

REPLIKIN PEPTIDES AND USES THEREOF

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CROSS REFERENCE TO OTHER APPLICATIONS

[0001] This application is a Continuation-In-Part of PCT Application
No.PCT/US02/09240, filed March 26, 2002, which is a Continuation-In-Part of
Applications Nos. US 09/984,057 and US 09/984,056, both filed October 26,
10 2001, which claims priority from Provisional Applications 60/303,396, filed July
9, 2001, the subject matter of which is incorporated herein by reference.

FIELD OF THE INVENTION

[0002] This invention relates to the identification and use of Replikins, a newly
15 discovered class of peptides that share structural characteristics. In particular, this
invention relates to Replikins which have been found in viruses, bacteria, fungus,
cancer associated proteins, plants and unicellular parasites and their use as targets
in the development of methods of treating or preventing diseases. Further, this
invention relates to the use of Replikins in the detection of these diseases. Also
20 this invention relates to the use of Replikins to stimulate growth of plants used for
food.

INTRODUCTION AND BACKGROUND OF THE INVENTION

[0003] Rapid replication is characteristic of virulence in certain bacteria, viruses
25 and malignancies, but no chemistry common to rapid replication in different
organisms has been described previously. This patent application discloses a new
class of protein structures related to rapid replication. A new family of conserved
small proteins related to rapid replication, named Replikins, which are used to

predict and control rapid replication in multiple organisms and diseases and to induce rapid replication in plant and animal life.

[0004] We constructed an algorithm search for Replikins. In applying the
5 algorithm invented herein not only was the function of the epitope revealed - rapid replication, but an entire family of homologues whose function is related to rapid replication was discovered, which we named Replikins.

[0005] The algorithm is based on the following: 1) Evidence that the immune
10 system looks to parts rather than a whole protein in recognition. Protein chains are first hydrolyzed by the immune system into smaller pieces, frequently six (6) to ten (10) amino acids long, as part of the immune systems' process of recognition of foreign structures against which it may mount an immune defense. By way of example, the immune system recognizes the presence of disease by chopping up
15 proteins of the disease agent into smaller peptide sequences and reading them.

This principle is used as a basis for the algorithm with which to search for homologues of the malignin cancer epitope, once the structure of the epitope was known; 2) The specific structure of the malignin epitope, in which two of the three lysines (K's) are eight residues apart is in accordance with the apparent 'rules'
20 used by the immune system for recognition referred to above (6-10 amino acids long); 3) The fact that the malignin cancer epitope was shown to be a very strong antigen, that is - a generator of a strong immune response; that there are three lysines (K's) in the 10-mer peptide glioma Replikin and that K's are known to bind frequently to DNA and RNA as potential anchors for the entry of viruses; and
25 4) One histidine (H) is included in the sequence of the malignin epitope, between

the two K's which are eight (8) residues apart, suggesting a connection to the metals of redox systems which are required to provide the energy for replication.

[0006] Engineered enzymes and catalytic antibodies, possessing tailored binding
5 pockets with appropriately positioned functional groups have been successful in catalyzing a number of chemical transformations, sometimes with impressive efficiencies. Just as two or more separate proteins with specific and quite different functions are now often recognized to be synthesized together by organisms, and then separately cleaved to 'go about their separate functions', so the Replikin
10 structure is a unique protein with a unique function that appears to be recognized separately by the immune system and may be now rationally engineered- e.g. synthesized to produce a functional unit.

[0007] From a proteomic point of view, this template based on the newly
15 determined glioma peptide sequence has led to the discovery of a wide class of proteins with related conserved structures and a particular function, in this case replication. Examples of the increase in Replikin concentration with virulence of a disease appear in diseases including, influenza, HIV, cancer and tomato leaf curl virus. This class of structures is related to the phenomenon of rapid replication in
20 organisms as diverse as yeast, algae, plants, the gemini curl leaf tomato virus, HIV and cancer.

[0008] In addition to detecting the presence of Replikins in rapidly replicating organisms, we found that 1) Replikin concentration (number of Replikins per 100
25 amino acids) and 2) Replikin compositions in specific functional states dependant

on rapid replication, provide the basis for the finding that Replikins are related quantitatively as well as qualitatively to the rate of replication of the organism in which they reside. Examples of these functional proofs include the relationship found between rapid replication and virulence in glioblastoma cells, between
5 Replikins in influenza virus and the prediction of influenza pandemics and epidemics, and the relationship between Replikin concentration and rapid replication in HIV.

[0009] The first functional basis for Replikins' role in rapid replication was found
10 in the properties of the glioma Replikin, a 10KD peptide called Malignin in brain glioblastoma multiforme (glioma) - a 250KD cell protein. Antimalignin antibody increased in concentration in serum (AMAS), measured by an early stage diagnostic test for cancer now used for most or all cell types. Malignin was so named because in tissue culture the expression of this peptide and its concentration
15 per milligram membrane protein extractable increased with increased rate of cell division per unit time. Not only is there an increase in the amount of malignin in proportion to the cell number increase but the amount of malignin is enriched, that is - increased ten fold whereas the cell number increased only five fold.

[0010] The structure of malignin protein was determined through hydrolysis and
20 mass spectrometry which revealed what proved to be a novel 16 mer peptide sequence. We searched for the 16 mer peptide sequence which we have named a Glioma Replikin protein in databases for the healthy human genome and found that it was not present in these databases.

[0011] As such, the fixed requirement algorithm was used to search in other organisms for the Glioma Replikin protein or homologues thereof. Over 4,000 protein sequences in the "Pub Med" database were searched and homologues were found in viruses and plant forms specifically associated with rapid replication. Homologues of such Replikin proteins occurred frequently in proteins called 'replicating proteins' by their investigators.

[0012] Homologues of the Replikin sequence were found in all tumor viruses (that is viruses that cause cancer), and in 'replicating proteins' of algae, plants, fungi, viruses and bacteria.

[0013] That malignin is enriched ten-fold compared to the five-fold increase in cell number and membrane protein concentration in rapid replication of glioma cells suggests an integral relationship of the Replikins to replication. When the glioma replikin was synthesized in vitro and administered as a synthetic vaccine to rabbits, abundant antimalignin antibody was produced - establishing rigourously the antigenic basis of the antimalignin antibody in serum (AMAS) test, and providing the first potential synthetic cancer vaccine and the prototype for Replikin vaccines in other organisms.

[0014] The demonstration of the relationship of the Replikins to replication and the natural immune response to cancer Replikins (overriding cell type) based upon the shared specificity of cancer Replikins, permits passive augmentation of immunity with antimalignin antibody and active augmentation with synthetic Replikin vaccines.

[0015] A study of 8,090 serum specimens from cancer patients and controls has demonstrated that the concentration of antimalignin antibody increases with age in healthy individuals, as the incidence of cancer in the population increases, and increases further two to three-fold in early malignancy, regardless of cell type. In vitro this antibody is cytotoxic to cancer cells at picograms (femtomoles) per cancer cell, and in vivo the concentration of antimalignin antibody relates quantitatively to the survival of cancer patients. As shown in glioma cells, the stage in cancer at which cells only have been transformed to the immortal malignant state but remain quiescent or dormant, now can be distinguished from the more active life-threatening replicating state which is characterized by the increased concentration of Replikins. In addition, clues to the viral pathogenesis of cancer may be found in the fact that glioma glycoprotein 10B has a 50% reduction in carbohydrate residues when compared to the normal 10B. This reduction is associated with virus entry in other instances and so may be evidence of the attachment of virus for the delivery of virus Replikins to the 10B of glial cells as a step in the transformation to the malignant state.

[0016] The sharing of immunological specificity by diverse members of the class, as demonstrated with antimalignin antibody for the glioma and related cancer Replikins, suggests that B cells and their product antibodies may recognize Replikins by means of a similar recognition 'language'. With the discovery of the Replikins, this shared immunological specificity may explain what was previously difficult to understand: why the antimalignin antibody is elevated in all cancers, and is cytotoxic to cancer cells and related to survival of cancer patients in most or

all cell types. Thus antimaligin antibody is produced against cancer Replikins, which share immunological specificity and which are related to the phenomenon of rapid replication, not to cell type.

5 [0017] A second functional basis for the Replikins' role in rapid replication is the study of data from the past 100 years on influenza virus hemagglutinin protein sequences and epidemiology of influenza epidemics and pandemics. To date, only serological hemagglutinin and antibody classification, but no strain-specific conserved peptide sequences have previously been described in influenza, and no
10 changes in concentration and composition of any strain-specific peptide sequences have been described previously which correlate with epidemiologically documented epidemics or rapid replication.

[0018] A four to ten-fold increase in the concentration of strain-specific influenza
15 Replikins in one of each of the four major strains, influenza B, (A)H1N1, (A)H2N2 and (A)H3N2 was found, and that such increase of Replikin concentration was related to influenza epidemics caused specifically by each strain from 1902 to 2001. These increases in concentration were then shown to be due to the reappearance of at least one specific Replikin composition from 1 to up to 64
20 years after its disappearance, plus the emergence of new strain-specific Replikin compositions. Previously, no strain-specific chemical structures were known with which to predict which strains would predominate in coming influenza seasons, nor to devise annual mixtures of whole-virus strains for vaccines. The recent sharp increase in H3N2 Replikin concentration (1997 to 2000), the largest in
25 H3N2's history, and the reappearance of specific Replikin compositions which

were last seen in the high mortality H3N2 pandemic of 1968 and in the two high mortality epidemics of 1975 and 1977, but were absent for 20-25 years, together may be a warning of coming epidemics.

