn	Asp	Leu	Gly	Pro	Ala	Thr	Ala	
530						535					540					
caa	atg	gca	ctc	caa	ctc	ttc	att	aag	gat	tat	cgg	tac	aca	tac	cgg	1680
Gln	Met	Ala	Leu	Gln	Leu	Phe	Ile	Lys	Asp	Tyr	Arg	Tyr	Thr	Tyr	Arg	
545					550					555					560	
tgc	cat	aga	ggt	gat	acc	cag	ata	caa	acc	aga	aga	tct	ttt	gag	ttg	1728
Cys	His	Arg	Gly	Asp	Thr	Gln	Ile	Gln	Thr	Arg	Arg	Ser	Phe	Glu	Leu	
				565					570					575		
aag	aaa	ctg	tgg	gaa	cag	act	cga	tca	aag	act	ggt	cta	ctg	gta	tca	1776
Lys	Lys	Leu	Trp	Glu	Gln	Thr	Arg	Ser	Lys	Thr	Gly	Leu	Leu	Val	Ser	
			580					585					590			
gat	ggg	ggt	cca	aac	cta	tat	aac	atc	aga	aac	cta	cac	atc	ccg	gaa	1824
Asp	Gly	Gly	Pro	Asn	Leu	Tyr	Asn	Ile	Arg	Asn	Leu	His	Ile	Pro	Glu	
		595					600					605				
gtc	tgt	tta	aaa	tgg	gag	cta	atg	gat	gaa	gat	tat	aag	ggg	agg	cta	1872
Val	Cys	Leu	Lys	Trp	Glu	Leu	Met	Asp	Glu	Asp	Tyr	Lys	Gly	Arg	Leu	
	610					615					620					
tgc	aat	cca	ttg	aat	cct	ttc	gtt	agt	cac	aaa	gaa	att	gaa	tca	gtc	1920
Cys	Asn	Pro	Leu	Asn	Pro	Phe	Val	Ser	His	Lys	Glu	Ile	Glu	Ser	Val	
625					630					635					640	
aac	agt	gca	gta	gta	atg	cct	gct	cat	ggc	cct	gcc	aaa	agc	atg	gag	1968
Asn	Ser	Ala	Val	Val	Met	Pro	Ala	His	Gly	Pro	Ala	Lys	Ser	Met	Glu	
				645					650					655		
tat	gat	gct	gtt	gca	aca	aca	cat	tct	tgg	atc	ccc	aag	agg	aac	cgg	2016
Tyr	Asp	Ala	Val	Ala	Thr	Thr	His	Ser	Trp	Ile	Pro	Lys	Arg	Asn	Arg	
			660					665					670			
tcc	ata	ttg	aac	aca	agc	caa	agg	gga	ata	cta	gaa	gat	gag	cag	atg	2064
Ser	Ile	Leu	Asn	Thr	Ser	Gln	Arg	Gly	Ile	Leu	Glu	Asp	Glu	Gln	Met	
		675					680					685				
tat	cag	aaa	tgc	tgc	aac	ctg	ttt	gaa	aaa	ttc	ttc	ccc	agc	agc	tca	2112
Tyr	Gln	Lys	Cys	Cys	Asn	Leu	Phe	Glu	Lys	Phe	Phe	Pro	Ser	Ser	Ser	
	690					695					700					
tac	aga	aga	cca	gtc	gga	att	tct	agt	atg	gtt	gag	gcc	atg	gta	tcc	2160
Tyr	Arg	Arg	Pro	Val	Gly	Ile	Ser	Ser	Met	Val	Glu	Ala	Met	Val	Ser	
705					710					715					720	
agg	gcc	cgc	att	gat	gca	cga	att	gac	ttc	gaa	tct	gga	cgg	ata	aag	2208
Arg	Ala	Arg	Ile	Asp	Ala	Arg	Ile	Asp	Phe	Glu	Ser	Gly	Arg	Ile	Lys	
				725				730						735		
aag	gat	gag	ttc	gct	gag	atc	atg	aag	atc	tgt	tcc	acc	att	gaa	gag	2256
Lys	Asp	Glu	Phe	Ala	Glu	Ile	Met	Lys	Ile	Cys	Ser	Thr	Ile	Glu	Glu	
			740					745						750		

ctc aga cgg caa aaa tag
 Leu Arg Arg Gln Lys
 755

2274

<210> 50
 <211> 757
 <212> PRT
 <213> Influenza virus

<400> 50

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 Asp 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 Ala 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

107

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
Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys			
	725	730	735
Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu			
	740	745	750
Leu Arg Arg Gln Lys			
	755		

<210> 51
 <211> 2151
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(2151)

<400> 51	
atg gaa gac ttt gtg cga cag tgc ttc aat cca atg atc gtc gag ctt	48
Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu	
1 5 10 15	
gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca	96

108

Ala	Glu	Lys	Ala	Met	Lys	Glu	Tyr	Gly	Glu	Asn	Pro	Lys	Ile	Glu	Thr		
			20					25					30				
aac	aaa	ttt	gca	gca	ata	tgc	act	cac	ttg	gaa	gtc	tgc	ttc	atg	tac		144
Asn	Lys	Phe	Ala	Ala	Ile	Cys	Thr	His	Leu	Glu	Val	Cys	Phe	Met	Tyr		
		35					40					45					
tgc	gat	ttc	cac	ttt	ata	aat	gaa	ctg	ggc	gag	tca	gtg	gtc	ata	gag		192
Ser	Asp	Phe	His	Phe	Ile	Asn	Glu	Leu	Gly	Glu	Ser	Val	Val	Ile	Glu		
	50					55					60						
tct	ggc	gac	cca	aat	gct	ctt	ttg	aaa	cac	aga	ttt	gaa	atc	att	gag		240
Ser	Gly	Asp	Pro	Asn	Ala	Leu	Leu	Lys	His	Arg	Phe	Glu	Ile	Ile	Glu		
65					70					75					80		
ggg	aga	gat	cga	aca	atg	gca	tgg	aca	gta	gta	aac	agc	atc	tgc	aac		288
Gly	Arg	Asp	Arg	Thr	Met	Ala	Trp	Thr	Val	Val	Asn	Ser	Ile	Cys	Asn		
				85					90					95			
acc	aca	aga	gct	gaa	aaa	cct	aaa	ttt	ctt	cca	gat	tta	tac	gac	tat		336
Thr	Thr	Arg	Ala	Glu	Lys	Pro	Lys	Phe	Leu	Pro	Asp	Leu	Tyr	Asp	Tyr		
			100					105					110				
aaa	gag	aac	aga	ttt	gtt	gaa	att	ggc	gtg	aca	agg	aga	gaa	gtt	cac		384
Lys	Glu	Asn	Arg	Phe	Val	Glu	Ile	Gly	Val	Thr	Arg	Arg	Glu	Val	His		
		115					120					125					
ata	tac	tac	ctg	gag	aag	gcc	aac	aaa	ata	aag	tct	gag	aaa	aca	cat		432
Ile	Tyr	Tyr	Leu	Glu	Lys	Ala	Asn	Lys	Ile	Lys	Ser	Glu	Lys	Thr	His		
	130					135					140						
atc	cac	att	ttc	tca	ttt	aca	gga	gaa	gaa	atg	gct	aca	aaa	gcg	gac		480
Ile	His	Ile	Phe	Ser	Phe	Thr	Gly	Glu	Glu	Met	Ala	Thr	Lys	Ala	Asp		
145					150					155					160		
tat	act	ctt	gat	gaa	gag	agt	aga	gcc	agg	atc	aag	acc	aga	cta	ttc		528
Tyr	Thr	Leu	Asp	Glu	Glu	Ser	Arg	Ala	Arg	Ile	Lys	Thr	Arg	Leu	Phe		
				165					170					175			
act	ata	aga	caa	gaa	atg	gcc	agt	aga	ggc	ctc	tgg	gat	tcc	ttt	cgt		576
Thr	Ile	Arg	Gln	Glu	Met	Ala	Ser	Arg	Gly	Leu	Trp	Asp	Ser	Phe	Arg		
			180					185					190				
cag	tcc	gag	aga	ggc	gaa	gag	aca	att	gaa	gaa	aga	ttt	gaa	atc	aca		624
Gln	Ser	Glu	Arg	Gly	Glu	Glu	Thr	Ile	Glu	Glu	Arg	Phe	Glu	Ile	Thr		
			195				200					205					
ggg	acg	atg	cgc	aag	ctt	gcc	aat	tac	agt	ctc	cca	ccg	aac	ttc	tcc		672
Gly	Thr	Met	Arg	Lys	Leu	Ala	Asn	Tyr	Ser	Leu	Pro	Pro	Asn	Phe	Ser		
	210					215					220						
agc	ctt	gaa	aat	ttt	aga	gtc	tat	ata	gat	gga	ttc	gaa	ccg	aac	ggc		720
Ser	Leu	Glu	Asn	Phe	Arg	Val	Tyr	Ile	Asp	Gly	Phe	Glu	Pro	Asn	Gly		
225					230					235					240		

tgc att gag agt aag ctt tct caa atg tcc aaa gaa gta aat gcc aaa	768
Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys	
245 250 255	
ata gaa cca ttt tca aag aca aca ccc cga cca ctc aaa atg cca ggt	816
Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
260 265 270	
ggt cca ccc tgc cat cag cga tcc aaa ttc ttg cta atg gat gct ctg	864
Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
275 280 285	
aaa ctg agc att gag gac cca agt cac gag gga gag ggg ata cca cta	912
Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
290 295 300	
tat gat gca atc aaa tgc atg aaa act ttc ttt gga tgg aaa gag ccc	960
Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
305 310 315 320	
agt att gtt aaa cca cat aaa aag ggt ata aac ccg aac tat ctc caa	1008
Ser Ile Val Lys Pro His Lys Lys Gly Ile Asn Pro Asn Tyr Leu Gln	
325 330 335	
act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa	1056
Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu	
340 345 350	
agg acc ccc aag acc aag aat atg aaa aaa aca agc caa ttg aaa tgg	1104
Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
355 360 365	
gca cta ggt gaa aat atg gca cca gag aaa gtg gat ttt gag gat tgt	1152
Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
370 375 380	
aaa gac atc aat gat tta aaa caa tat gac agt gat gag cca gaa gca	1200
Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala	
385 390 395 400	
agg tct ctt gca agt tgg att caa agt gag ttc aac aag gct tgt gag	1248
Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
405 410 415	
ctg aca gat tca agc tgg ata gag ctc gat gaa att ggg gag gat gtc	1296
Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val	
420 425 430	
gcc cca ata gaa tac att gcg agc atg agg aga aat tat ttt act gct	1344
Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
435 440 445	
gag att tcc cat tgt aga gca aca gaa tat ata atg aaa gga gtg tac	1392
Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr	
450 455 460	

atc aac act gct cta ctc aat gca tcc tgt gct gcg atg gat gaa ttt Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe 465 470 475 480	1440
caa tta att ccg atg ata agt aaa tgc agg acc aaa gaa ggg aga agg Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg 485 490 495	1488
aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg 500 505 510	1536
aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct ctc act Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr 515 520 525	1584
gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu 530 535 540	1632
att gga gac atg ctt tta aga act gct gta ggt caa gtg tca aga ccc Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro 545 550 555 560	1680
atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys 565 570 575	1728
tgg gga atg gaa atg agg cgc tgc ctc ctt cag tct ctg caa cag att Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile 580 585 590	1776
gaa agc atg atc gaa gct gag tcc tca gtc aaa gaa aag gac atg acc Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr 595 600 605	1824
aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser 610 615 620	1872
ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu 625 630 635 640	1920
tta gca aaa tct gtg ttt aac agt tta tat gca tct cca caa ctg gaa Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu 645 650 655	1968
gga ttt tca gct gaa tct agg aaa tta ctt ctc att gtt cag gct ctt Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu 660 665 670	2016
aga gat gac ctg gaa cct gga acc ttt gat att ggg ggg tta tat gaa Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu	2064