5 [0019] Synthetic Replikins are new vaccines. This high degree of conservation of Replikin structures observed whereby the identical structure can persist for 100 years, or reappear after an absence of from one to 64 years reappears indicates that what was previously thought to be change in virulence due to random substitution of amino acids in influenza proteins is more likely to be change due to an
10 organized process of conservation of Replikins. In fact, if random substitutions of each amino acid occurred, the chance against an average length influenza Replikin sequence being conserved for one year (let alone 100) is calculated to be in the order of 2 to the 27th power to 1.

15 [0020] The significant conservation of Replikins is not unique to influenza virus is also present in foot and mouth disease virus type O and in HIV, as well as in wheat.

[0021] A third functional basis for Replikins' role in rapid replication is the
20 increase in Replikin concentration shown to be related to rapid replication in HIV. The Replikin concentration in the slow-growing low-titre strain of HIV (NS1, "Bru"), prevalent in early stage infection, was found to be one-sixth of the Replikin concentration in the rapidly-growing high-titre strain of HIV (SI, "Lai"), prevalent in late stage HIV infection.

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[0022] Other examples are given of the relation of Replikins to rapid replication.

For example, in tomato curl leaf gemini virus, which devastates tomato crops, the first 161 amino acids of the 'replicating protein', which have been shown to bind to DNA, contain five Replikins.

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[0023] In malaria, legendary for rapid replication, trypanosomes are released from the liver in tens of thousands from one trypanosome. Multiple, novel, almost 'flamboyant' Replikin structures with concentrations of up to 36 overlapping Replikins per 100 amino acids are found therein.

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[0024] The increase in Replikin concentration in influenza epidemics is functionally comparable to the glioma Replikin's increase in concentration during rapid replication of malignant glioma cells and comparable to rapid replication in HIV and in a diverse range of other organisms. Replikins thus are associated with and appear to be part of the structural bases of rapid replication in different organisms.

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[0025] Replikin concentration and composition therefore provide new methods to detect and to control the process of replication, which is central to the survival and dominance of each biological population. The discovery of these new proteins related to rapid replication provides new opportunities 1) for detection of pathogens by qualitative and quantitative determinations of Replikins, 2) for the control of a broad range of diseases in which rapid replication is a key factor by targeting native Replikins and by using synthetic Replikins as vaccines, and 3) for the use of Replikins to foster growth of algal and plant foods.

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[0026] There is a significant number of diseases and pathogens which have proved difficult to detect and treat and for which there is no effective vaccine. Thus, for each disorder there is a need for developing a target that will provide effective methods of detecting, treating or preventing these diseases and pathogens.

SUMMARY OF THE INVENTION

[0027] The present invention provides a method for identifying nucleotide or amino acid sequences that include a Replikin sequence. The method is referred to herein as a 3-point-recognition method. By use of the "3-point recognition" method, namely, peptides comprising from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues (Replikin) – constituting a new class of peptides was revealed in algae, yeast, fungi, amoebae, bacteria, plant and virus proteins having replication, transformation, or redox functions.

[0028] In one aspect of the invention there are provided isolated or synthesized peptides containing a Replikin sequence. The peptides comprise from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid residues from a second lysine residues; (2) at least one histidine residue; and (3) at least 6% lysine residues.

[0029] The present invention also provides methods for detecting the presence

of a contaminating organism in a body sample or environmental sample comprising:

- (1) isolating nucleic acids from the body sample or environmental sample;
- (2) screening the nucleic acids for the presence of a Replikin structure; and
- 5 (3) correlating the presence of a Replikin structure with the presence of the contaminating organism.

[0030] In another aspect of the invention there is provided a process for stimulating the immune system of a subject to produce antibodies that bind specifically to a Replikin sequence, said process comprising administering to the
10 subject an effective amount of a dosage of a composition comprising at least one Replikin peptide. One embodiment comprises at least one peptide that is present in an emerging strain of the organism if such new strain emerges.

15 [0031] The present invention also provides antibodies that bind specifically to a Replikin, as defined herein, as well as antibody cocktails containing a plurality of antibodies that specifically bind to Replikins. In one embodiment of the invention, there are provided compositions comprising an antibody or antibodies that specifically bind to a Replikin and a pharmaceutically acceptable carrier.

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[0032] In one aspect of the invention there are provided isolated, or separated from other proteins, recombinant, or synthesized peptides or other methods containing a viral Replikin sequence. The viral Replikin peptides comprise from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid

residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues. (viral Replikin).

[0033] The present invention also provides methods for detecting the presence of a contaminating virus in a body sample or environmental sample comprising:

- (1) isolating nucleic acids from the body sample or environmental sample;
- (2) screening the nucleic acids for the presence of a viral Replikin structure; and
- (3) correlating the presence of viral Replikin structures, their concentration and composition, with the presence of the contaminating virus.

[0034] In another aspect of the invention there is provided a process for stimulating the immune system of a subject to produce antibodies that bind specifically to a viral Replikin sequence, said process comprising administering to the subject an effective amount of a dosage of a composition comprising at least one Replikin peptide. One embodiment comprises at least one peptide that is present in an emerging strain of the virus if such new strain emerges.

[0035] The present invention also provides antibodies that bind specifically to a viral Replikin, as defined herein, as well as antibody cocktails containing a plurality of antibodies that specifically bind to viral Replikins. In one embodiment of the invention, there are provided compositions comprising an antibody or antibodies that specifically bind to a viral Replikin and a pharmaceutically acceptable carrier.

[0036] The present invention also provides therapeutic compositions comprising one or more of isolated virus peptides having from 7 to about 50 amino acids comprising: (1) at least one lysine residue located six to ten residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues, and a pharmaceutically acceptable carrier.

[0037] In another aspect of the invention there is provided an antisense nucleic acid molecule complementary to a virus Replikin mRNA sequence, said Replikin mRNA sequence denoting from 7 to about 50 amino acids comprising:

(1) at least one lysine residue located six to ten residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues.

[0038] In yet another aspect of the invention there is provided a method of simulating the immune system of a subject to produce antibodies to viruses, said method comprising: administering an effective amount of at least one virus Replikin peptide having from 7 to about 50 amino acids comprising (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; (3) and at least 6% lysine residues.

[0039] In another aspect, there is provided a method of selecting a virus peptide for inclusion in a preventive or therapeutic virus vaccine comprising:

- (1) obtaining at least one isolate of each strain of a plurality of strains of said virus;

- (2) analyzing the amino acid sequence of the at least one isolate of each strain of the plurality of strains of the virus for the presence and concentration of Replikin sequences;
- 5 (3) comparing the concentration of Replikin sequences in the amino acid sequence of the at least one isolate of each strain of the plurality of strains of the virus to the concentration of Replikin sequences observed in the amino acid sequence of each of the strains at least one earlier time period to provide the concentration of Replikins for at least two time periods, said at least one earlier time period being within about six
- 10 months to about three years prior to step (1);
- (4) indentifying the strain of the virus having the highest increase in concentration of Replikin sequences during the at least two time periods; and
- (5) selecting at least one Replikin sequence present in the strain of the
- 15 virus peptide identified in step (4) as a peptide for inclusion in the virus vaccine.

[0040] The present invention also provides a method of making a preventive or therapeutic virus vaccine comprising:

- 20 (1) identifying a strain of a virus as an emerging strain;
- (2) selecting at least one Replikin sequence present in the emerging strain as a peptide template for the virus vaccine manufacture,
- (3) synthesizing peptides having the amino acid sequence of the at least one Replikin sequence selected in step (2), and

- (4) combining a therapeutically effective amount of the peptides of step (3) with a pharmaceutically acceptable carrier and/or adjuvant.

[0041] In another aspect, the invention is directed to a method of identifying an emerging strain of a virus for diagnostic, preventive or therapeutic purposes comprising:

- (1) obtaining at least one isolate of each strain of a plurality of strains of the virus;
- (2) analyzing the amino acid sequence of the at least one isolate of each strain of the plurality of strains of the virus for the presence and concentration of Replikin sequences;
- (3) comparing the concentration of Replikin sequences in the amino acid sequence of the at least one isolate of each strain of the plurality of strains of the virus to the concentration of Replikin sequences observed in the amino acid sequence of each of the strains at at least one earlier time period to provide the concentration of Replikins for at least two time periods, said at least one earlier time period being within about six months to about three years prior to step (1); and
- (4) identifying the strain of the virus having the highest increase in concentration of Replikin sequences during the at least two time periods.

[0042] In yet another aspect of the invention, there is provided a preventive or therapeutic virus vaccine comprising at least one isolated Replikin present in a

protein of an emerging strain of the virus and a pharmaceutically acceptable carrier and/or adjuvant.

[0043] Also provided by the present invention is a method of preventing or
5 treating a virus infection comprising administering to a patient in need thereof a preventive or therapeutic virus vaccine comprising at least one isolated Replikin present in a protein of an emerging strain of the virus and a pharmaceutically acceptable carrier and/or adjuvant.

10 INFLUENZA

[0044] Influenza is an acute respiratory illness of global importance. Despite international attempts to control influenza virus outbreaks through vaccination, influenza infections remain an important cause of morbidity and mortality. Worldwide influenza epidemics and pandemics have occurred at irregular and
15 previously unpredictable intervals throughout history and it is expected that they will continue to occur in the future. The impact of both pandemic and epidemic influenza is substantial in terms of morbidity, mortality and economic cost.