111

675	680	685	
tca att gag gag tgc ctg att aat gat ccc tgg gtt ttg ctt aat gca			2112
Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala			
690	695	700	
tct tgg ttc aac tcc ttc ctc aca cat gca ctg aag tag			2151
Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys			
705	710	715	

<210> 52
 <211> 716
 <212> PRT
 <213> Influenza virus

<400> 52

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
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

112

145		150		155		160
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	240
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	320
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
 385 390 395 400

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
 465 470 475 480

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

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

Met 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> 53
<211> 844
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(690)

<400> 53
atg gat tcc aac act gtg tca agc ttt cag gta gac tgt ttt ctt tgg 48
Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp
1 5 10 15
cat gtc cgt aaa cga ttc gca gac caa gaa ctg ggt gat gcc cca ttc 96
His Val Arg Lys Arg Phe Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe
20 25 30
ctt gac cgg ctt cgc cga gac cag aag tcc cta agg gga aga ggt agc 144
Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser
35 40 45

act ctt ggt ctg gac atc gaa aca gcc act cat gca gga aag cag ata	192
Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr His Ala Gly Lys Gln Ile	
50 55 60	
gtg gag cag att ctg gaa aag gaa tca gat gag gca ctt aaa atg acc	240
Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr	
65 70 75 80	
att gcc tct gtt cct gct tca cgc tac tta act gac atg act ctt gat	288
Ile Ala Ser Val Pro Ala Ser Arg Tyr Leu Thr Asp Met Thr Leu Asp	
85 90 95	
gag atg tca aga gac tgg ttc atg ctc atg ccc aag caa aaa gta aca	336
Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Thr	
100 105 110	
ggc tcc cta tgt ata aga atg gac cag gca atc atg gat aag aac atc	384
Gly Ser Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile	
115 120 125	
ata ctt aaa gca aac ttt agt gtg att ttc gaa agg ctg gaa aca cta	432
Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Arg Leu Glu Thr Leu	
130 135 140	
ata cta ctt aga gcc ttc acc gaa gaa gga gca gtc gtt ggc gaa att	480
Ile Leu Leu Arg Ala Phe Thr Glu Glu Gly Ala Val Val Gly Glu Ile	
145 150 155 160	
tca cca tta cct tct ctt cca gga cat act aat gag gat gtc aaa aat	528
Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn	
165 170 175	
gca att ggg gtc ctc atc gga gga ctt aaa tgg aat gat aat acg gtt	576
Ala Ile Gly Val Leu Ile Gly Gly Leu Lys Trp Asn Asp Asn Thr Val	
180 185 190	
aga atc tct gaa act cta cag aga ttc gct tgg aga agc agt cat gaa	624
Arg Ile Ser Glu Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser His Glu	
195 200 205	
aat ggg aga cct tca ttc cct tca aaa cag aaa cga aaa atg gag aga	672
Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg	
210 215 220	
aca att aag cca gaa att tgaagaaata agatggttga ttgaagaagt	720
Thr Ile Lys Pro Glu Ile	
225 230	
gcgacataga ttgaaaaata cagaaaatag ttttgaacaa ataacattta tgcaagcctt	780
acaactattg cttgaagtag aacaagagat aagaactttc tcgttttcagc ttattttaatg	840
ataa	844

<210> 54
 <211> 230
 <212> PRT
 <213> Influenza virus

<400> 54

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
 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

117

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> 55
 <211> 1497
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1497)

<400> 55
 atg gcg tct caa. ggc acc aaa cga tcc tat gaa cag atg gaa act gat 48
 Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 1 5 10 15
 ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
 Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30
 gtg gga gga atc gga cgg ttt tat gtc cag atg tgt act gag ctt aaa 144
 Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45
 cta aac gac cat gaa ggg cgg ctg att cag aac agc ata aca ata gaa 192
 Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60
 agg atg gtg ctt tgc gca ttc gac gaa aga aga aac aag tat ctc gag 240
 Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu
 65 70 75 80
 gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc ccg ata 288
 Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile
 85 90 95
 tac aga aga aaa gat ggg aaa tgg atg agg gaa ctc atc ctc cat gat 336
 Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp
 100 105 110
 aaa gaa gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac 384
 Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp
 115 120 125

gct act gct ggt ctt act cat atg atg atc tgg cac tcc aat ctc aat	432
Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn	
130 135 140	
gac acc aca tac caa aga aca agg gct ctt gtt cgg act ggg atg gat	480
Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp	
145 150 155 160	
ccc aga atg tgc tct ctg atg caa ggc tca acc ctc cca cgg aga tct	528
Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser	
165 170 175	
gga gcc gct ggt gct gca gta aaa ggc gtt gga aca atg gta atg gaa	576
Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu	
180 185 190	
ctc atc aga atg atc aag cgc gga ata aat gat cgg aat ttc tgg aga	624
Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg	
195 200 205	
ggt gaa aat ggt cga aga acc aga att gct tat gaa aga atg tgc aat	672
Gly Glu Asn Gly Arg Arg Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn	
210 215 220	
atc ctc aaa ggg aaa ttt cag aca gca gca caa cgg gct atg atg gac	720
Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp	
225 230 235 240	
cag gtg agg gaa ggc cgc aat cct gga aac gct gag att gag gat ctc	768
Gln Val Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu	
245 250 255	
att ttc ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat	816
Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His	
260 265 270	
aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gca gta acc agt ggg	864
Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Val Thr Ser Gly	
275 280 285	
tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc	912
Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe	
290 295 300	
aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa	960
Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu	
305 310 315 320	
aac cca gca cac aaa agc cag ttg gtg tgg atg gca tgc cat tct gca	1008
Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala	
325 330 335	
gca ttt gag gat ctg aga gtt tta aat ttc att aga gga acc aaa gta	1056
Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val	

119

340	345	350	
atc cca aga gga cag tta aca acc aga gga gtt caa att gct tca aat			1104
Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn			
355	360	365	
gaa aac atg gag aca ata aat tct agc aca ctt gaa ctg aga agc aaa			1152
Glu Asn Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys			
370	375	380	
tat tgg gca ata agg acc aga agc gga gga aac acc agt caa cag aga			1200
Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg			
385	390	395	400
gca tct gca gga cag ata agt gtg caa cct act ttc tca gta cag aga			1248
Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg			
405	410	415	
aat ctt ccc ttt gag aga gca acc att atg gct gca ttc act ggt aac			1296
Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn			
420	425	430	
act gaa gga agg act tcc gac atg aga acg gaa atc ata agg atg atg			1344
Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met			
435	440	445	
gaa aat gcc aaa tca gaa gat gtg tct ttc cag ggg cgg gga gtc ttc			1392
Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe			
450	455	460	
gag ctc tcg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac			1440
Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp			
465	470	475	480
atg agc aat gaa ggg tct tat ttc ttc gga gac aat gct gag gag ttt			1488
Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe			
485	490	495	
gac agt taa			1497
Asp Ser			

<210> 56

<211> 498

<212> PRT

<213> Influenza virus

<400> 56

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

120

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
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					240

121

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
305 310 315 320

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
385 390 395 400

Ala Ser 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

122

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp
 465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
 485 490 495

Asp Ser

<210> 57
 <211> 1413
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1413)

<400> 57
 atg aat cca aat caa aag ata ata gca att gga ttt gca tca ttg ggg 48
 Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
 1 5 10 15
 ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca 96
 Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
 20 25 30
 gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144
 Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
 35 40 45
 atc ata aga gaa tac aat gaa aca gta aga gta gaa aaa ctt act caa 192
 Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu Thr Gln
 50 55 60
 tgg tat aat acc agt aca att aag tac ata gag aga cct tca aat gaa 240
 Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu
 65 70 75 80
 tac tac atg aat aac act gaa cca ctt tgt gag gcc caa ggc ttt gca 288
 Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala
 85 90 95
 cca ttt tcc aaa gat aat gga ata cga att ggg tcg aga ggc cat gtt 336
 Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val
 100 105 110
 ttt gtg ata aga gaa cct ttt gta tca tgt tcg ccc tca gaa tgt aga 384
 Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg
 115 120 125

acc ttt ttc ctc aca cag ggc tca tta ctc aat gac aaa cat tct aac	432
Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn	
130 135 140	
ggc aca ata aag gat cga agt ccg tat agg act ttg atg agt gtc aaa	480
Gly Thr Ile Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys	
145 150 155 160	
ata ggg caa tca cct aat gta tat caa gct agg ttt gaa tcg gtg gca	528
Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala	
165 170 175	
tgg tca gca aca gca tgc cat gat gga aaa aaa tgg atg aca gtt gga	576
Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly	
180 185 190	
gtc aca ggg ccc gac aat caa gca att gca gta gtg aac tat gga ggt	624
Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly	
195 200 205	
gtt ccg gtt gat att att aat tca tgg gca ggg gat att tta aga acc	672
Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr	
210 215 220	
caa gaa tca tca tgc acc tgc att aaa gga gac tgt tat tgg gta atg	720
Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met	
225 230 235 240	
act gat gga ccg gca aat agg caa gct aaa tat agg ata ttc aaa gca	768
Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala	
245 250 255	
aaa gat gga aga gta att gga caa act gat ata agt ttc aat ggg gga	816
Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly	
260 265 270	
cac ata gag gag tgt tct tgt tac ccc aat gaa ggg aag gtg gaa tgc	864
His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys	
275 280 285	
ata tgc agg gac aat tgg act gga aca aat aga cca att ctg gta ata	912
Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile	
290 295 300	
tct tct gat cta tcg tac aca gtt gga tat ttg tgt gct ggc att ccc	960
Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro	
305 310 315 320	
act gac act cct agg gga gag gat agt caa ttc aca ggc tca tgt aca	1008
Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr	
325 330 335	
agt cct ttg gga aat aaa gga tac ggt gta aaa ggc ttc ggg ttt cga	1056
Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg	

124

340	345	350	
caa gga act gac gta tgg gcc gga agg aca att agt agg act tca aga			1104
Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg			
355	360	365	
tca gga ttc gaa ata ata aaa atc agg aat ggt tgg aca cag aac agt			1152
Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser			
370	375	380	
aag gac caa atc agg agg caa gtg att atc gat gac cca aat tgg tca			1200
Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser			
385	390	395	400
gga tat agc ggt tct ttc aca ttg ccg gtt gaa ctg aca aaa aag gga			1248
Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly			
405	410	415	
tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa			1296
Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu			
420	425	430	
gaa aca aca ata tgg acc tct agc agc tcc att gtg atg tgt gga gta			1344
Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val			
435	440	445	
gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att ctt ccc			1392
Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro			
450	455	460	
ttt gac atc gat aag atg taa			1413
Phe Asp Ile Asp Lys Met			
465	470		

<210> 58

<211> 470

<212> PRT

<213> Influenza virus

<400> 58

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

125

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	Ile	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				

126

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

Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
 325 330 335

Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
 340 345 350

Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
 355 360 365

Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
 370 375 380

Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
 385 390 395 400

Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
 405 410 415

Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
 420 425 430

Glu Thr Thr Ile Trp Thr Ser Ser Ser Ile Val Met Cys Gly Val
 435 440 445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460

Phe Asp Ile Asp Lys Met
 465 470

<210> 59
 <211> 981
 <212> DNA

127

<213> Influenza virus

<220>

<221> CDS

<222> (1)..(756)

<400> 59

atg agt ctt cta acc gag gtc gaa acg tac gtt ctc tct atc gta cca	48
Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro	
1 5 10 15	
tca ggc ccc ctc aaa gcc gag atc gcg cag aga ctt gaa gat gtc ttt	96
Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe	
20 25 30	
gcg gga aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca	144
Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr	
35 40 45	
aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc	192
Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe	
50 55 60	
acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc	240
Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val	
65 70 75 80	
caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gca	288
Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala	
85 90 95	
gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gca	336
Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala	
100 105 110	
aaa gag gtg gca ctc agc tat tcc act ggt gca cta gcc agc tgc atg	384
Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met	
115 120 125	
gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gca ttt	432
Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe	
130 135 140	
ggc ctg gta tgc gcc aca tgt gaa cag att gct gat tcc cag cat cga	480
Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg	
145 150 155 160	
tct cac agg cag atg gtg aca aca acc aac cca tta atc aga cat gaa	528
Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu	
165 170 175	
aac aga atg gta tta gcc agt acc acg gct aaa gcc atg gaa cag atg	576
Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met	
180 185 190	

gca gga tgc agt gag cag gca gca gag gcc atg gag gtt gct agt agg 624
Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg
195 200 205

gct agg cag atg gta cag gca atg aga acc att ggg acc cac cct agc 672
Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser
210 215 220

tcc agt gcc ggt ttg aaa gat gat ctc ctt gaa aat tta cag gcc tac 720
Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr
225 230 235 240

cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctctc 766
Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys
245 250

gtcattgcag caagtatcat tgggatcttg cacttgatat tgtggattct tgatcgtctt 826

ttcttcaa at tcatttatcg tcgccttaaa tacgggttga aaagagggcc ttctacggaa 886

ggagtacctg agtctatgag ggaagaatat cggcaggaac agcagaatgc tgtggatggt 946

gacgatggtc attttgtcaa catagagctg gagta 981

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<210> 60
<211> 252
<212> PRT
<213> Influenza virus
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<400> 60

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

129

Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly 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> 61
 <211> 1698
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1698)

<400> 61
 atg aag aca acc att att tta ata cta ctg acc cat tgg gcc tac agt
 Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser

130

1	5	10	15	
caa aac cca atc agt ggc aat aac aca gcc aca ctg tgt ctg gga cac				96
Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His				
	20	25	30	
cat gca gta gca aat gga aca ttg gta aaa aca atg agt gat gat caa				144
His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln				
	35	40	45	
att gag gtg aca aat gct aca gaa tta gtt cag agc att tca atg ggg				192
Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly				
	50	55	60	
aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca				240
Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr				
	65	70	75	80
tta ata gat gca atg cta gga gac ccc cac tgt gac gcc ttt cag tat				288
Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr				
	85	90	95	
gag agt tgg gac ctc ttt ata gaa aga agc agc gct ttc agc aat tgc				336
Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys				
	100	105	110	
tac cca tat gac atc cct gac tat gca tcg ctc cga tcc att gta gca				384
Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Ser Leu Arg Ser Ile Val Ala				
	115	120	125	
tcc tca ggg aca gtg gaa ttc aca gca gag gga ttc aca tgg aca ggt				432
Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly				
	130	135	140	
gta act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat				480
Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp				
	145	150	155	160
agt ttc ttt agc cga ctg aat tgg cta aca aaa tct gga agc tct tac				528
Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Lys Ser Gly Ser Ser Tyr				
	165	170	175	
ccc aca ttg aat gtg aca atg cct aac aat aaa aat ttc gac aag cta				576
Pro Thr Leu Asn Val Thr Met Pro Asn Asn Lys Asn Phe Asp Lys Leu				
	180	185	190	
tac atc tgg ggg att cat cac ccg agc tca aat caa gag cag aca aaa				624
Tyr Ile Trp Gly Ile His His Pro Ser Ser Asn Gln Glu Gln Thr Lys				
	195	200	205	
ttg tac atc caa gaa tca gga cga gta aca gtc tca aca aaa aga agt				672
Leu Tyr Ile Gln Glu Ser Gly Arg Val Thr Val Ser Thr Lys Arg Ser				
	210	215	220	
caa caa aca ata atc cct aac atc gga tct aga ccg ttg gtc aga ggt				720

131

Gln	Gln	Thr	Ile	Ile	Pro	Asn	Ile	Gly	Ser	Arg	Pro	Leu	Val	Arg	Gly	
225					230					235					240	
caa	tca	ggc	agg	ata	agc	ata	tac	tgg	acc	att	gta	aaa	cct	gga	gat	768
Gln	Ser	Gly	Arg	Ile	Ser	Ile	Tyr	Trp	Thr	Ile	Val	Lys	Pro	Gly	Asp	
				245					250					255		
atc	cta	atg	ata	aac	agt	aat	ggc	aac	tta	gtt	gca	ccg	cgg	gga	tat	816
Ile	Leu	Met	Ile	Asn	Ser	Asn	Gly	Asn	Leu	Val	Ala	Pro	Arg	Gly	Tyr	
			260					265					270			
ttt	aaa	ttg	aac	aca	ggg	aaa	agc	tct	gta	atg	aga	tcc	gat	gta	ccc	864
Phe	Lys	Leu	Asn	Thr	Gly	Lys	Ser	Ser	Val	Met	Arg	Ser	Asp	Val	Pro	
		275					280					285				
ata	gac	att	tgt	gtg	tct	gaa	tgt	att	aca	cca	aat	gga	agc	atc	tcc	912
Ile	Asp	Ile	Cys	Val	Ser	Glu	Cys	Ile	Thr	Pro	Asn	Gly	Ser	Ile	Ser	
	290					295					300					
aac	gac	aag	cca	ttc	caa	aat	gtg	aac	aaa	gtt	aca	tat	gga	aaa	tgc	960
Asn	Asp	Lys	Pro	Phe	Gln	Asn	Val	Asn	Lys	Val	Thr	Tyr	Gly	Lys	Cys	
305					310					315					320	
ccc	aag	tat	atc	agg	caa	aac	act	tta	aag	ctg	gcc	act	ggg	atg	agg	1008
Pro	Lys	Tyr	Ile	Arg	Gln	Asn	Thr	Leu	Lys	Leu	Ala	Thr	Gly	Met	Arg	
				325					330					335		
aat	gta	cca	gaa	aag	caa	acc	aga	gga	atc	ttt	gga	gca	ata	gcg	gga	1056
Asn	Val	Pro	Glu	Lys	Gln	Thr	Arg	Gly	Ile	Phe	Gly	Ala	Ile	Ala	Gly	
			340					345					350			
ttc	atc	gaa	aac	ggc	tgg	gaa	gga	atg	gtt	gat	ggg	tgg	tat	ggg	ttc	1104
Phe	Ile	Glu	Asn	Gly	Trp	Glu	Gly	Met	Val	Asp	Gly		Tyr	Gly	Phe	
		355				360						365				
cga	tat	caa	aac	tct	gaa	gga	aca	ggg	caa	gct	gca	gat	cta	aag	agc	1152
Arg	Tyr	Gln	Asn	Ser	Glu	Gly	Thr	Gly	Gln	Ala	Ala	Asp	Leu	Lys	Ser	
	370					375					380					
act	caa	gca	gcc	atc	gac	cag	att	aat	gga	aag	tta	aac	aga	gtg	att	1200
Thr	Gln	Ala	Ala	Ile	Asp	Gln	Ile	Asn	Gly	Lys	Leu	Asn	Arg	Val	Ile	
385					390					395					400	
gaa	aga	acc	aat	gag	aaa	ttc	cat	caa	ata	gag	aag	gaa	ttc	tca	gaa	1248
Glu	Arg	Thr	Asn	Glu	Lys	Phe	His	Gln	Ile	Glu	Lys	Glu	Phe	Ser	Glu	
				405					410					415		
gta	gaa	gga	aga	att	cag	gac	ttg	gag	aaa	tat	gta	gaa	gac	acc	aaa	1296
Val	Glu	Gly	Arg	Ile	Gln	Asp	Leu	Glu	Lys	Tyr	Val	Glu	Asp	Thr	Lys	
			420					425					430			
ata	gac	cta	tgg	tcc	tac	aat	gca	gaa	ttg	ctg	gtg	gct	cta	gaa	aat	1344
Ile	Asp	Leu	Trp	Ser	Tyr	Asn	Ala	Glu	Leu	Leu	Val	Ala	Leu	Glu	Asn	
		435					440					445				

132

caa cat aca att gac tta aca gat gca gaa atg aat aaa tta ttt gag 1392
 Gln His Thr Ile Asp Leu Thr Asp Ala Glu Met Asn Lys Leu Phe Glu
 450 455 460

aag act aga cgc cag tta aga gaa aac gca gaa gac atg gga ggt gga 1440
 Lys Thr Arg Arg Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Gly Gly
 465 470 475 480

tgt ttc aag att tac cac aaa tgt gat aat gca tgc att gaa tca ata 1488
 Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Glu Ser Ile
 485 490 495

aga act ggg aca tat gac cat tac ata tac aaa gat gaa gca tta aac 1536
 Arg Thr Gly Thr Tyr Asp His Tyr Ile Tyr Lys Asp Glu Ala Leu Asn
 500 505 510

aat cga ttt cag atc aaa ggt gta gag ttg aaa tca ggc tac aaa gat 1584
 Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Tyr Lys Asp
 515 520 525

tgg ata ctg tgg att tca ttc gcc ata tca tgc ttc tta att tgc gtt 1632
 Trp Ile Leu Trp Ile Ser Phe Ala Ile Ser Cys Phe Leu Ile Cys Val
 530 535 540

gtt cta ttg ggt ttc att atg tgg gct tgc caa aaa ggc aac atc aga 1680
 Val Leu Leu Gly Phe Ile Met Trp Ala Cys Gln Lys Gly Asn Ile Arg
 545 550 555 560

tgc aac att tgc att tga 1698
 Cys Asn Ile Cys Ile
 565

<210> 62
 <211> 565
 <212> PRT
 <213> Influenza virus

<400> 62

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

133

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 Phe 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 Gly Ser Arg Pro Leu Val Arg Gly
 225 230 235 240

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 Lys Asp Glu Ala Leu Asn

135

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> 63
 <211> 2280
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(2280)

<400> 63
 atg gag aga ata aaa gaa ctg aga gat ctg atg tta caa tcc cgc acc 48
 Met Glu Arg Ile Lys Glu Leu Arg Asp Leu Met Leu Gln Ser Arg Thr
 1 5 10 15
 cgc gag ata cta aca aaa act act gtg gac cac atg gcc ata atc aag 96
 Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys
 20 25 30
 aaa tac aca tca gga aga caa gag aag aac cct gca ctt agg atg aaa 144
 Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ala Leu Arg Met Lys
 35 40 45
 tgg atg atg gca atg aaa tac cca att aca gca gat aag agg ata atg 192
 Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Met
 50 55 60
 gag atg att cct gag aga aat gaa cag gga caa acc ctt tgg agc aaa 240
 Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys
 65 70 75 80
 acg aac gat gct ggc tca gac cgc gta atg gta tca cct ctg gca gtg 288
 Thr Asn Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val
 85 90 95
 aca tgg tgg aat agg aat gga cca aca acg aac aca att cat tat cca 336