[0045] Influenza vaccines remain the most effective defense against influenza
20 virus, but because of the ability of the virus to mutate and the availability of non-human host reservoirs, it is expected that influenza will remain an emergent or re-emergent infection. Global influenza surveillance indicates that influenza viruses may vary within a country and between countries and continents during an influenza season. Virological surveillance is of importance in monitoring
25 antigenic shift and drift. Disease surveillance is also important in assessing the

impact of epidemics. Both types of information have provided the basis of the vaccine composition and the correct use of antivirals. However, to date there has been only annual post hoc hematological classification of the increasing number of emerging influenza virus strains, and no specific chemical structure of the viruses has been identified as an indicator of approaching influenza epidemics or pandemics. Currently, the only basis for annual classification of influenza virus as active, inactive or prevalent in a given year is the activities of the virus hemagglutinin and neuraminidase proteins. No influenza viral chemical structure has been identified prior to this application that can be used for quantitative warning of epidemics or pandemics or to design more effective and safer vaccines.

[0046] Because of the annual administration of influenza vaccines and the short period of time when a vaccine can be administered, strategies directed at improving vaccine coverage are of critical importance.

[0047] In one aspect of the invention there are provided isolated or synthesized influenza virus peptides containing a Replikin sequence. The influenza Replikin virus peptides comprise from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues. (Influenza Replikin).

[0048] In another aspect of the invention, there is provided a process for stimulating the immune system of a subject to produce antibodies that bind specifically to an influenza virus Replikin sequence, said process comprising

administering to the subject an effective amount of dosage of a composition comprising at least one influenza virus Replikin peptide. In a preferred embodiment the composition comprises at least one peptide that is present in an emerging strain of influenza virus.

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[0049] The present invention also provides antibodies that bind specifically to an influenza virus Replikin, as defined herein, as well as antibody cocktails containing a plurality of antibodies that specifically bind to influenza virus Replikins. In one embodiment of the invention, there are provided compositions comprising an antibody or antibodies that specifically bind to an influenza Replikin and a pharmaceutically acceptable carrier.

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[0050] The present invention also provides therapeutic compositions comprising one or more of isolated influenza virus peptides having from 7 to about 50 amino acids comprising:

- (1) at least one lysine residue located six to ten residues from a second lysine residue;
- (2) at least one histidine residue; and
- (3) at least 6% lysine residues, and a pharmaceutical acceptable carrier.

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[0051] In another aspect of the invention there is provided an antisense nucleic acid molecule complementary to an influenza virus hemagglutinin Replikin mRNA sequence, said Replikin mRNA sequence denoting from 7 to about 50 amino acids comprising:

- (1) at least one lysine residue located six to ten residues from a second lysine residue;
- (2) at least one histidine residue; and
- (3) at least 6% lysine residues.

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[0052] In yet another aspect of the invention there is provided a method of simulating the immune system of a subject to produce antibodies to influenza virus comprising administering an effective amount of at least one influenza virus Replikin peptide having from 7 to about 50 amino acids comprising:

- 10 (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue;
- (2) at least one histidine residue; and
- (3) at least 6% lysine residues.

15 [0053] In another aspect, there is provided a method of selecting an influenza virus peptide for inclusion in a preventive or therapeutic influenza virus vaccine comprising:

- (1) obtaining at least one isolate of each strain of a plurality of strains of influenza virus;
- 20 (2) analyzing the hemagglutinin amino acid sequence of the at least one isolate of each strain of the plurality of strains of influenza virus for the presence and concentration of Replikin sequences;
- (3) comparing the concentration of Replikin sequences in the hemagglutinin amino acid sequence of the at least one isolate of each strain of the plurality of strains of influenza virus to the concentration
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of Replikin sequences observed in the hemagglutinin amino acid sequence of each of the strains at least one earlier time period to provide the concentration of Replikins for at least two time periods, said at least one earlier time period being within about six months to about three years prior to step (1);

- (4) identifying the strain of influenza virus having the highest increase in concentration of Replikin sequences during the at least two time periods;
- (5) selecting at least one Replikin sequence present in the strain of influenza virus peptide identified in step (4) as a peptide for inclusion in an influenza virus vaccine.

[0054] The present invention also provides a method of making a preventive or therapeutic influenza virus vaccine comprising:

- (1) identifying a strain of influenza virus as an emerging strain;
- (2) selecting at least one Replikin sequence present in the emerging strain as a peptide template for influenza virus vaccine manufacture,
- (3) synthesizing peptides having the amino acid sequence of the at least one Replikin sequence selected in step (2), and
- (4) combining a therapeutically effective amount of the peptides of step (3) with a pharmaceutically acceptable carrier and/or adjuvant

[0055] In another aspect, the invention is directed to a method of identifying an emerging strain of influenza virus for diagnostic, preventive or therapeutic purposes comprising:

- (1) obtaining at least one isolate of each strain of a plurality of strains of influenza virus;
- (2) analyzing the hemagglutinin amino acid sequence of the at least one isolate of each strain of the plurality of strains of influenza virus for the presence and concentration of Replikin sequences;
- (3) comparing the concentration of Replikin sequences in the hemagglutinin amino acid sequence of the at least one isolate of each strain of the plurality of strains of influenza virus to the concentration of Replikin sequences observed in the hemagglutinin amino acid sequence of each of the strains at at least one earlier time period to provide the concentration of Replikins for at least two time periods, said at least one earlier time period being within about six months to about three years prior to step (1); and
- (4) identifying the strain of influenza virus having the highest increase in concentration of Replikin sequences during the at least two time periods.

[0056] In yet another aspect of the invention, there is provided a preventive or therapeutic influenza virus vaccine comprising at least one isolated Replikin present in the hemagglutinin protein of an emerging strain of influenza virus and a pharmaceutically acceptable carrier and/or adjuvant.

[0057] Also provided by the present invention is a method of preventing or treating influenza virus infection comprising administering to a patient in need thereof a preventive or therapeutic vaccine comprising at least one isolated

Replikin present in the hemagglutinin protein of an emerging strain of influenza virus and a pharmaceutically acceptable carrier and/or adjuvant.

TRYPANOSOMES

5 [0058] In one aspect of the invention there are provided isolated or synthesized trypanosome peptides containing a Replikin sequence. The trypanosome Replikin peptides comprise from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues. (Trypanosome
10 Replikins).

MALARIA

[0059] One trypanosome disorder which has proved difficult to treat and for which there is no effective vaccine is malaria. Malaria causes much death, and physical
15 and economic hardship in tropical regions. Malaria is caused mainly by *Plasmodium falciparum*, which has proved to be extremely resistant to treatment and to date, a vaccine for malaria has remained elusive. Thus there is a need for effective malaria vaccines and methods of treating or preventing the disease. This application provides the basis for such vaccines and methods of treatment and
20 prevention. All of the methods described above for production of and treatment with Replikin virus vaccines and Replikin influenza virus vaccines are applicable to the production of and treatment with Replikin malaria vaccines.

[0060] In the present invention, there are provided vaccines and methods for
25 preventing or treating malaria. The malaria vaccines comprise at least one isolated

Plasmodium falciparum Replikin. The present invention also provides methods for treating or preventing malaria comprising administering to a patient an effective amount of preventive or therapeutic vaccine comprising at least one isolated Plasmodium falciparum Replikin.

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[0061] Also provided by the present invention are antibodies, antibody cocktails and compositions that comprise antibodies that specifically bind to a Replikin or Replikins present in a malaria antigen of Plasmodium falciparum.

10 [0062] Another example of a trypanosome which may be treated under the present invention as is the case for malaria, the Replikins of Treponema Pallidum (syphilis), can be used for detection, prevention, treatment of syphilis.

BACTERIA

15 [0063] In one aspect of the invention there are provided isolated or synthesized bacterial peptides containing a Replikin sequence (bacterial Replikins). The bacterial peptides comprise from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues.
20 (bacterial Replikins). US Application Serial No. 10/105,232 filed March 26, 2002 is incorporated by reference in its entirety, including but not limited to the bacterial sequence listing and information.

[0064] The present invention also provides methods for detecting the presence

of a contaminating bacterial organism in a body sample or environmental sample comprising:

- (1) isolating nucleic acids from the body sample or environmental sample;
- (2) screening the nucleic acids for the presence of a Replikin structure; and
- 5 (3) correlating the presence of a Replikin structure with the presence of the contaminating organism.

[0065] In another aspect of the invention there is provided a process for stimulating the immune system of a subject to produce antibodies that bind
10 specifically to a bacterial Replikin sequence, said process comprising administering to the subject an effective amount of a dosage of a composition comprising at least one bacterial Replikin peptide. One embodiment comprises at least one bacterial peptide that is present in an emerging strain of the bacterial organism if such new strain emerges.

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[0066] The present invention also provides antibodies that bind specifically to a bacterial Replikin, as defined herein, as well as antibody cocktails containing a plurality of antibodies that specifically bind to bacterial Replikins. In one embodiment of the invention, there are provided compositions comprising an
20 antibody or antibodies that specifically bind to a bacterial Replikin and a pharmaceutically acceptable carrier.

[0067] The present invention also provides therapeutic compositions comprising one or more of isolated bacterial peptides having from 7 to about 50 amino acids
25 comprising:

- (1) at least one lysine residue located six to ten residues from a second lysine residue;
- (2) at least one histidine residue;
- (3) at least 6% lysine residues; and
- 5 (4) a pharmaceutically acceptable carrier.