136

Thr	Trp	Trp	Asn	Arg	Asn	Gly	Pro	Thr	Thr	Asn	Thr	Ile	His	Tyr	Pro	
			100					105					110			
aaa	gtc	tac	aaa	act	tat	ttt	gaa	aag	gtt	gaa	aga	ttg	aaa	cac	gga	384
Lys	Val	Tyr	Lys	Thr	Tyr	Phe	Glu	Lys	Val	Glu	Arg	Leu	Lys	His	Gly	
		115					120					125				
acc	ttt	ggc	ccc	gtt	cat	ttt	agg	aat	caa	gtc	aag	ata	aga	cga	aga	432
Thr	Phe	Gly	Pro	Val	His	Phe	Arg	Asn	Gln	Val	Lys	Ile	Arg	Arg	Arg	
	130					135					140					
gtt	gat	gta	aac	cct	ggc	cac	gcg	gac	ctc	agt	gct	aaa	gaa	gca	caa	480
Val	Asp	Val	Asn	Pro	Gly	His	Ala	Asp	Leu	Ser	Ala	Lys	Glu	Ala	Gln	
145					150					155					160	
gat	gtg	atc	atg	gaa	gtt	gtt	ttc	cca	aat	gaa	gtg	gga	gcc	aga	att	528
Asp	Val	Ile	Met	Glu	Val	Val	Phe	Pro	Asn	Glu	Val	Gly	Ala	Arg	Ile	
				165					170					175		
cta	aca	tca	gaa	tca	caa	cta	aca	ata	acc	aaa	gag	aaa	aag	gaa	gaa	576
Leu	Thr	Ser	Glu	Ser	Gln	Leu	Thr	Ile	Thr	Lys	Glu	Lys	Lys	Glu	Glu	
			180					185					190			
ctt	cag	gac	tgc	aaa	att	gct	ccc	ttg	atg	gta	gca	tac	atg	cta	gaa	624
Leu	Gln	Asp	Cys	Lys	Ile	Ala	Pro	Leu	Met	Val	Ala	Tyr	Met	Leu	Glu	
		195					200					205				
aga	gag	ttg	gtc	cga	aaa	aca	agg	ttc	ctc	cca	gta	gta	ggc	gga	aca	672
Arg	Glu	Leu	Val	Arg	Lys	Thr	Arg	Phe	Leu	Pro	Val	Val	Gly	Gly	Thr	
	210					215					220					
agc	agt	gta	tac	att	gaa	gtg	ttg	cat	ctg	act	cag	gga	aca	tgc	tg	720
Ser	Ser	Val	Tyr	Ile	Glu	Val	Leu	His	Leu	Thr	Gln	Gly	Thr	Cys	Trp	
225					230					235					240	
gag	caa	atg	tac	acc	cca	gga	gga	aaa	gtt	aga	aac	gat	gat	att	gat	768
Glu	Gln	Met	Tyr	Thr	Pro	Gly	Gly	Lys	Val	Arg	Asn	Asp	Asp	Ile	Asp	
				245					250					255		
caa	agt	tta	att	att	gca	gcc	cgg	aac	ata	gtg	aga	aga	gca	aca	gta	816
Gln	Ser	Leu	Ile	Ile	Ala	Ala	Arg	Asn	Ile	Val	Arg	Arg	Ala	Thr	Val	
			260					265					270			
tca	gca	gat	cca	cta	gca	tcc	cta	ctg	gaa	atg	tgc	cac	agt	aca	cag	864
Ser	Ala	Asp	Pro	Leu	Ala	Ser	Leu	Leu	Glu	Met	Cys	His	Ser	Thr	Gln	
		275					280					285				
att	ggc	gga	aca	agg	atg	gta	gac	atc	ctt	aag	cag	aac	cca	aca	gag	912
Ile	Gly	Gly	Thr	Arg	Met	Val	Asp	Ile	Leu	Lys	Gln	Asn	Pro	Thr	Glu	
	290					295					300					
gaa	caa	gct	gtg	gat	ata	tgc	aaa	gca	gca	atg	gga	ttg	aga	att	agc	960
Glu	Gln	Ala	Val	Asp	Ile	Cys	Lys	Ala	Ala	Met	Gly	Leu	Arg	Ile	Ser	
305					310					315					320	

tca tca ttc agc ttt ggt gga ttc acc ttc aaa agg aca agt gga tca	1008
Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser	
325 330 335	
tca gtc aag aga gaa gaa gaa atg ctt acg ggc aac ctt caa aca ttg	1056
Ser Val Lys Arg Glu Glu Glu Met Leu Thr Gly Asn Leu Gln Thr Leu	
340 345 350	
aaa ata aga gtg cat gag ggc tat gaa gaa ttc aca atg gtc gga aga	1104
Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Arg	
355 360 365	
aga gca aca gcc att atc aga aag gca acc aga aga ttg att caa ttg	1152
Arg Ala Thr Ala Ile Ile Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu	
370 375 380	
ata gta agt ggg aga gat gaa caa tca att gct gaa gca ata att gta	1200
Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val	
385 390 395 400	
gcc atg gtg ttt tcg caa gaa gat tgc atg ata aaa gca gtt cga ggc	1248
Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly	
405 410 415	
gat ttg aac ttt gtt aat aga gca aat cag cgt ttg aac ccc atg cat	1296
Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His	
420 425 430	
caa ctc ttg agg cat ttc caa aaa gat gca aaa gtg ctt ttc caa aat	1344
Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn	
435 440 445	
tgg gga att gaa ccc atc gac aat gta atg ggg atg att gga ata ttg	1392
Trp Gly Ile Glu Pro Ile Asp Asn Val Met Gly Met Ile Gly Ile Leu	
450 455 460	
cct gac atg acc cca agc acc gag atg tca ttg aga gga gtg aga gtc	1440
Pro Asp Met Thr Pro Ser Thr Glu Met Ser Leu Arg Gly Val Arg Val	
465 470 475 480	
agc aaa atg gga gtg gat gag tac tcc agc act gag aga gtg gtg gtg	1488
Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Thr Glu Arg Val Val Val	
485 490 495	
agc att gac cgt ttt tta aga gtt cgg gat caa agg gga aac ata cta	1536
Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Ile Leu	
500 505 510	
ctg tcc cct gaa gaa gtc agt gaa aca caa gga acg gaa aag ctg aca	1584
Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr	
515 520 525	
ata att tat tcg tca tca atg atg tgg gag att aat ggt ccc gaa tca	1632
Ile Ile Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser	
530 535 540	

gtg ttg gtc aat act tat caa tgg atc atc aga aac tgg gaa att gta	1680
Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Ile Val	
545 550 555 560	
aaa att cag tgg tca cag gac ccc aca atg tta tac aat aag ata gaa	1728
Lys Ile Gln Trp Ser Gln Asp Pro Thr Met Leu Tyr Asn Lys Ile Glu	
565 570 575	
ttt gaa cca ttc caa tcc ctg gtc cct agg gcc acc aga agc caa tac	1776
Phe Glu Pro Phe Gln Ser Leu Val Pro Arg Ala Thr Arg Ser Gln Tyr	
580 585 590	
agc ggt ttc gta aga acc ctg ttt cag caa atg cga gat gta ctt gga	1824
Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly	
595 600 605	
aca ttt gat act gct caa ata ata aaa ctc ctc cct ttt gcc gct gct	1872
Thr Phe Asp Thr Ala Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala	
610 615 620	
cct ccg gaa cag agt agg atg cag ttc tct tct ttg act gtt aat gta	1920
Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val	
625 630 635 640	
aga ggt tcg gga atg agg ata ctt gta aga ggc aat tcc cca gtg ttc	1968
Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Val Phe	
645 650 655	
aac tac aat aaa gtc act aaa agg ctc aca gtc ctc gga aag gat gca	2016
Asn Tyr Asn Lys Val Thr Lys Arg Leu Thr Val Leu Gly Lys Asp Ala	
660 665 670	
ggg gcg ctt act gag gac cca gat gaa ggt acg gct gga gta gag tct	2064
Gly Ala Leu Thr Glu Asp Pro Asp Glu Gly Thr Ala Gly Val Glu Ser	
675 680 685	
gct gtt cta aga ggg ttt ctc att tta ggt aaa gaa aac aag aga tat	2112
Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asn Lys Arg Tyr	
690 695 700	
ggc cca gca cta agc atc aat gaa ctt agc aaa ctt gca aaa ggg gag	2160
Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Lys Leu Ala Lys Gly Glu	
705 710 715 720	
aaa gcc aat gta cta att ggg caa ggg gac gta gtg ttg gta atg aaa	2208
Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys	
725 730 735	
cgg aaa cgt gac tct agc ata ctt act gac agc cag aca gcg acc aaa	2256
Arg Lys Arg Asp Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys	
740 745 750	
agg att cgg atg gcc atc aat tag	2280
Arg Ile Arg Met Ala Ile Asn	

755

<210> 64
 <211> 759
 <212> PRT
 <213> Influenza virus

<400> 64

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

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

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 Lys 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

[illegible]

141

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
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

142

Pro Pro Glu Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val
625 630 635 640

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
705 710 715 720

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

<210> 65
<211> 2274
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(2274)

<400> 65
atg gat gtc aat ccg act cta ctt ttc tta aag gtg cca gcg caa aat 48
Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn
1 5 10 15

gct ata agc aca aca ttc cct tat act gga gat cct ccc tac agt cat 96
Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His
20 25 30

143

gga aca ggg aca gga tac acc atg gat act gtc aac aga aca cac caa	144
Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln	
35 40 45	
tat tca gaa aaa ggg aaa tgg aca aca aac act gag att gga gca cca	192
Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Ile Gly Ala Pro	
50 55 60	
caa ctt aat cca atc gat gga cca ctt cct gaa gac aat gaa cca agt	240
Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser	
65 70 75 80	
ggg tac gcc caa aca gat tgt gta ttg gaa gca atg gct ttc ctt gaa	288
Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu	
85 90 95	
gaa tcc cat ccc gga atc ttt gaa aat tcg tgt ctt gaa acg atg gag	336
Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu	
100 105 110	
gtg att cag cag aca aga gtg gac aaa cta aca caa ggc cga caa act	384
Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr	
115 120 125	
tat gat tgg acc ttg aat agg aat caa cct gcc gca aca gca ctt gct	432
Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala	
130 135 140	
aat acg att gaa gta ttc aga tca aat ggt ctg acc tcc aat gaa tcg	480
Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ser Asn Glu Ser	
145 150 155 160	
ggg aga ttg atg gac ttc ctc aaa gat gtc atg gag tcc atg aac aag	528
Gly Arg Leu Met Asp Phe Leu Lys Asp Val Met Glu Ser Met Asn Lys	
165 170 175	
gag gaa atg gaa ata aca aca cac ttc caa cgg aag aga aga gta aga	576
Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg	
180 185 190	
gac aac atg aca aag aga atg ata aca cag aga acc ata gga aag aaa	624
Asp Asn Met Thr Lys Arg Met Ile Thr Gln Arg Thr Ile Gly Lys Lys	
195 200 205	
aaa caa cga tta agc aga aag agc tat cta atc aga aca tta acc cta	672
Lys Gln Arg Leu Ser Arg Lys Ser Tyr Leu Ile Arg Thr Leu Thr Leu	
210 215 220	
aac aca atg acc aag gac gct gag aga ggg aaa ttg aaa cga cga gca	720
Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala	
225 230 235 240	
atc gct acc cca ggg atg cag ata aga gga ttt gta tat ttt gtt gaa	768
Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu	

144

245								250				255				
aca	cta	gct	cga	aga	ata	tgt	gaa	aag	ctt	gaa	caa	tca	gga	ttg	cca	816
Thr	Leu	Ala	Arg	Arg	Ile	Cys	Glu	Lys	Leu	Glu	Gln	Ser	Gly	Leu	Pro	
			260						265				270			
ggt	ggc	ggt	aat	gag	aaa	aag	gcc	aaa	ctg	gct	aat	gtc	gtc	aga	aaa	864
Val	Gly	Gly	Asn	Glu	Lys	Lys	Ala	Lys	Leu	Ala	Asn	Val	Val	Arg	Lys	
			275				280					285				
atg	atg	act	aat	tcc	caa	gac	act	gaa	ctc	tcc	ttc	acc	atc	act	ggg	912
Met	Met	Thr	Asn	Ser	Gln	Asp	Thr	Glu	Leu	Ser	Phe	Thr	Ile	Thr	Gly	
			290				295					300				
gac	aat	acc	aaa	tgg	aat	gaa	aat	cag	aac	cca	cgc	ata	ttc	ctg	gca	960
Asp	Asn	Thr	Lys	Trp	Asn	Glu	Asn	Gln	Asn	Pro	Arg	Ile	Phe	Leu	Ala	
305					310					315					320	
atg	atc	aca	tac	ata	act	aga	gat	cag	cca	gaa	tgg	ttc	aga	aat	gtt	1008
Met	Ile	Thr	Tyr	Ile	Thr	Arg	Asp	Gln	Pro	Glu	Trp	Phe	Arg	Asn	Val	
				325					330					335		
cta	agc	att	gca	ccg	att	atg	ttc	tca	aat	aaa	atg	gca	aga	ctg	ggg	1056
Leu	Ser	Ile	Ala	Pro	Ile	Met	Phe	Ser	Asn	Lys	Met	Ala	Arg	Leu	Gly	
			340					345					350			
aaa	gga	tat	atg	ttt	gaa	agc	aaa	agt	atg	aaa	ttg	aga	act	caa	ata	1104
Lys	Gly	Tyr	Met	Phe	Glu	Ser	Lys	Ser	Met	Lys	Leu	Arg	Thr	Gln	Ile	
			355				360					365				
cca	gca	gaa	atg	cta	gca	agc	att	gac	cta	aaa	tat	ttc	aat	gat	tca	1152
Pro	Ala	Glu	Met	Leu	Ala	Ser	Ile	Asp	Leu	Lys	Tyr	Phe	Asn	Asp	Ser	
			370				375					380				
aca	aaa	aag	aaa	att	gaa	aag	ata	cga	cca	ctc	ctg	gtt	gac	ggg	act	1200
Thr	Lys	Lys	Lys	Ile	Glu	Lys	Ile	Arg	Pro	Leu	Leu	Val	Asp	Gly	Thr	
385					390					395					400	
gct	tca	ctg	agt	cct	ggc	atg	atg	atg	gga	atg	ttc	aac	atg	ttg	agc	1248
Ala	Ser	Leu	Ser	Pro	Gly	Met	Met	Met	Gly	Met	Phe	Asn	Met	Leu	Ser	
				405					410					415		
act	gtg	ctg	ggt	gta	tcc	ata	tta	aac	ctg	ggc	cag	agg	aaa	tat	aca	1296
Thr	Val	Leu	Gly	Val	Ser	Ile	Leu	Asn	Leu	Gly	Gln	Arg	Lys	Tyr	Thr	
			420					425					430			
aag	acc	aca	tac	tgg	tgg	gat	ggt	ctg	caa	tca	tcc	gat	gac	ttt	gct	1344
Lys	Thr	Thr	Tyr	Trp	Trp	Asp	Gly	Leu	Gln	Ser	Ser	Asp	Asp	Phe	Ala	
			435				440					445				
ttg	ata	gtg	aat	gcg	cct	aat	cat	gaa	gga	ata	caa	gct	gga	gta	gac	1392
Leu	Ile	Val	Asn	Ala	Pro	Asn	His	Glu	Gly	Ile	Gln	Ala	Gly	Val	Asp	
			450				455				460					
aga	ttc	tat	aga	act	tgc	aaa	ctg	gtc	ggg	atc	aac	atg	agc	aaa	aag	1440

145

Arg	Phe	Tyr	Arg	Thr	Cys	Lys	Leu	Val	Gly	Ile	Asn	Met	Ser	Lys	Lys		
465					470					475					480		
aag	tcc	tac	ata	aat	aga	act	gga	aca	ttc	gaa	ttc	aca	agc	ttt	ttc	1488	
Lys	Ser	Tyr	Ile	Asn	Arg	Thr	Gly	Thr	Phe	Glu	Phe	Thr	Ser	Phe	Phe		
				485					490					495			
tac	cgg	tat	ggt	ttt	gta	gcc	aat	ttc	agc	atg	gaa	cta	ccc	agt	ttt	1536	
Tyr	Arg	Tyr	Gly	Phe	Val	Ala	Asn	Phe	Ser	Met	Glu	Leu	Pro	Ser	Phe		
			500					505					510				
ggg	gtt	tcc	gga	ata	aat	gaa	tct	gca	gac	atg	agc	att	gga	gtg	aca	1584	
Gly	Val	Ser	Gly	Ile	Asn	Glu	Ser	Ala	Asp	Met	Ser	Ile	Gly	Val	Thr		
		515					520					525					
gtc	atc	aaa	aac	aac	atg	ata	aat	aat	gat	ctc	ggt	cct	gcc	acg	gca	1632	
Val	Ile	Lys	Asn	Asn	Met	Ile	Asn	Asn	Asp	Leu	Gly	Pro	Ala	Thr	Ala		
	530						535					540					
caa	atg	gca	ctc	caa	ctc	ttc	att	aag	gat	tat	cgg	tac	aca	tac	cgg	1680	
Gln	Met	Ala	Leu	Gln	Leu	Phe	Ile	Lys	Asp	Tyr	Arg	Tyr	Thr	Tyr	Arg		
545					550					555					560		
tgc	cat	aga	ggt	gat	acc	cag	ata	caa	acc	aga	aga	tct	ttt	gag	ttg	1728	
Cys	His	Arg	Gly	Asp	Thr	Gln	Ile	Gln	Thr	Arg	Arg	Ser	Phe	Glu	Leu		
				565					570					575			
aag	aaa	ctg	tgg	gaa	cag	act	cga	tca	aag	act	ggt	cta	ctg	gta	tca	1776	
Lys	Lys	Leu	Trp	Glu	Gln	Thr	Arg	Ser	Lys	Thr	Gly	Leu	Leu	Val	Ser		
			580					585					590				
gat	ggg	ggt	cca	aac	cta	tat	aac	atc	aga	aac	cta	cac	atc	ccg	gaa	1824	
Asp	Gly	Gly	Pro	Asn	Leu	Tyr	Asn	Ile	Arg	Asn	Leu	His	Ile	Pro	Glu		
		595					600					605					
gtc	tgt	tta	aaa	tgg	gag	cta	atg	gat	gaa	gat	tat	aag	ggg	agg	cta	1872	
Val	Cys	Leu	Lys	Trp	Glu	Leu	Met	Asp	Glu	Asp	Tyr	Lys	Gly	Arg	Leu		
	610					615					620						
tgc	aat	cca	ttg	aat	cct	ttc	gtt	agt	cac	aaa	gaa	att	gaa	tca	gtc	1920	
Cys	Asn	Pro	Leu	Asn	Pro	Phe	Val	Ser	His	Lys	Glu	Ile	Glu	Ser	Val		
625					630					635					640		
aac	agt	gca	gta	gta	atg	cct	gct	cat	ggc	cct	gcc	aaa	agc	atg	gag	1968	
Asn	Ser	Ala	Val	Val	Met	Pro	Ala	His	Gly	Pro	Ala	Lys	Ser	Met	Glu		
				645					650					655			
tat	gat	gct	gtt	gca	aca	aca	cat	tct	tgg	atc	ccc	aag	agg	aac	cgg	2016	
Tyr	Asp	Ala	Val	Ala	Thr	Thr	His	Ser	Trp	Ile	Pro	Lys	Arg	Asn	Arg		
			660					665					670				
tcc	ata	ttg	aac	aca	agc	caa	agg	gga	ata	cta	gaa	gat	gag	cag	atg	2064	
Ser	Ile	Leu	Asn	Thr	Ser	Gln	Arg	Gly	Ile	Leu	Glu	Asp	Glu	Gln	Met		
		675					680					685					

146

tat cag aaa tgc tgc aac ctg ttt gaa aaa ttc ttc ccc agc agc tca 2112
 Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser
 690 695 700

tac aga aga cca gtc gga att tct agt atg gtt gag gcc atg gta tcc 2160
 Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser
 705 710 715 720

agg gcc cgc att gat gca cga att gac ttc gaa tct gga cgg ata aag 2208
 Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
 725 730 735

aag gat gag ttc gct gag atc atg aag atc tgt tcc acc att gaa gag 2256
 Lys Asp Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu
 740 745 750

ctc aga cgg caa aaa tag 2274
 Leu Arg Arg Gln Lys
 755

<210> 66
 <211> 757
 <212> PRT
 <213> Influenza virus

<400> 66

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

147

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	Asp	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 Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg

149

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 Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu						
	740			745		750
Leu Arg Arg Gln Lys						
	755					

150

<210> 67
 <211> 2151
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(2151)

<400> 67
 atg gaa gac ttt gtg cga cag tgc ttc aat cca atg atc gtc gag ctt 48
 Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu
 1 5 10 15

gcg gaa aag gca atg aaa gaa tat gga gag aac ccg aaa atc gaa aca 96
 Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asn Pro Lys Ile Glu Thr
 20 25 30

aac aaa ttt gca gca ata tgc act cac ttg gaa gtc tgc ttc atg tac 144
 Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr
 35 40 45

tcg gat ttc cac ttt ata aat gaa ctg ggt gag tca gtg gtc ata gag 192
 Ser Asp Phe His Phe Ile Asn Glu Leu Gly Glu Ser Val Val Ile Glu
 50 55 60

tct ggt gac cca aat gct ctt ttg aaa cac aga ttt gaa atc att gag 240
 Ser Gly Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu
 65 70 75 80

ggg aga gat cga aca atg gca tgg aca gta gta aac agc atc tgc aac 288
 Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn
 85 90 95

acc aca aga gct gaa aaa cct aaa ttt ctt cca gat tta tac gac tat 336
 Thr Thr Arg Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr
 100 105 110

aaa gag aac aga ttt gtt gaa att ggt gtg aca agg aga gaa gtt cac 384
 Lys Glu Asn Arg Phe Val Glu Ile Gly Val Thr Arg Arg Glu Val His
 115 120 125

ata tac tac ctg gag aag gcc aac aaa ata aag tct gag aaa aca cat 432
 Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His
 130 135 140

atc cac att ttc tca ttt aca gga gaa gaa atg gct aca aaa gcg gac 480
 Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp
 145 150 155 160

tat act ctt gat gaa gag agt aga gcc agg atc aag acc aga cta ttc 528
 Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe
 165 170 175

151

act ata aga caa gaa atg gcc agt aga ggc ctc tgg gat tcc ttt cgt	576
Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe Arg	
180 185 190	
cag tcc gag aga ggc gaa gag aca att gaa gaa aga ttt gaa atc aca	624
Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr	
195 200 205	
ggg acg atg cgc aag ctt gcc aat tac agt ctc cca ccg aac ttc tcc	672
Gly Thr Met Arg Lys Leu Ala Asn Tyr Ser Leu Pro Pro Asn Phe Ser	
210 215 220	
agc ctt gaa aat ttt aga gtc tat ata gat gga ttc gaa ccg aac ggc	720
Ser Leu Glu Asn Phe Arg Val Tyr Ile Asp Gly Phe Glu Pro Asn Gly	
225 230 235 240	
tgc att gag agt aag ctt tct caa atg tcc aaa gaa gta aat gcc aaa	768
Cys Ile Glu Ser Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys	
245 250 255	
ata gaa cca ttt tca aag aca aca ccc cga cca ctc aaa atg cca ggt	816
Ile Glu Pro Phe Ser Lys Thr Thr Pro Arg Pro Leu Lys Met Pro Gly	
260 265 270	
ggt cca ccc tgc cat cag cga tcc aaa ttc ttg cta atg gat gct ctg	864
Gly Pro Pro Cys His Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu	
275 280 285	
aaa ctg agc att gag gac cca agt cac gag gga gag ggg ata cca cta	912
Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu	
290 295 300	
tat gat gca atc aaa tgc atg aaa act ttc ttt gga tgg aaa gag ccc	960
Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro	
305 310 315 320	
agt att gtt aaa cca cat aaa aag ggt ata aac ccg aac tat ctc caa	1008
Ser Ile Val Lys Pro His Lys Lys Gly Ile Asn Pro Asn Tyr Leu Gln	
325 330 335	
act tgg aag caa gta tta gaa gaa ata caa gac ctt gag aac gaa gaa	1056
Thr Trp Lys Gln Val Leu Glu Glu Ile Gln Asp Leu Glu Asn Glu Glu	
340 345 350	
agg acc ccc aag acc aag aat atg aaa aaa aca agc caa ttg aaa tgg	1104
Arg Thr Pro Lys Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp	
355 360 365	
gca cta ggt gaa aat atg gca cca gag aaa gtg gat ttt gag gat tgt	1152
Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Glu Asp Cys	
370 375 380	
aaa gac atc aat gat tta aaa caa tat gac agt gat gag cca gaa gca	1200
Lys Asp Ile Asn Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Ala	
385 390 395 400	