[0068] In another aspect of the invention there is provided an antisense nucleic acid molecule complementary to a bacterial Replikin mRNA sequence, said Replikin mRNA sequence denoting from 7 to about 50 amino acids comprising:

- 10 (1) at least one lysine residue located six to ten residues from a second lysine residue;
- (2) at least one histidine residue; and
- (3) at least 6% lysine residues.

15 [0069] In yet another aspect of the invention there is provided a method of simulating the immune system of a subject to produce antibodies to bacteria comprising administering an effective amount of at least one bacterial Replikin peptide having from 7 to about 50 amino acids comprising:

- 20 (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue;
- (2) at least one histidine residue; and
- (3) at least 6% lysine residues.

[0070] In another aspect, there is provided a method of selecting a bacterial Replikin peptide for inclusion in a preventive or therapeutic bacterial vaccine comprising:

- 5 (1) obtaining at least one isolate of each strain of a plurality of strains of the bacteria;
- (2) analyzing the amino acid sequence of the at least one isolate of each strain of the plurality of strains of the bacteria for the presence and concentration of bacterial Replikin sequences;
- 10 (3) comparing the concentration of bacterial Replikin sequences in the amino acid sequence of the at least one isolate of each strain of the plurality of strains of the bacteria to the concentration of bacterial Replikin sequences observed in the amino acid sequence of each of the strains at least one earlier time period to provide the concentration of
15 bacterial Replikins for at least two time periods, said at least one earlier time period being within about six months to about three years prior to step (1), or earlier in rapidly mutating bacteria;
- (4) indentifying the strain of the bacteria having the highest increase in concentration of bacterial Replikin sequences during the at least two
20 time periods; and
- (5) selecting at least one bacterial Replikin sequence present in the strain of the bacterial peptide identified in step (4) as a peptide for inclusion in the bacterial vaccine.

[0071] The present invention also provides a method of making a preventive or therapeutic bacterial vaccine comprising:

- (1) identifying a strain of a bacteria as an emerging strain;
- (2) selecting at least one bacterial Replikin sequence present in the
5 emerging strain as a peptide template for the bacterial vaccine
manufacture;
- (3) synthesizing peptides having the amino acid sequence of the at least
one bacterial Replikin sequence selected in step (2); and
- (4) combining a therapeutically effective amount of the peptides of step (3)
10 with a pharmaceutically acceptable carrier and/or adjuvant.

[0072] In another aspect, the invention is directed to a method of identifying an emerging strain of bacteria for diagnostic, preventive or therapeutic purposes comprising:

- 15 (1) obtaining at least one isolate of each strain of a plurality of strains of
the bacteria;
- (2) analyzing the amino acid sequence of the at least one isolate of each
strain of the plurality of strains of the bacteria for the presence and
concentration of bacterial Replikin sequences;
- 20 (3) comparing the concentration of bacterial Replikin sequences in the
amino acid sequence of the at least one isolate of each strain of the
plurality of strains of the bacteria to the concentration of bacterial
Replikin sequences observed in the amino acid sequence of each of the
strains at at least one earlier time period to provide the concentration of
25 bacterial Replikins for at least two time periods, said at least one earlier

time period being within about six months to about three years prior to
step (1); and

- (4) identifying the strain of the bacteria having the highest increase in
concentration of bacterial Replikin sequences during the at least two
time periods.

[0073] In yet another aspect of the invention, there is provided a preventive or
therapeutic bacterial vaccine comprising at least one isolated bacterial Replikin
present in a protein of an emerging strain of the bacteria and a pharmaceutically
acceptable carrier and/or adjuvant.

[0074] Two important sub-species of bacteria, classified under mycobacteria, are
Mycobacterium leprae (leprosy) whose 30-s ribosomal protein has a C-terminal
Replikin and Mycobacterium tuberculosis (tuberculosis) whose ATPase has three
Replikins.

Replikin in 30s ribosomal protein s6 of Mycobacterium leprae (leprosy) is:

kvmrtdkh

Replikins in the ATPase of Mycobacterium tuberculosis are:

hprpkvaaalkdsyrlk

hprpkvaaalk

ksaqkwpdkflagaaqvah

Replikins in the B-D-galactosidase of E. coli:

hawqhqqktlfisrk

hqgktlfisrk

Replikins in Agrobacterium tumefaciens:

5 hsdqqlavmiaakrlddyk

hlldhpsvgqldlramlaveevkidnpvymek

hpsvgqldlramlaveevkidnpvymek

kcvmakncnikcpaglttnqcafgdpralaqylmniah

kcnikcpaglttnqcafgdpralaqylmniah

10 hhdtsiedlaqlihdakaarvrivk

hdtsiedlaqlihdakaarvrivk

hdakaarvrivk

kigqgakpgeggqlpspktveiaaarggtpgvelvsppph

kigqgakpgeggqlpspktveiaaarggtpgvelvsppph

15 kaseitktlasgamshgalvaaheavahgtmvggmsnsgeggeh

kaseitktlasgamshgalvaaheavah

kaseitktlasgamshgalvaaah

kaseitktlasgamsh

kryfpnvktpvggvtfaviaqavadwh

20 hhiaaglgfgasavypigvqfraeckfgadadkafkrfakaaekslmk

hhiaaglgfgasavypigvqfraeckfgadadkafkrfakaaekslmk

hhiaaglgfgasavypigvqfraeckfgadadkafkrfakaaek

hhiaaglgfgasavypigvqfraeckfgadadkafkrfak

hhiaaglgfgasavypigvqfraeckfgadadk

25 hiaaglgfgasavypigvqfraeckfgadadkafkrfakaaekslmk

hiaaglgfgasavypigvqfrageekfgadadkafrfakaaek

hiaaglgfgasavypigvqfrageekfgadadkafrfak

hiaaglgfgasavypigvqfrageekfgadadk

kfglydaafeksscgvqftrkdgvqth

5

[0075] Also provided by the present invention is a method of preventing or treating a bacterial infection comprising administering to a patient in need thereof a preventive or therapeutic vaccine comprising at least one isolated bacterial Replikin present in a protein of an emerging strain of the bacteria and a

10 pharmaceutically acceptable carrier and/or adjuvant.

FUNGUS

[0076] In one aspect of the invention there are provided isolated or synthesized fungal peptides containing a Replikin sequence. The fungal Replikin peptides

15 comprise from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues (fungal Replikins).

[0077] All of the methods described above for production of and treatment with

20 bacterial Replikin vaccines are applicable to the production of and treatment with fungal Replikin vaccines.

[0078] In another aspect of the invention there is provided a process for stimulating the immune system of a subject to produce antibodies that bind

specifically to a fungal Replikin sequence, said process comprising administering to the subject an effective amount of a dosage of a composition comprising at least one fungal Replikin peptide.

5 [0079] The present invention also provides antibodies that bind specifically to a fungal Replikin, as defined herein, as well as antibody cocktails containing a plurality of antibodies that specifically bind to viral Replikins. In one embodiment of the invention, there are provided compositions comprising an antibody or antibodies that specifically bind to a fungal Replikin and a
10 pharmaceutically acceptable carrier.

[0080] The present invention also provides therapeutic compositions comprising one or more of isolated fungal peptides having from 7 to about 50 amino acids comprising:

- 15 (1) at least one lysine residue located six to ten residues from a second lysine residue;
- (2) at least one histidine residue;
- (3) at least 6% lysine residues; and
- (4) a pharmaceutically acceptable carrier.

20

[0081] In another aspect of the invention there is provided an antisense nucleic acid molecule complementary to an fungal Replikin mRNA sequence, said Replikin mRNA sequence having from 7 to about 50 amino acids comprising:

- (1) at least one lysine residue located six to ten residues from a second
25 lysine residue;

- (2) at least one histidine residue; and
- (3) at least 6% lysine residues.

[0082] In another aspect of the invention there is provided a process for stimulating the immune system of a subject to produce antibodies that bind specifically to a fungal Replikin sequence, said process comprising administering to the subject an effective amount of a dosage of a composition comprising at least one Replikin peptide.

10 INCREASING REPLICATION

[0083] In yet another aspect of the invention there is provided a method for increasing the replication rate of an organism comprising transforming a gene encoding an enzyme or other protein having a replication function in the organism with at least one Replikin structure.

15

DEFINITIONS

[0084] As used herein, the term "peptide" or "protein" refers to a compound of two or more amino acids in which the carboxyl group of one is united with an amino group of another, forming a peptide bond. The term peptide is also used to denote the amino acid sequence encoding such a compound. As used herein, "isolated" or "synthesized" peptide or biologically active portion thereof refers to a peptide that is substantially free of cellular material or other contaminating peptides from the cell or tissue source from which the peptide is derived, or substantially free from chemical precursors or other chemicals when chemically

20

synthesized by any method, or substantially free from contaminating peptides when synthesized by recombinant gene techniques.

[0085] As used herein, a Replikin peptide or Replikin protein is an amino acid sequence having 7 to about 50 amino acids comprising:

- (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue;
- (2) at least one histidine residue;
- (3) at least 6% lysine residues.

Similarly, a Replikin sequence is the amino acid sequence encoding such a peptide or protein.