152

agg tct ctt gca agt tgg att caa agt gag ttc aac aag gct tgt gag	1248
Arg Ser Leu Ala Ser Trp Ile Gln Ser Glu Phe Asn Lys Ala Cys Glu	
405 410 415	
ctg aca gat tca agc tgg ata gag ctc gat gaa att ggg gag gat gtc	1296
Leu Thr Asp Ser Ser Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val	
420 425 430	
gcc cca ata gaa tac att gcg agc atg agg aga aat tat ttt act gct	1344
Ala Pro Ile Glu Tyr Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala	
435 440 445	
gag att tcc cat tgt aga gca aca gaa tat ata atg aaa gga gtg tac	1392
Glu Ile Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr	
450 455 460	
atc aac act gct cta ctc aat gca tcc tgt gct gcg atg gat gaa ttt	1440
Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Glu Phe	
465 470 475 480	
caa tta att ccg atg ata agt aaa tgc agg acc aaa gaa ggg aga agg	1488
Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg	
485 490 495	
aaa aca aat tta tat gga ttc ata ata aag gga agg tcc cat tta aga	1536
Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg	
500 505 510	
aat gat act gac gtg gtg aac ttt gta agt atg gaa ttt tct ctc act	1584
Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr	
515 520 525	
gat cca aga ttt gag cca cac aaa tgg gaa aaa tac tgc gtt cta gaa	1632
Asp Pro Arg Phe Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu	
530 535 540	
att gga gac atg ctt tta aga act gct gta ggt caa gtg tca aga ccc	1680
Ile Gly Asp Met Leu Leu Arg Thr Ala Val Gly Gln Val Ser Arg Pro	
545 550 555 560	
atg ttt ttg tat gta agg aca aat gga acc tct aaa att aaa atg aaa	1728
Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys	
565 570 575	
tgg gga atg gaa atg agg cgc tgc ctc ctt cag tct ctg caa cag att	1776
Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile	
580 585 590	
gaa agc atg atc gaa gct gag tcc tca gtc aaa gaa aag gac atg acc	1824
Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr	
595 600 605	
aaa gaa ttt ttt gag aac aaa tca gag aca tgg cct ata gga gag tcc	1872
Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser	

153

610	615	620	
ccc aaa gga gtg gaa gag ggc tca atc ggg aag gtt tgc agg acc tta			1920
Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu			
625	630	635	640
tta gca aaa tct gtg ttt aac agt tta tat gca tct cca caa ctg gaa			1968
Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu			
	645	650	655
gga ttt tca gct gaa tct agg aaa tta ctt ctc att gtt cag gct ctt			2016
Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Ile Val Gln Ala Leu			
	660	665	670
aga gat gac ctg gaa cct gga acc ttt gat att ggg ggg tta tat gaa			2064
Arg Asp Asp Leu Glu Pro Gly Thr Phe Asp Ile Gly Gly Leu Tyr Glu			
	675	680	685
tca att gag gag tgc ctg att aat gat ccc tgg gtt ttg ctt aat gca			2112
Ser Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala			
	690	695	700
tct tgg ttc aac tcc ttc ctc aca cat gca ctg aag tag			2151
Ser Trp Phe Asn Ser Phe Leu Thr His Ala Leu Lys			
705	710	715	

<210> 68

<211> 716

<212> PRT

<213> Influenza virus

<400> 68

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
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

154

				85					90					95			
Thr	Thr	Arg	Ala	Glu	Lys	Pro	Lys	Phe	Leu	Pro	Asp	Leu	Tyr	Asp	Tyr		
			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					160		
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					240		
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						

155

Tyr Asp Ala Ile Lys Cys Met Lys Thr Phe Phe Gly Trp Lys Glu Pro
 305 310 315 320

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
 385 390 395 400

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
 465 470 475 480

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

156

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

Met 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> 69

<211> 844

<212> DNA

<213> Influenza virus

157

<220>

<221> CDS

<222> (1)..(690)

<400> 69

atg	gat	tcc	aac	act	gtg	tca	agc	ttt	cag	gta	gac	tgt	ttt	ctt	tgg	48
Met	Asp	Ser	Asn	Thr	Val	Ser	Ser	Phe	Gln	Val	Asp	Cys	Phe	Leu	Trp	
1				5					10					15		

cat	gtc	cgt	aaa	cga	ttc	gca	gac	caa	gaa	ctg	ggt	gat	gcc	cca	ttc	96
His	Val	Arg	Lys	Arg	Phe	Ala	Asp	Gln	Glu	Leu	Gly	Asp	Ala	Pro	Phe	
			20					25					30			

ctt	gac	cgg	ctt	cgc	cga	gac	cag	aag	tcc	cta	agg	gga	aga	ggt	agc	144
Leu	Asp	Arg	Leu	Arg	Arg	Asp	Gln	Lys	Ser	Leu	Arg	Gly	Arg	Gly	Ser	
		35				40					45					

act	ctt	ggt	ctg	gac	atc	gaa	aca	gcc	act	cat	gca	gga	aag	cag	ata	192
Thr	Leu	Gly	Leu	Asp	Ile	Glu	Thr	Ala	Thr	His	Ala	Gly	Lys	Gln	Ile	
	50					55					60					

gtg	gag	cag	att	ctg	gaa	aag	gaa	tca	gat	gag	gca	ctt	aaa	atg	acc	240
Val	Glu	Gln	Ile	Leu	Glu	Lys	Glu	Ser	Asp	Glu	Ala	Leu	Lys	Met	Thr	
65					70					75				80		

att	gcc	tct	gtt	cct	gct	tca	cgc	tac	tta	act	gac	atg	act	ctt	gat	288
Ile	Ala	Ser	Val	Pro	Ala	Ser	Arg	Tyr	Leu	Thr	Asp	Met	Thr	Leu	Asp	
				85					90					95		

gag	atg	tca	aga	gac	tgg	ttc	atg	ctc	atg	ccc	aag	caa	aaa	gta	aca	336
Glu	Met	Ser	Arg	Asp	Trp	Phe	Met	Leu	Met	Pro	Lys	Gln	Lys	Val	Thr	
			100					105					110			

ggc	tcc	cta	tgt	ata	aga	atg	gac	cag	gca	atc	atg	gat	aag	aac	atc	384
Gly	Ser	Leu	Cys	Ile	Arg	Met	Asp	Gln	Ala	Ile	Met	Asp	Lys	Asn	Ile	
		115					120					125				

ata	ctt	aaa	gca	aac	ttt	agt	gtg	att	ttc	gaa	agg	ctg	gaa	aca	cta	432
Ile	Leu	Lys	Ala	Asn	Phe	Ser	Val	Ile	Phe	Glu	Arg	Leu	Glu	Thr	Leu	
	130					135					140					

ata	cta	ctt	aga	gcc	ttc	acc	gaa	gaa	gga	gca	gtc	gtt	ggc	gaa	att	480
Ile	Leu	Leu	Arg	Ala	Phe	Thr	Glu	Glu	Gly	Ala	Val	Val	Gly	Glu	Ile	
145					150					155					160	

tca	cca	tta	cct	tct	ctt	cca	gga	cat	act	aat	gag	gat	gtc	aaa	aat	528
Ser	Pro	Leu	Pro	Ser	Leu	Pro	Gly	His	Thr	Asn	Glu	Asp	Val	Lys	Asn	
				165					170					175		

gca	att	ggg	gtc	ctc	atc	gga	gga	ctt	aaa	tgg	aat	gat	aat	acg	gtt	576
Ala	Ile	Gly	Val	Leu	Ile	Gly	Gly	Leu	Lys	Trp	Asn	Asp	Asn	Thr	Val	
			180					185					190			

aga	atc	tct	gaa	act	cta	cag	aga	ttc	gct	tgg	aga	agc	agt	cat	gaa	624
Arg	Ile	Ser	Glu	Thr	Leu	Gln	Arg	Phe	Ala	Trp	Arg	Ser	Ser	His	Glu	

158

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195          200          205
aat ggg aga cct tca ttc cct tca aaa cag aaa cga aaa atg gag aga      672
Asn Gly Arg Pro Ser Phe Pro Ser Lys Gln Lys Arg Lys Met Glu Arg
210          215          220

aca att aag cca gaa att tgaagaaata agatggttga ttgaagaagt      720
Thr Ile Lys Pro Glu Ile
225          230

gcgacataga ttgaaaaata cagaaaatag ttttgaacaa ataacattta tgcaagcctt      780

acaactattg cttgaagtag aacaagagat aagaactttc tcgtttcagc ttatttaatg      840

ataa      844

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<210> 70
<211> 230
<212> PRT
<213> Influenza virus

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<400> 70

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Met Asp Ser Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp
1          5          10          15

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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

```

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Val Glu Gln Ile Leu Glu Lys Glu Ser Asp Glu Ala Leu Lys Met Thr
65          70          75          80

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```

Ile Ala Ser Val Pro Ala Ser Arg Tyr Leu Thr Asp Met Thr Leu Asp
85          90          95

```

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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

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159

Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Glu Arg Leu Glu Thr Leu
 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> 71
 <211> 1497
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1497)

<400> 71
 atg gcg tct caa ggc acc aaa cga tcc tat gaa cag atg gaa act gat 48
 Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp
 1 5 10 15
 ggg gaa cgc cag aat gca act gaa atc aga gca tct gtc gga agg atg 96
 Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Arg Met
 20 25 30
 gtg gga gga atc gga cgg ttt tat gtc cag atg tgt act gag ctt aaa 144
 Val Gly Gly Ile Gly Arg Phe Tyr Val Gln Met Cys Thr Glu Leu Lys
 35 40 45
 cta aac gac cat gaa ggg cgg ctg att cag aac agc ata aca ata gaa 192
 Leu Asn Asp His Glu Gly Arg Leu Ile Gln Asn Ser Ile Thr Ile Glu
 50 55 60

160

agg atg gtg ctt tcg gca ttc gac gaa aga aga aac aag tat ctc gag	240
Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu	
65 70 75 80	
gag cat ccc agt gct ggg aaa gac cct aag aaa acg gga ggc ccg ata	288
Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile	
85 90 95	
tac aga aga aaa gat ggg aaa tgg atg agg gaa ctc atc ctc cat gat	336
Tyr Arg Arg Lys Asp Gly Lys Trp Met Arg Glu Leu Ile Leu His Asp	
100 105 110	
aaa gaa gaa atc atg aga atc tgg cgt cag gcc aac aat ggt gaa gac	384
Lys Glu Glu Ile Met Arg Ile Trp Arg Gln Ala Asn Asn Gly Glu Asp	
115 120 125	
gct act gct ggt ctt act cat atg atg atc tgg cac tcc aat ctc aat	432
Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn	
130 135 140	
gac acc aca tac caa aga aca agg gct ctt gtt cgg act ggg atg gat	480
Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp	
145 150 155 160	
ccc aga atg tgc tct ctg atg caa ggc tca acc ctc cca cgg aga tct	528
Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser	
165 170 175	
gga gcc gct ggt gct gca gta aaa ggc gtt gga aca atg gta atg gaa	576
Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu	
180 185 190	
ctc atc aga atg atc aag cgc gga ata aat gat cgg aat ttc tgg aga	624
Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg	
195 200 205	
ggt gaa aat ggt cga aga acc aga att gct tat gaa aga atg tgc aat	672
Gly Glu Asn Gly Arg Arg Thr Arg Ile Ala Tyr Glu Arg Met Cys Asn	
210 215 220	
atc ctc aaa ggg aaa ttt cag aca gca gca caa cgg gct atg atg gac	720
Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp	
225 230 235 240	
cag gtg agg gaa ggc cgc aat cct gga aac gct gag att gag gat ctc	768
Gln Val Arg Glu Gly Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu	
245 250 255	
att ttc ttg gca cga tca gca ctt att ttg aga gga tca gta gcc cat	816
Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His	
260 265 270	
aaa tca tgc cta cct gcc tgt gtt tat ggc ctt gca cta acc agt ggg	864
Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Leu Ala Leu Thr Ser Gly	