[0086] As used herein, "emerging strain" as used herein refers to a strain of a virus, bacterium, fungus, or other organisms identified as having an increased increasing concentration of Replikin sequences in one or more of its protein sequences relative to the concentration of Replikins in other strains of such organism. The increase or increasing concentration of Replikins occurs over a period of at least about six months, and preferably over a period of at least about one year, most preferably over a period of at least about three years or more, for example, in influenza virus, but may be a much shorter period of time for bacteria and other organisms.

[0087] As used herein, "mutation" refers to change in this structure and properties of an organism caused by substitution of amino acids. In contrast, the term

"conservation" as used herein, refers to conservation of particular amino acids due to lack of substitution.

BRIEF DESCRIPTION OF THE DRAWINGS

5 [0088] Figure 1 is a bar graph depicting the frequency of occurrence of Replikins in various organisms.

[0089] Figure 2 is a graph depicting the percentage of malignin per milligram total membrane protein during anaerobic replication of glioblastoma cells.

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[0090] Figure 3 is a bar graph showing amount of antimalignin antibody produced in response to exposure to the recognin 16-mer.

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[0091] Figure 4A is a photograph of a blood smear taken with ordinary and fluorescent light. Figure 4B is a photograph of a blood smear taken with ordinary and fluorescent light illustrating the presence of two leukemic cells. Figure 4C is a photograph of a dense layer of glioma cells in the presence of antimalignin antibody. Figure 4D and Figure 4E are photographs of the layer of cells in Figure 4C taken at 30 and 45 minutes following addition of antimalignin antibody

20

[0092] Figure 4F is a bar graph showing the inhibition of growth of small cell lung carcinoma cells in vitro by antimalignin antibody.

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[0093] Figure 5 is a plot of the amount of antimalignin antibody present in the serum of patients with benign or malignant breast disease pre-and post surgery.

[0094] Figure 6 is a box diagram depicting an embodiment of the invention wherein a computer is used to carry out the 3-point-recognition method of identifying Replikin sequences.

5

[0095] Figure 7 is a graph showing the concentration of Replikins observed in hemagglutinin of influenza B and influenza A strain, H1N1, on a year by year basis from 1918 through 2001.

10

[0096] Figure 8 is a graph of the Replikin concentration observed in hemagglutinin of influenza A strains, H2N2 and H3N2, as well as an emerging strain defined by its constituent Replikins, designated H3N2(R), on a year by year basis from 1950 to 2001.

15

DETAILED DESCRIPTION OF THE INVENTION

[0097] The identification of a new family of small peptides related to the phenomenon of rapid replication, referred to herein as Replikins, provides targets for detection of pathogens in a sample and developing therapies, including vaccine development. In general, knowledge of and identification of this family of peptides enables development of effective therapies and vaccines for any organism that harbors Replikins. Identification of this family of peptides also provides for the detection of viruses and virus vaccine development.

20

[0098] For example, identification of this family of peptides provides for the detection of influenza virus and provides new targets for influenza treatment.

25

Identification of this family of peptides also provides for example, for the detection of malaria and provides new targets for malaria vaccine development. Further examples provided by the identification of this family of peptides include the detection of infectious disease Replikins, cancer immune Replikins and structural protein Replikins.

[0099] Rapid replication is characteristic of virulence in certain bacteria, viruses and malignancies, but no chemistry common to rapid replication in different organisms has been described. We have found a family of conserved small protein sequences related to rapid replication, which we have named Replikins. Such Replikins offer new targets for developing effective detection methods and therapies. The first Replikin found was the glioma Replikin, which was identified in brain glioblastoma multiforme (glioma) cell protein called malignin.

[00100] Hydrolysis and mass spectrometry of malignin revealed the novel 16 mer peptide sequence which contains the glioma Replikin. This Replikin was not found in databases for the normal healthy human genome and therefore appeared to be derived from some source outside the body.

[0101] We have devised an algorithm to search for the glioma Replikin or homologue thereof. Homologues were not common in over 4,000 protein sequences, but were found, surprisingly, in all tumor viruses, and in the replicating proteins of algae, plants, fungi, viruses and bacteria.

[0102] We have identified that both 1) Replikin concentration (number of Replikins per 100 amino acids) and 2) Replikin composition correlate with the functional phenomenon of rapid replication. These relationships provide functional basis for the determination that Replikins are related quantitatively as well as qualitatively to the rate of replication.

[0103] The first functional basis for Replikins role to rapid replication is seen in glioma replication. The fact that glioma malignin is enriched ten-fold compared to the five-fold increase in cell number and membrane protein concentration in rapid replication of glioma cells suggests an integral relationship of the Replikins to replication. When the glioma Replikin was synthesized in vitro and administered as a synthetic vaccine to rabbits, abundant antimalignin antibody was produced. This establishes the antigenic basis of the antimalignin antibody in serum (AMAS) test, and provides the first potential synthetic cancer vaccine and the prototype for Replikin vaccines in other organisms. With the demonstration of this natural immune relationship of the Replikins to replication and this natural immune response to cancer Replikins, which overrides cell type, based upon the shared specificity of cancer Replikins and rapid replication, both passive augmentation of this immunity with antimalignin antibody and active augmentation with synthetic Replikin vaccines now is possible.

[0104] The relationship between the presence of antimalignin antibody and survival in patients was shown in a study of 8,090 serum specimens from cancer patients. The study showed that the concentration of antimalignin antibody increases with age, as the incidence of cancer in the population increases, and

increases further two to three-fold in early malignancy, regardless of cell type. In vitro, the antimalignin antibody is cytotoxic to cancer cells at picograms (femtomoles) per cancer cell, and in vivo the concentration of antimalignin antibody relates quantitatively to the survival of cancer patients. As shown in glioma cells, the stage in cancer at which cells have only been transformed to the immortal malignant state but remain quiescent or dormant, now can be distinguished from the more active life-threatening replicating state, which is characterized by the increased concentration of Replikins. In addition, clues to the viral pathogenesis of cancer may be found in the fact that glioma glycoprotein 10B has a 50% reduction in carbohydrate residues when compared to the normal 10B. This reduction is associated with virus entry in other instances, and so may be evidence of the attachment of virus for the delivery of virus Replikins to the 10B of glial cells as a step in the transformation to the malignant state.

[0105] Our study concerning influenza virus hemagglutinin protein sequences and influenza epidemiology over the past 100 years, has provided a second functional basis for the relations of Replikins to rapid replication. Only serological hemagglutinin and antibody classification, but no strain-specific conserved peptide sequences have previously been described in influenza. Further, no changes in concentration and composition of any strain-specific peptide sequences have been described previously that correlate with epidemiologically documented epidemics or rapid replication. In this study, a four to ten-fold increase in the concentration of strain-specific influenza Replikins in one of each of the four major strains, influenza B, (A)H1N1, (A)H2N2 and (A)143N2, is shown to relate to influenza epidemics caused by each strain from 1902 to 2001.

[0106] We then showed that these increases in concentration are due to the reappearance of at least one specific Replikin composition from 1 to up to 64 years after its disappearance, plus the emergence of new strain-specific Replikin compositions. Previously, no strain-specific chemical structures were known with which to predict the strains that would predominate in coming influenza seasons, nor to devise annual mixtures of whole-virus strains for vaccines. The recent sharp increase in H3N2 Replikin concentration (1997 to 2000), the largest in H3N2's history, and the reappearance of specific Replikin compositions that were last seen in the high mortality H3N2 pandemic of 1968, and in the two high mortality epidemics of 1975 and 1977, but were absent for 20-25 years, together may be a warning of coming epidemics. This high degree of conservation of Replikin structures observed, whereby the identical structure can persist for 100 years, or reappear after an absence of from one to 64 years, indicate that what was previously thought to be change due to random substitution of amino acids in influenza proteins is more likely to be change due to an organized process of conservation of Replikins.

[0107] The conservation of Replikins is not unique to influenza virus but was also observed in other sources, for example in foot and mouth disease virus, type O, HIV tat, and wheat.

[0108] A third functional basis for Replikins' role in rapid replication is seen in the increase in rapid replication in HIV. Replikin concentration was shown to be related to rapid replication in HIV. We found the Replikin concentration in the

slow growing low-titre strain of HIV (NSI, "Bru"), which is prevalent in early stage infection, to be one-sixth of the Replikin concentration in the rapidly-growing high-titre strain of HIV (SI, "Lai") (prevalent in late stage HIV infection).

5 [0109] Further examples demonstrate the relationship of Replikins to rapid replication. In the "replicating protein," of tomato curl leaf gemini virus which devastates tomato crops, the first 161 amino acids, the sequence which has been shown to bind to DNA, was shown to contain five Replikins. In malaria, legendary for rapid replication when trypanosomes are released from the liver in
10 the tens of thousands from one trypanosome, multiple, novel, almost 'flamboyant' Replikin structures have been found with concentrations of up to 36 overlapping Replikins per 100 amino acids.

[0110] The conservation of any structure is critical to whether that
15 structure provides a stable invariant target to attack and destroy or to stimulate. When a structure is tied in some way to a basic survival mechanism of the organism, the structures tend to be conserved. A varying structure provides an inconstant target, which is a good strategy for avoiding attackers, such as antibodies that have been generated specifically against the prior structure and thus
20 are ineffective against the modified form. This strategy is used by influenza virus, for example, so that a previous vaccine may be quite ineffective against the current virulent virus.

REPLIKINS AS STABLE TARGETS FOR TREATMENT

[0111] Both bacteria and HIV have both Replikin and non-Replikin amino acids.

In HIV, for example, there has been a recent increase in drug-resistance from 9% to 13% due to mutation, that is substitution of non-Replikin amino acids. (See

5 detailed analysis of TAT protein of HIV discussed herein). In bacteria, the

development of 'resistant strains' is due to a similar mechanism. However, we

have found that Replikin structures do not mutate or change to the same degree as

non Replikin amino acids (see also discussion of foot and mouth disease virus

conservation of Replikins discussed herein). The Replikin structures, as opposed

10 to the non-Replikin structures are conserved and thus provide new constant targets for treatment.

[0112] Certain structures too closely related to survival functions apparently

cannot change constantly. Because an essential component of the Replikin

15 structure is histidine (h), which is know for its frequent binding to metal groups in

redox enzymes and probable source of energy needed for replication, and since

this histidine structure remains constant, this structure remains all the more

attractive a target for destruction or stimulation.

20 [0113] From a proteomic point of view, inventors construction of a template based

on the newly determined glioma peptide sequence led them to the discovery of a

wide class of proteins with related conserved structures and a particular function,

in this case replication. Examples of the increase in Replikin concentration with

virulence of a disease include, influenza, HIV, cancer and tomato leaf curl virus.

25 This newly recognized class of structures is related to the phenomenon of rapid

replication in organisms as diverse as yeast, algae, plants, the gemini curl leaf tomato virus, HIV and cancer.

5 [0114] Replikin concentration and composition provide new quantitative methods to detect and control the process of replication, which is central to the survival and dominance of each biological population. The sharing of immunological specificity by diverse members of the class, as demonstrated with antimalignin antibody for the glioma and related cancer Replikins, suggests that B cells and their product antibodies may recognize Replikins by means of a similar
10 recognition language.

[0115] Examples of peptide sequences of cancer Replikins or as containing a Replikin, i.e., a homologue of the glioma peptide, kagvafihkk, may be found in such cancers of, but not limited to, the lung, brain, liver, soft-tissue, salivary gland,
15 nasopharynx, esophagus, stomach, colon, rectum, gallbladder, breast, prostate, uterus, cervix, bladder, eye, forms of melanoma, lymphoma, leukemia, and kidney.

[0116] Replikins provide for: 1) detection of pathogens by qualitative and quantitative determinations of Replikins; 2) treatment and control of a broad range
20 of diseases in which rapid replication is a key factor by targeting native Replikins and by using synthetic Replikins as vaccines; and 3) fostering increased growth rates of algal and plant foods.

[0117] The first Replikin sequence to be identified was the cancer cell Replikin
25 found in a brain cancer protein, malignin, which was demonstrated to be enriched

ten-fold during rapid anaerobic replication of glioblastoma multiforme (glioma) cells. (Figure 2) Malignin is a 10KDa portion of the 250 KDa glycoprotein 10B, which was isolated in vivo and in vitro from membranes of glioblastoma multiforme (glioma) cells. Hydrolysis and mass spectroscopy of malignin revealed a 16-mer peptide sequence, ykagvafhkkndide (SEQ ID NO.:4), which is referred to herein as the glioma Replikin and which includes the shorter peptide, kagvafhkk (SEQ ID NO.: 1), both of which apparently are absent in the normal human genome.

Table 1

16-mer peptide sequence ykagvafhkkndide obtained from malignin by hydrolysis and mass spectrometry

Seq. NO.	Fragment Identified	MH ⁺ (mass)	Sequence	Method By Which Fragment Obtained	Auto-hydrolysis of malignin immobilized on bromoacetyl cellulose	Microwaved 30 seconds	Microwaved 30 seconds
19	1-3	374.10	Oyka(g)				+
20	1-5	527.10	Oykagv(a)		+		
21	2-6	552.10	(y)kagva(f)		+		
22	2-7	599.10	(Y)kagva(f)				
23	4-11	899.10	(a)gvafhkk(n)				+
24	5-7	336.10	(g)va(f)				+
25	6-7	226.09	(v)af(f)				
26	6-10	381.09	(v)afhkk(k)				+
27	6-10	381.09	(v)afhkk(k)				
28	6-12	533.10	(v)afhkknd(d)		+		
29	6-12	533.10	(v)afhkknd(d)				
30	7-8	279.10	(a)fl(h)				
31	10-16	867.10	(h)kkndide()		+		
32	11-14	533.10	(k)kndid(d)		+		
33	12-15	476.09	(k)ndid(e)				

[0118] When the 16-mer glioma Replikin was synthesized and injected as a synthetic vaccine into rabbits, abundant antimalignin antibody was produced.

5 (Bogoch et al., Cancer Detection and Prevention, 26 (Suppl. 1): 402 (2002)). The concentration of antimalignin antibody in serum in vivo has been shown to relate quantitatively to the survival of cancer patients. (Bogoch et al., Protides of Biological Fluids, 31:739-747 (1984). In vitro antimalignin antibodies have been shown to be cytotoxic to cancer cells at a concentration of picograms (femtomolar) per cancer cell. (Bogoch et al., Cancer Detection and Prevention, 26 (Suppl. 1):
10 402 (2002).

[0119] Studies carried out by the inventors showed that the glioma Replikin is not represented in the normal healthy human genome. Consequently, a search for the
15 origin and possible homologues of the Replikin sequence was undertaken by analysis of published sequences of various organisms.

[0120] By using the 16-mer glioma Replikin sequence as a template and constructing a recognition proteomic system to visually scan the amino acid
20 sequences of proteins of several different organisms, a new class of peptides, the Replikins, was identified. The present invention provides a method for identifying nucleotide or amino acid sequences that include a Replikin sequence. The method is referred to herein as a 3-point-recognition method. The three point recognition method comprises: a peptide from 7 to about 50 amino acids including
25 (1) at least one lysine residue located six to ten amino acid residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues. (Replikin). These peptides or proteins constitute a new class of peptides

in species including algae, yeast, fungi, amoebae, bacteria, plant, virus and cancer proteins having replication, transformation, or redox functions. Replikin peptides have been found to be concentrated in larger 'replicating' and 'transforming' proteins (so designated by their investigators, See Table 2) and cancer cell

5 proteins. No sequences were found to be identical to the malignin 16-mer peptide.

Table 2:
Examples of Replikins in various organisms - prototype: Glioma Replikin* kagvaflhkk
 (SEQ ID No.:1)

Algae:	SEQ ID NO.		
	34	Caldophera prolifera	kaskfikh
	35	Isotriplisprolifera	kaqaetgeikgh
Yeast:	36	Schizosaccharomyces pombe	kskypkckhk
	37	Oryza sativa	kkaygnethk
	2	Sacch. cerevisiae replication binding protein	hsikrelgiifdk
Fungi:		Isocitrate lyase ICI 1, Penicillium marneffei	kvdivthqk
	38	DNA-dependent RNA polymerase II, Discula destructiva	kkeedaayhrkk
	39	Ophiostoma novo-ulm I, RNA in Dutch elm disease fungus	kvilplrgnikgiffkh
	40		
Amoeba:	41	Entamoeba invadens, histone H2B	klikgdinkh
Bacteria:	42	Pribosomal protein replication factor, Helicobacter pylori	ksvhaflk
		Replication-associated protein Staph. aureus	
	10	Mycoplasma pulmonis, chromosome replication	kkektthnk
	43	Macrophage infectivity potentiator, L. legionella	kvhffqlkk
	90	Bacillus anthracis	khlisvkk
	91	Bacillus anthracis	hvkckekcnk
	92	Bacillus anthracis	khivkievk
	93	Bacillus anthracis	kdddkdiygkdalfh
	94	Bacillus anthracis	kwckikqh
	95	Bacillus anthracis	kklqippiepkddiifh
	96	Bacillus anthracis	hmrysnivesaylilnew-kniqsdlikk
	97	Bacillus anthracis	havddyagyldknqsdly-trskk
	98	Bacillus anthracis	haerikvqknspk
Plants:	44	Arabidopsis thaliana, prolifera	kdhdfdgdk
	45	Arabidopsis thaliana, cytoplasmic ribosomal	knkgllqldcah
	46	Arabidopsis thaliana, DNA binding protein	kelsttqeksh
Viruses:	9	Replication associated protein A [Maize streak virus]	Keldpskdeimrdiish
	11	Bovine herpes virus 4, DNA replication protein	hkinutgqk
	12	Meleagrid herpesvirus 1, replication binding protein	hkdlyrlmk
	47	Feline immunodeficiency	hkdylklv
	3	Foot and Mouth Disease (O)	hkqkivapvk
	5	HIV Type 1	kefncgkegh
	7	HIV Type 2	kwncgkegh
	99	Small Pox Virus (Variola)	khymitwyk
	100	Small Pox Virus (Variola)	kysqtgkeliifh
	101	Small Pox Virus (Variola)	hyddvrikndivvsrek
	102	Small Pox Virus (Variola)	hrfdildski
	103	Small Pox Virus (Variola)	kerghnyyfe