161

275	280	285	
tat gac ttt gag aag gaa gga tac tct ctg gtt gga att gat cct ttc Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe 290 295 300			912
aaa cta ctc cag aac agt caa att ttc agt cta atc aga cca aaa gaa Lys Leu Leu Gln Asn Ser Gln Ile Phe Ser Leu Ile Arg Pro Lys Glu 305 310 315 320			960
aac cca gca cac aaa agc cag ttg gtg tgg atg gca tgc cat tct gca Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys His Ser Ala 325 330 335			1008
gca ttt gag gat ctg aga gtt tta aat ttc att aga gga acc aaa gta Ala Phe Glu Asp Leu Arg Val Leu Asn Phe Ile Arg Gly Thr Lys Val 340 345 350			1056
atc cca aga gga cag tta aca acc aga gga gtt caa att gct tca aat Ile Pro Arg Gly Gln Leu Thr Thr Arg Gly Val Gln Ile Ala Ser Asn 355 360 365			1104
gaa aac atg gag aca ata aat tct agc aca ctt gaa ctg aga agc aaa Glu Asn Met Glu Thr Ile Asn Ser Ser Thr Leu Glu Leu Arg Ser Lys 370 375 380			1152
tat tgg gca ata agg acc aga agc gga gga aac acc agt caa cag aga Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Ser Gln Gln Arg 385 390 395 400			1200
gca tct gca gga cag ata agt gtg caa cct act ttc tca gta cag aga Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg 405 410 415			1248
aat ctt ccc ttt gag aga gca acc att atg gct gca ttc act ggt aac Asn Leu Pro Phe Glu Arg Ala Thr Ile Met Ala Ala Phe Thr Gly Asn 420 425 430			1296
act gaa gga agg act tcc gac atg aga acg gaa atc ata agg atg atg Thr Glu Gly Arg Thr Ser Asp Met Arg Thr Glu Ile Ile Arg Met Met 435 440 445			1344
gaa aat gcc aaa tca gaa gat gtg tct ttc cag ggg cgg gga gtc ttc Glu Asn Ala Lys Ser Glu Asp Val Ser Phe Gln Gly Arg Gly Val Phe 450 455 460			1392
gag ctc tcg gac gaa aag gca acg aac ccg atc gtg cct tcc ttt gac Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp 465 470 475 480			1440
atg agc aat gaa ggg tct tat ttc ttc gga gac aat gct gag gag ttt Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe 485 490 495			1488
gac agt taa			1497

162

Asp Ser

<210> 72
 <211> 498
 <212> PRT
 <213> Influenza virus

<400> 72

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
 145 150 155 160

Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser
 165 170 175

163

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
 225 230 235 240

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 Leu 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
 305 310 315 320

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
 385 390 395 400

164

Ala Ser 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
465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Phe
485 490 495

Asp Ser

<210> 73
<211> 1413
<212> DNA
<213> Influenza virus

<220>
<221> CDS
<222> (1)..(1413)

<400> 73
atg aat cca aat caa aag ata ata gca att gga ttt gca tca ttg ggg 48
Met Asn Pro Asn Gln Lys Ile Ile Ala Ile Gly Phe Ala Ser Leu Gly
1 5 10 15

ata tta atc att aat gtc att ctc cat gta gtc agc att ata gta aca 96
Ile Leu Ile Ile Asn Val Ile Leu His Val Val Ser Ile Ile Val Thr
20 25 30

gta ctg gtc ctc aat aac aat aga aca gat ctg aac tgc aaa ggg acg 144
Val Leu Val Leu Asn Asn Asn Arg Thr Asp Leu Asn Cys Lys Gly Thr
35 40 45

atc ata aga gaa tac aat gaa aca gta aga gta gaa aaa ctt act caa 192
Ile Ile Arg Glu Tyr Asn Glu Thr Val Arg Val Glu Lys Leu Thr Gln
50 55 60

165

tgg tat aat acc agt aca att aag tac ata gag aga cct tca aat gaa	240
Trp Tyr Asn Thr Ser Thr Ile Lys Tyr Ile Glu Arg Pro Ser Asn Glu	
65 70 75 80	
tac tac atg aat aac act gaa cca ctt tgt gag gcc caa ggc ttt gca	288
Tyr Tyr Met Asn Asn Thr Glu Pro Leu Cys Glu Ala Gln Gly Phe Ala	
85 90 95	
cca ttt tcc aaa gat aat gga ata cga att ggg tcg aga ggc cat gtt	336
Pro Phe Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Arg Gly His Val	
100 105 110	
ttt gtg ata aga gaa cct ttt gta tca tgt tcg ccc tca gaa tgt aga	384
Phe Val Ile Arg Glu Pro Phe Val Ser Cys Ser Pro Ser Glu Cys Arg	
115 120 125	
acc ttt ttc ctc aca cag ggc tca tta ctc aat gac aaa cat tct aac	432
Thr Phe Phe Leu Thr Gln Gly Ser Leu Leu Asn Asp Lys His Ser Asn	
130 135 140	
ggc aca ata aag gat cga agt ccg tat agg act ttg atg agt gtc aaa	480
Gly Thr Ile Lys Asp Arg Ser Pro Tyr Arg Thr Leu Met Ser Val Lys	
145 150 155 160	
ata ggg caa tca cct aat gta tat caa gct agg ttt gaa tcg gtg gca	528
Ile Gly Gln Ser Pro Asn Val Tyr Gln Ala Arg Phe Glu Ser Val Ala	
165 170 175	
tgg tca gca aca gca tgc cat gat gga aaa aaa tgg atg aca gtt gga	576
Trp Ser Ala Thr Ala Cys His Asp Gly Lys Lys Trp Met Thr Val Gly	
180 185 190	
gtc aca ggg ccc gac aat caa gca att gca gta gtg aac tat gga ggt	624
Val Thr Gly Pro Asp Asn Gln Ala Ile Ala Val Val Asn Tyr Gly Gly	
195 200 205	
gtt ccg gtt gat att att aat tca tgg gca ggg gat att tta aga acc	672
Val Pro Val Asp Ile Ile Asn Ser Trp Ala Gly Asp Ile Leu Arg Thr	
210 215 220	
caa gaa tca tca tgc acc tgc att aaa gga gac tgt tat tgg gta atg	720
Gln Glu Ser Ser Cys Thr Cys Ile Lys Gly Asp Cys Tyr Trp Val Met	
225 230 235 240	
act gat gga ccg gca aat agg caa gct aaa tat agg ata ttc aaa gca	768
Thr Asp Gly Pro Ala Asn Arg Gln Ala Lys Tyr Arg Ile Phe Lys Ala	
245 250 255	
aaa gat gga aga gta att gga caa act gat ata agt ttc aat ggg gga	816
Lys Asp Gly Arg Val Ile Gly Gln Thr Asp Ile Ser Phe Asn Gly Gly	
260 265 270	
cac ata gag gag tgt tct tgt tac ccc aat gaa ggg aag gtg gaa tgc	864
His Ile Glu Glu Cys Ser Cys Tyr Pro Asn Glu Gly Lys Val Glu Cys	

166

275	280	285	
ata tgc agg gac aat tgg act gga aca aat aga cca att ctg gta ata Ile Cys Arg Asp Asn Trp Thr Gly Thr Asn Arg Pro Ile Leu Val Ile 290 295 300			912
tct tct gat cta tcg tac aca gtt gga tat ttg tgt gct ggc att ccc Ser Ser Asp Leu Ser Tyr Thr Val Gly Tyr Leu Cys Ala Gly Ile Pro 305 310 315 320			960
act gac act cct agg gga gag gat agt caa ttc aca ggc tca tgt aca Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr 325 330 335			1008
agt cct ttg gga aat aaa gga tac ggt gta aaa ggc ttc ggg ttt cga Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg 340 345 350			1056
caa gga act gac gta tgg gcc gga agg aca att agt agg act tca aga Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg 355 360 365			1104
tca gga ttc gaa ata ata aaa atc agg aat ggt tgg aca cag aac agt Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser 370 375 380			1152
aag gac caa atc agg agg caa gtg att atc gat gac cca aat tgg tca Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser 385 390 395 400			1200
gga tat agc ggt tct ttc aca ttg ccg gtt gaa ctg aca aaa aag gga Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly 405 410 415			1248
tgt ttg gtc ccc tgt ttc tgg gtt gaa atg att aga ggt aaa cct gaa Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu 420 425 430			1296
gaa aca aca ata tgg acc tct agc agc tcc att gtg atg tgt gga gta Glu Thr Thr Ile Trp Thr Ser Ser Ser Ile Val Met Cys Gly Val 435 440 445			1344
gat cat aaa att gcc agt tgg tca tgg cac gat gga gct att ctt ccc Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro 450 455 460			1392
ttt gac atc gat aag atg taa Phe Asp Ile Asp Lys Met 465 470			1413

<210> 74

<211> 470

<212> PRT

<213> Influenza virus

167

<400> 74

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

168

Val Pro Val Asp Ile 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
 Thr Asp Thr Pro Arg Gly Glu Asp Ser Gln Phe Thr Gly Ser Cys Thr
 325 330 335
 Ser Pro Leu Gly Asn Lys Gly Tyr Gly Val Lys Gly Phe Gly Phe Arg
 340 345 350
 Gln Gly Thr Asp Val Trp Ala Gly Arg Thr Ile Ser Arg Thr Ser Arg
 355 360 365
 Ser Gly Phe Glu Ile Ile Lys Ile Arg Asn Gly Trp Thr Gln Asn Ser
 370 375 380
 Lys Asp Gln Ile Arg Arg Gln Val Ile Ile Asp Asp Pro Asn Trp Ser
 385 390 395 400
 Gly Tyr Ser Gly Ser Phe Thr Leu Pro Val Glu Leu Thr Lys Lys Gly
 405 410 415
 Cys Leu Val Pro Cys Phe Trp Val Glu Met Ile Arg Gly Lys Pro Glu
 420 425 430

169

Glu Thr Thr Ile Trp Thr Ser Ser Ser Ser Ile Val Met Cys Gly Val
 435 440 445

Asp His Lys Ile Ala Ser Trp Ser Trp His Asp Gly Ala Ile Leu Pro
 450 455 460

Phe Asp Ile Asp Lys Met
 465 470

<210> 75
 <211> 981
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(756)

<400> 75
 atg agt ctt cta acc gag gtc gaa acg tac gtt ctc tct atc gta cca 48
 Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Val Pro
 1 5 10 15
 tca ggc ccc ctc aaa gcc gag atc gcg cag aga ctt gaa gat gtc ttt 96
 Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
 20 25 30
 gcg gga aag aac acc gat ctt gag gca ctc atg gaa tgg cta aag aca 144
 Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr
 35 40 45
 aga cca atc ctg tca cct ctg act aaa ggg att tta gga ttt gta ttc 192
 Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe
 50 55 60
 acg ctc acc gtg ccc agt gag cga gga ctg cag cgt aga cgc ttt gtc 240
 Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val
 65 70 75 80
 caa aat gcc ctt agt gga aac gga gat cca aac aac atg gac aga gca 288
 Gln Asn Ala Leu Ser Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala
 85 90 95
 gta aaa ctg tac agg aag ctt aaa aga gaa ata aca ttc cat ggg gca 336
 Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala
 100 105 110
 aaa gag gtg gca ctc agc tat tcc act ggt gca cta gcc agc tgc atg 384
 Lys Glu Val Ala Leu Ser Tyr Ser Thr Gly Ala Leu Ala Ser Cys Met
 115 120 125