Tumor Viruses:	48	Rous sarcoma virus tyrosine-protein kinase	kdrhek
	49	v-yes, avian sarcoma	kdrhdk
	50	c-yes, colon cancer, malignant melanoma	kdrhdk
	51	v-src, avian sarcoma	kdrhek
	52	c-src, colon, mammary, pancreatic cancer	kdrhek
	53	Neuroblastoma RAS viral (v-ras) oncogene	kqabelak
	54	VPI (major capsid protein) [Polyomavirus sp.]	khrfskh
	55	Sindbis	knhekik
	56	E1 [Human papillomavirus type 71]	khrptqk
	57	v-erbB from AEV and c-erb	kspnhvk
	58	v-fms (feline sarcoma)	knihlek
	59	c-fms (acute and chronic myelomonocytic tumors)	knihlek
	60	large t-antigen I [Polyomavirus sp.]	kphlaqlek
	61	middle t-antigen [Polyomavirus sp.]	kqhrlek
	62	small t-antigen [Polyomavirus sp.]	kqhrlek
	63	v-abl, murine acute leukemia	kvpvlspthk
	64	Human T-cell lymphotropic virus type 2	kalllevdkdsh
	65	c-kit, GI tumors, small cell lung carcinoma	kagitmvrkryh
	18	Hepatitis C	hyppkpgcivpak
Trans-Forming Proteins:	66	Transforming protein myb	Ksgkhgk
	67	Transforming protein myc, Burkitt lymphoma	kneqlkhk
	68	Ras-related GTP-binding protein	ksefvkvih
	69	Transforming protein ras (teratocarcinoma)	kklhvk
	70	TRAP-associated NF-kB activator TANK	kqkdhlsk
	71	RFP transforming protein	hkrvkdsk
	72	Transforming protein D (S.C.)	kygspkhrk
	73	Papilloma virus type 11, transforming protein	kklhlgkarfk
	74	Protein tyrosine kinase (EC 2.7.1.12)sk	kgdhvkhykirk
	75	Transforming protein (axl(-))	kckrdvmvdrhk
Cancer Cell Proteins:	76	Transforming protein (N-myc)	klqarqqllkckeh
	77	Fibroblast growth factor 4 (Kaposi sarcoma)	kkgnrsvptmkvth
	78	Matrix metalloproteinase 7 (uterine)	kcpilhrk
	79	Transcription factor 7-like	kklphlk
	80	Breast cancer antigen NY-BR-87	ktrhdplak
	81	BRCA-1-Associated Ring Domain Protein (breast)	khhpkdnlk
	82	'Autoantigen from a breast tumor'	khlrkkfrk
	83	Glioma Replikin (this study)	kagvafhkk
	84	Ovarian cancer antigen	khlrkkfrk
	85	EE L Leukemia	kckskdhkdk
	86	Proto-oncogene tyrosine-protein kinase C-ABL	hksckpalprk
	87	Adenomatosis polyposis coli	kckkpsrlkgdnek
	88	Gastric cancer transforming protein	kklkgnrsvptmkvth
	89	Transforming protein (K-RAS 2B),lung	khlkckmskdgkdkdkk

[0121] Identification of an amino acid sequence as a Replikin or as containing a Replikin, i.e., a homologue of the glioma peptide, kagvafhkk, requires that the three following requirements be met. According to the three point recognition system the sequences have three elements: (1) at least one lysine residue located six to ten residues from another lysine residue; (2) at least one histidine residue; and (3) a composition of at least 6% lysine within an amino acid sequence of 7 to about 50 residues.

[0122] Databases were searched using the National Library of Medicine keyword "PubMed" descriptor for protein sequences containing Replikin sequences. Over 4,000 protein sequences were visually examined for homologues. Sequences of all individual proteins within each group of PubMed-classified proteins were visually scanned for peptides meeting the three above-listed requirements. An infrequent occurrence of homologues was observed in "virus peptides" as a whole (1.5%) (N=953), and in other peptides not designated as associated with malignant transformation or replication such as "brain peptides" and "neuropeptides" (together 8.5%) (N=845). However, surprisingly, homologues were significantly more frequently identified in large "replicating proteins," which were identified as having an established function in replication in bacteria, algae, and viruses. Even more surprising was the finding that Replikin homologues occurred in 100% of "tumor viruses" (N=250), in 97% of "cancer proteins" (N=401), and in 85% of "transforming viruses" (N=248). These results suggest that there are shared properties of cancer pathogenesis regardless of cell type and suggest a role of viruses in carcinogenesis, i.e., conversion of cells from a transformed albeit dormant state to a more virulent actively replicating state.

[0123] Homologues of the following amino acid sequence, kagvafhhkk, as defined by the three point recognition method, were found in such viruses, or viral peptides, as, but not limited to, adenovirus, lentivirus, a-virus, retrovirus, andeno-associated virus, human immunodeficiency virus, hepatitis virus, influenza virus, maize streak virus, herpes virus, bovine herpes virus, feline immunodeficiency virus, foot and mouth disease virus, small pox virus, rous sarcoma virus, neuroblastoma RAS viral oncogene, polyomavirus, sindbis, human papilloma

virus, myelomonocytic tumor virus, murine acute leukemia, T-cell lymphotropic virus, and tomato leaf curl virus.

[0124] Replikins are present in such bacteria as, but not limited to, Acetobacter,
5 Achromobacter, Actinomyces, Aerobacter, Alcaligenes, Arthrobacter,
Azotobacter, Bacillus, Brevibacterium, Chainia, Clostridium, Corynebacterium,
Erwinia, Escheria, Lebsiella, Lactobacillus, Haemophilus, Flavobacterium,
Methylomonas, Micrococcus, Mycobacterium, Micronomspora, Mycoplasma,
Neisseria, Nocardia, Proteus, Pseudomonas, Rhizobium, Salmonella, Serratia,
10 Staphylococcus, Streptocossus, Streptomyces, Streptosporangium,
Streptovirticillium, Vibrio, peptide, and Xanthomas.

[0125] Replikins are present in such fungi as, but not limited to, Penicillium,
Diseula, Ophiostoma novo-ulim, Mycophycophta, Phytophthora infestans,
15 Absidia, Aspergillus, Candida, Cephalosporium, Fusarium, Hansenula, Mucor,
Paecilomyces, Pichia, Rhizopus, Torulopsis, Trichoderma, and Erysiphe.

[0126] Replikins are present in such yeast as, but not limited to, Saccharomyces,
Cryptococcus, including Cryptococcus neoformas, Schizosaccharomyces, and
20 Oryza.

[0127] Replikins are present in algae such as, but not limited to, Caldophera,
Isolepisprolifera, Chondrus, Gracilaria, Gelidium, Caulerpa, Laurencia,
Cladophexa, Sargassum, Penicillos, Halimeda, Laminaria, Fucus, Ascophyllum,
25 Undari, Rhodymenia, Macrocystis, Eucheuma, Ahnfeltia, and Pteroclasia.

[0128] Replikins are present in amoeba such as, but not limited to, *Entamoeba* (including *Entamoeba invadens*), *Amoebidae*, *Acanthamoeba* and *Naegleria*.

5 [0129] Replikins are present in plants such as, but not limited to, *Arabidopsis*, wheat, rice, and maize.

AUXILIARY SPECIFICATIONS

10 [0130] To permit classification of subtypes of Replikins, additional or "auxiliary specifications" to the basic "3-point-recognition" requirements may be added: (a) on a structural basis, such as the common occurrence of adjacent di- and polylysines in cancer cell proteins (e.g., transforming protein P21B(K-RAS 2B), lung, Table 2, SEQ ID NO.: 89), and other adjacent di-amino acids in TOLL-like
15 receptors, or b) on a functional basis, such as exhibiting ATPase, tyrosine kinase or redox activity as seen in Table 2.

FUNCTIONAL DERIVATIVES

[0131] "Functional derivatives" of the Replikins as described herein are
20 fragments, variants, analogs, or chemical derivatives of the Replikins, which retain at least a portion of the immunological cross reactivity with an antibody specific for the Replikin. A fragment of the Replikin peptide refers to any subset of the molecule. Variant peptides may be made by direct chemical synthesis, for example, using methods well known in the art. An analog of a Replikin to a non-
25 natural protein substantially similar to either the entire protein or a fragment

thereof. Chemical derivatives of a Replikin contain additional chemical moieties not normally a part of the peptide or peptide fragment.

[0132] As seen in Figure 2, during anaerobic respiration when the rate of cell replication is increased, malignin is enriched. That is, malignin is found to increase not simply in proportion to the increase in cell number and total membrane proteins, but is enriched as much as ten-fold in concentration, starting with 3% at rest and reaching 30% of total membrane protein. This clear demonstration of a marked increase in Replikin concentration with glioma cell replication points to, and is consistent with, the presence of Replikins identified with the 3-point recognition method in various organisms. For example, Replikins were identified in such proteins as "Saccharomyces cerevisiae replication binding protein" (SEQ ID NO.: 2) (hsikrelgiifdk); the "replication associated protein A of maize streak virus" (SEQ ID NO.: 8) (kyivcareahk) and (SEQ ID NO.: 9) (kekkpskdeimrdiish); the "replication-associated protein of Staphylococcus aureus" (SEQ ID NO.: 10) (kkekttlmk); the "DNA replication protein of bovine herpes virus 4" (SEQ ID NO.: 11) (hkinitngqk); and the "Mealigrad herpes virus 1 replication binding protein" (SEQ ID NO.: 12) (hkdlyrllmk). Previous studies of tomato leaf curl gemini virus show that the regulation of virus accumulation appears to involve binding of amino acids 1-160 of the "replicating protein" of that virus to leaf DNA and to other replication protein molecules during virus replication. Analysis of this sequence showed that amino acids 1-163 of this "replicating protein" contain five Replikins, namely: (SEQ ID NO.: 13) kfrinaknyfltyph, (SEQ ID NO.: 14) knletpvnlfricrefh, (SEQ ID NO.: 15)

hpniqaaksstdvk, (SEQ ID NO.: 16) ksstdvkaymdkdgdvldh, and (SEQ ID NO.:
17) kasalnirekapkdfvlqfh.