170

gga ctc ata tac aac aga atg gga act gtt aca acc gaa gtg gca ttt 432
 Gly Leu Ile Tyr Asn Arg Met Gly Thr Val Thr Thr Glu Val Ala Phe
 130 135 140

ggc ctg gta tgc gcc aca tgt gaa cag att gct gat tcc cag cat cga 480
 Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg
 145 150 155 160

tct cac agg cag atg gtg aca aca acc aac cca tta atc aga cat gaa 528
 Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu
 165 170 175

aac aga atg gta tta gcc agt acc acg gct aaa gcc atg gaa cag atg 576
 Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met
 180 185 190

gca gga tcg agt gag cag gca gca gag gcc atg gag gtt gct agt agg 624
 Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Arg
 195 200 205

gct agg cag atg gta cag gca atg aga acc att ggg acc cac cct agc 672
 Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser
 210 215 220

tcc agt gcc ggt ttg aaa gat gat ctc ctt gaa aat tta cag gcc tac 720
 Ser Ser Ala Gly Leu Lys Asp Asp Leu Leu Glu Asn Leu Gln Ala Tyr
 225 230 235 240

cag aaa cgg atg gga gtg caa atg cag cga ttc aag tgatcctctc 766
 Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys
 245 250

gtcatcgcag caagtatcat tgggatcttg cacttgatat tgtggattct tgatcgtctt 826

ttcttcaaatt tcatttatcg tcgccttaaa tacgggttga aaagagggcc ttctacggaa 886

ggagtacctg agtctatgag ggaagaatat cggcaggaac agcagaatgc tgtggatggt 946

gacgatggtc attttgtcaa catagagctg gagta 981

<210> 76
 <211> 252
 <212> PRT
 <213> Influenza virus

<400> 76

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 Gly 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

172

245

250

<210> 77
 <211> 1698
 <212> DNA
 <213> Influenza virus

<220>
 <221> CDS
 <222> (1)..(1698)

<400> 77
 atg aag aca acc att att tta ata cta ctg acc cat tgg gcc tac agt 48
 Met Lys Thr Thr Ile Ile Leu Ile Leu Leu Thr His Trp Ala Tyr Ser
 1 5 10 15
 caa aac cca atc agt ggc aat aac aca gcc aca ctg tgt ctg gga cac 96
 Gln Asn Pro Ile Ser Gly Asn Asn Thr Ala Thr Leu Cys Leu Gly His
 20 25 30
 cat gca gta gca aat gga aca ttg gta aaa aca atg agt gat gat caa 144
 His Ala Val Ala Asn Gly Thr Leu Val Lys Thr Met Ser Asp Asp Gln
 35 40 45
 att gag gtg aca aat gct aca gaa tta gtt cag agc att tca atg ggg 192
 Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ile Ser Met Gly
 50 55 60
 aaa ata tgc aac aaa tca tat aga att cta gat gga aga aat tgc aca 240
 Lys Ile Cys Asn Lys Ser Tyr Arg Ile Leu Asp Gly Arg Asn Cys Thr
 65 70 75 80
 tta ata gat gca atg cta gga gac ccc cac tgt gac gcc ttt cag tat 288
 Leu Ile Asp Ala Met Leu Gly Asp Pro His Cys Asp Ala Phe Gln Tyr
 85 90 95
 gag agt tgg gac ctc ttt ata gaa aga agc agc gct ttc agc aat tgc 336
 Glu Ser Trp Asp Leu Phe Ile Glu Arg Ser Ser Ala Phe Ser Asn Cys
 100 105 110
 tac cca tat gac atc cct gac tat gca ccg ctc cga tcc att gta gca 384
 Tyr Pro Tyr Asp Ile Pro Asp Tyr Ala Pro Leu Arg Ser Ile Val Ala
 115 120 125
 tcc tca ggg aca gtg gaa ttc aca gca gag gga ttc aca tgg aca ggt 432
 Ser Ser Gly Thr Val Glu Phe Thr Ala Glu Gly Phe Thr Trp Thr Gly
 130 135 140
 gta act caa aac gga aga agt gga gcc tgc aaa agg gga tca gcc gat 480
 Val Thr Gln Asn Gly Arg Ser Gly Ala Cys Lys Arg Gly Ser Ala Asp
 145 150 155 160
 agt ttc ttt agc cga ctg aat tgg cta aca aaa tct gga agc tct tac 528

173

Ser	Phe	Phe	Ser	Arg	Leu	Asn	Trp	Leu	Thr	Lys	Ser	Gly	Ser	Ser	Tyr		
				165					170					175			
ccc	aca	ttg	aat	gtg	aca	atg	cct	aac	aat	aaa	aat	ttc	gac	aag	cta	576	
Pro	Thr	Leu	Asn	Val	Thr	Met	Pro	Asn	Asn	Lys	Asn	Phe	Asp	Lys	Leu		
			180					185					190				
tac	atc	tgg	ggg	att	cat	cac	ccg	agc	tca	aat	caa	gag	cag	aca	aaa	624	
Tyr	Ile	Trp	Gly	Ile	His	His	Pro	Ser	Ser	Asn	Gln	Glu	Gln	Thr	Lys		
		195					200					205					
ttg	tac	atc	caa	gaa	tca	gga	cga	gta	aca	gtc	tca	aca	aaa	aga	agt	672	
Leu	Tyr	Ile	Gln	Glu	Ser	Gly	Arg	Val	Thr	Val	Ser	Thr	Lys	Arg	Ser		
		210				215					220						
caa	caa	aca	ata	atc	cct	aac	atc	gga	tct	aga	ccg	ttg	gtc	aga	ggt	720	
Gln	Gln	Thr	Ile	Ile	Pro	Asn	Ile	Gly	Ser	Arg	Pro	Leu	Val	Arg	Gly		
225					230					235					240		
caa	tca	ggc	agg	ata	agc	ata	tac	tgg	acc	att	gta	aaa	cct	gga	gat	768	
Gln	Ser	Gly	Arg	Ile	Ser	Ile	Tyr	Trp	Thr	Ile	Val	Lys	Pro	Gly	Asp		
			245					250						255			
atc	cta	atg	ata	aac	agt	aat	ggc	aac	tta	gtt	gca	ccg	cgg	gga	tat	816	
Ile	Leu	Met	Ile	Asn	Ser	Asn	Gly	Asn	Leu	Val	Ala	Pro	Arg	Gly	Tyr		
			260				265						270				
ttt	aaa	ttg	aac	aca	ggg	aaa	agc	tct	gta	atg	aga	tcc	gat	gta	ccc	864	
Phe	Lys	Leu	Asn	Thr	Gly	Lys	Ser	Ser	Val	Met	Arg	Ser	Asp	Val	Pro		
		275					280					285					
ata	gac	att	tgt	gtg	tct	gaa	tgt	att	aca	cca	aat	gga	agc	atc	tcc	912	
Ile	Asp	Ile	Cys	Val	Ser	Glu	Cys	Ile	Thr	Pro	Asn	Gly	Ser	Ile	Ser		
		290				295					300						
aac	gac	aag	cca	ttc	caa	aat	gtg	aac	aaa	gtt	aca	tat	gga	aaa	tgc	960	
Asn	Asp	Lys	Pro	Phe	Gln	Asn	Val	Asn	Lys	Val	Thr	Tyr	Gly	Lys	Cys		
305					310					315					320		
ccc	aag	tat	atc	agg	caa	aac	act	tta	aag	ctg	gcc	act	ggg	atg	agg	1008	
Pro	Lys	Tyr	Ile	Arg	Gln	Asn	Thr	Leu	Lys	Leu	Ala	Thr	Gly	Met	Arg		
				325					330					335			
aat	gta	cca	gaa	aag	caa	acc	aga	gga	atc	ttt	gga	gca	ata	gcg	gga	1056	
Asn	Val	Pro	Glu	Lys	Gln	Thr	Arg	Gly	Ile	Phe	Gly	Ala	Ile	Ala	Gly		
			340					345					350				
ttc	atc	gaa	aac	ggc	tgg	gaa	gga	atg	gtt	gat	ggg	tgg	tat	ggg	ttc	1104	
Phe	Ile	Glu	Asn	Gly	Trp	Glu	Gly	Met	Val	Asp	Gly	Trp	Tyr	Gly	Phe		
		355					360					365					
cga	tat	caa	aac	tct	gaa	gga	aca	ggg	caa	gct	gca	gat	cta	aag	agc	1152	
Arg	Tyr	Gln	Asn	Ser	Glu	Gly	Thr	Gly	Gln	Ala	Ala	Asp	Leu	Lys	Ser		
		370				375					380						

174

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act  caa  gca  gcc  atc  gac  cag  att  aat  gga  aag  tta  aac  aga  gtg  att      1200
Thr  Gln  Ala  Ala  Ile  Asp  Gln  Ile  Asn  Gly  Lys  Leu  Asn  Arg  Val  Ile
385                                390                                395                                400

gaa  aga  acc  aat  gag  aaa  ttc  cat  caa  ata  gag  aag  gaa  ttc  tca  gaa      1248
Glu  Arg  Thr  Asn  Glu  Lys  Phe  His  Gln  Ile  Glu  Lys  Glu  Phe  Ser  Glu
                                405                                410                                415

gta  gaa  gga  aga  att  cag  gac  ttg  gag  aaa  tat  gta  gaa  gac  acc  aaa      1296
Val  Glu  Gly  Arg  Ile  Gln  Asp  Leu  Glu  Lys  Tyr  Val  Glu  Asp  Thr  Lys
                                420                                425                                430

ata  gac  cta  tgg  tcc  tac  aat  gca  gaa  ttg  ctg  gtg  gct  cta  gaa  aat      1344
Ile  Asp  Leu  Trp  Ser  Tyr  Asn  Ala  Glu  Leu  Leu  Val  Ala  Leu  Glu  Asn
                                435                                440                                445

caa  cat  aca  att  gac  tta  aca  gat  gca  gaa  atg  aat  aaa  tta  ttt  gag      1392
Gln  His  Thr  Ile  Asp  Leu  Thr  Asp  Ala  Glu  Met  Asn  Lys  Leu  Phe  Glu
                                450                                455                                460

aag  act  aga  cgc  cag  tta  aga  gaa  aac  gca  gaa  gac  atg  gga  ggt  gga      1440
Lys  Thr  Arg  Arg  Gln  Leu  Arg  Glu  Asn  Ala  Glu  Asp  Met  Gly  Gly  Gly
465                                470                                475                                480

tgt  ttc  aag  att  tac  cac  aaa  tgt  gat  aat  gca  tgc  att  gaa  tca  ata      1488
Cys  Phe  Lys  Ile  Tyr  His  Lys  Cys  Asp  Asn  Ala  Cys  Ile  Glu  Ser  Ile
                                485                                490                                495

aga  act  ggg  aca  tat  gac  cat  tac  ata  tac  aaa  gat  gaa  gca  tta  aac      1536
Arg  Thr  Gly  Thr  Tyr  Asp  His  Tyr  Ile  Tyr  Lys  Asp  Glu  Ala  Leu  Asn
                                500                                505                                510

aat  cga  ttt  cag  atc  aaa  ggt  gta  gag  ttg  aaa  tca  ggc  tac  aaa  gat      1584
Asn  Arg  Phe  Gln  Ile  Lys  Gly  Val  Glu  Leu  Lys  Ser  Gly  Tyr  Lys  Asp
                                515                                520                                525

tgg  ata  ctg  tgg  att  tca  ttc  gcc  ata  tca  tgc  ttc  tta  att  tgc  gtt      1632
Trp  Ile  Leu  Trp  Ile  Ser  Phe  Ala  Ile  Ser  Cys  Phe  Leu  Ile  Cys  Val
                                530                                535                                540

gtt  cta  ttg  ggt  ttc  att  atg  tgg  gct  tgc  caa  aaa  ggc  aac  atc  aga      1680
Val  Leu  Leu  Gly  Phe  Ile  Met  Trp  Ala  Cys  Gln  Lys  Gly  Asn  Ile  Arg
545                                550                                555                                560

tgc  aac  att  tgc  att  tga
Cys  Asn  Ile  Cys  Ile
                                565                                1698

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<210>  78
<211>  565
<212>  PRT
<213>  Influenza virus

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<400>  78

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175

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 Phe 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 Pro 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 Gly Ser Arg Pro Leu Val Arg Gly
225 230 235 240

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 Lys 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
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20

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21

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<212> DNA
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<211> 40
<212> DNA
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tgtaatacga ctcaactatag ggcatttttg acaaagcgtc

40