[0133] Table 2 shows that Replikin-containing proteins also are associated
5 frequently with redox functions, and protein synthesis or elongation, as well as
with cell replication. The association with metal-based redox functions, the
enrichment of the Replikin-containing glioma malignin concentration during
anaerobic replication, and the cytotoxicity of antimalignin at low concentrations
(picograms/cell) (Figure 4c-f), all suggest that the Replikins are related to central
10 respiratory survival functions, have been found less often subjected to the
mutations characteristic of non-Replikin amino acids.

[0134] Of particular interest, it was observed that at least one Replikin per
100 amino acids was found to be present in the hemagglutinin proteins of almost
15 all of the individual strains of influenza viruses examined. The Replikin
sequences that were observed to occur in the hemagglutinin proteins of isolates of
each of the four prevalent strains of influenza virus, influenza B, H1N1, H2N2,
and H3N2, for each year that amino acid sequence data are available (1902-2001),
are shown in Tables 3, 4, 5 and 6, below.

Table 3

Replikin Sequences present in hemagglutinins of Influenza B viruses in each year for which amino acid sequences were available (1902-2001).

<i>Influenza B Replikins</i>		<i>Year Detected in Influenza B strain</i>	
(Peak in Figure 7:		EB1	EB2
kshfanlk (SEQ ID NO. 104)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
kshfanlkgtk (SEQ ID NO. 105)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
kshfanlkgtktrgkclpk (SEQ ID NO. 106)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hekygglnk (SEQ ID NO. 107)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hekygglnksk (SEQ ID NO. 108)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hekygglnkskpyygehak (SEQ ID NO. 109)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hakaigncpiwvk (SEQ ID NO. 110)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hakaigncpiwvktplkiangtk (SEQ ID NO. 111)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hakaigncpiwvktplkiangtkyrppak (SEQ ID NO. 112)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hakaigncpiwvktplkiangtkyrppakllk (SEQ ID NO. 113)		1902,19,24,38,40,43,51,59,75,76,77,89,90,93,97,98,99,00,01	
hfanlkgtktrgk (SEQ ID NO. 114)		1919,	76, 89,90, 99,00,01
hfanlkgtktrgkclpk (SEQ ID NO. 115)		1919,	76, 90 00,01
hsdneiqmrvklygdsk (SEQ ID NO. 116)		1919	
hsdneiqdkmrvklygdskpqk (SEQ ID NO. 117)		1919	
hsdneiqmrvklygdskpqk (SEQ ID NO. 118)		1919, 24,	97,98, 00
k(a/v)silhevk (SEQ ID NO. 119)		1919, 40, 59,	90,93
kctgtipsakasilh (SEQ ID NO. 120)		1919,	00
kctgtipsakasilhevk (SEQ ID NO. 121)		1919,	93

kygglnkskpyytgeh (SEQ ID NO. 122)	1919					
kywcasgrskvikgspligeadclh (SEQ ID NO. 123)	1919,	38,40,43,	59,75,76, <u>77</u> ,89,90,	98,99,00		
kpyytgehak (SEQ ID NO. 124)	1919,	38,40,	59,	89,90,93,97,98,	01	
kcimgtipsakasilhevk (SEQ ID NO. 125)	1924,	43,	75,76, <u>77</u> ,	93		
hnvinaekapggpyk (SEQ ID NO. 126)	1938,			93,97,	00	
hsdnetqmaklygds (SEQ ID NO. 127)	1938,			93,97,	00	
hgvavaadlkstqeaink (SEQ ID NO. 128)	1940,	59,	00			
hgvavaadlkstqeainkdtistqeaink (SEQ ID NO. 129)	1940					
klygdskpqkftssangvith (SEQ ID NO. 130)	1943,	75,76, <u>77</u> ,	93,97,	00		
hsdnetqmaklygdskpqk (SEQ ID NO. 131)	1943,	75,76, <u>77</u> ,	93			
hfanlkgqtgrgk (SEQ ID NO. 132)	1959					
kpysalkokgfh (SEQ ID NO. 133)	1988					
kskpyytgehakai(g/a)ncpiwvk (SEQ ID NO. 134)	2000					

1. Influenza B has not been responsible for any human pandemic (global distribution).
2. Abbreviation for years: eg. "19" = 1919, "01" = 2001.
3. The first year that a given Replikin appears is indicated at the beginning of the series of years in which that Replikin has been found.
4. Overlapping Replikin sequences are listed separately.
5. Increase in number of new Replikin structures occurs in years of epidemics (underlined): eg. 1951 and 1977 and correlates with increased total Replikin concentration (number of Replikins per 100 amino acid residues). See Figure 7.

Table 4

H1N1 Replicon Sequences present in H1N1 hemagglutinins of Influenza viruses in each year for which amino acid sequences were available (1918-2000)

H1N1 Replicon Year Detected in Influenza

H1N1 Strain

Peak in Figure 7: P1 E1 E1.1, 1.2, 1.3 E1.4)

	1918, 25, 28, 30, 31, 35, 47, 48, 51, 52, 55, 56, 57, 59, 63, 77, 79, 80, 81, 85, 87, 88, 89, 91, 92, 95, 96, 97, 98, 99, 00				
hp(v/i)tiqecpkyy(r/k)(s/t)(t/a)k (SEQ ID NO. 135)	1918, 25, 28, 30, 31, 35, 47, 48, 51, 52, 55, 56, 57, 59, 63, 77, 79, 80, 81, 85, 87, 88, 89, 91, 92, 95, 96, 97, 98, 99, 00				
hdsnvknly(e/g)kv(k/r)(n/s)ql(k/r)nnak (SEQ ID NO. 136)	1918, 28, 30, 31,	77, 79, 80,	88, 91, 95, 98		
hdsnvknly(e/g)kv(k/r)(n/s)qlk (SEQ ID NO. 137)	1918, 28, 30, 31,	77, 79, 80,	88, 91, 95, 98		
hkc(nn/dd)(a/t/e)cmesv(n/k)ngtydypkyseesklne(e/k)idgvk (SEQ ID NO. 138)	1918, 30, 35,	77, 80,			98
hkc(nn/dd)(a/t/e)cmesv(n/k)ngtydypkyseesk (SEQ ID NO. 139)	1918, 30, 35,	77, 80,			98
hqn(e/g)qgsqyaadqkstqnai(d/n)gimkvnsiekmtqfavgkefnklek (SEQ ID NO. 140)	1918, 28, 30, 31, 35,	59, 79,		95	
hqn(e/g)qgsqyaadqkstqnai(d/n)gimkvnsiek (SEQ ID NO. 141)	1918, 28, 30, 31, 35,	59, 79,		95	
hqn(e/g)qgsqyaadqkstqnai(d/n)gimk (SEQ ID NO. 142)	1918, 28, 30, 31, 35,	59, 79,		95	
kfeifpksawpnh (SEQ ID NO. 143)	1918,	77			
kg(n/s/t)sypkl(n/s)ksy(v/t)nnkgkevlvlwgvh (SEQ ID NO. 144)	1918, 35,	77,			96
ksy(v/t)nnkgkevlvlwgvh (SEQ ID NO. 145)	1918, 35,	77,			96
hkcnnecmesvknngtydypkyseesklneklidgvk (SEQ ID NO. 146)	1928, 31,			95	
hkcnnecmesvknngtydypkyseesk (SEQ ID NO. 147)	1928, 31,			95	
hkcnnecmesvknngtydypk (SEQ ID NO. 148)	1928, 31,			95	
hkcnnecmesvk (SEQ ID NO. 149)	1928, 31,			95	
hngkssfy(k/r)nilwlt(e/g)knglypnlsksyvnnek (SEQ ID NO. 150)	1928,			95,	00
hngkssfy(k/r)nilwlt(e/g)knglypnlsksyvnnk (SEQ ID NO. 151)	1928, 31,			95,	00
hngkssfy(k/r)nilwlt(e/g)knglypnlsk (SEQ ID NO. 152)	1928, 31,			95,	00

hngkssfy(k/r)nlilwit(e/g)k (SEQ ID NO. 153)

1928, 31,

95, 00

kssfyknllwiteknglypnlsksyvnkekevlwgvh (SEQ ID NO. 154)

1928, 31,

95

knllwiteknglypnlsksyvnkekevlwgvh (SEQ ID NO. 155)

1928, 31,

95

knglypnlsksyvnkekevlwgvh (SEQ ID NO. 156)

1928, 31,

95, 96, 00

kssy(w/a)nnkekev(l/-)(w/-)lwgvh (SEQ ID NO. 157)

1928, 31, 51,

95, 96, 98, 00

kesswpnhvtvk (SEQ ID NO. 158)

1928, 31,

95

het(t/n)kgvtaacpyagassfymllwlvkkensypklksyvnk (SEQ ID NO. 159)

1930, 35

het(t/n)kgvtaacpyagassfymllwlvkkensypklks (SEQ ID NO. 160)

1930, 35

kfeifpktsswpnevvlwgvh (SEQ ID NO. 161)

1930

kerswpkh (SEQ ID NO. 162)

1947, 51, 52, 55, 56, 72, 82

klksyvnkekevlwgvh (SEQ ID NO. 163)

1947, 51

28

knnkekevlwgvh (SEQ ID NO. 164)

1947

h(k/n)(g/q)kssfy(r/k)nlilwitekng(l/s)yp(n/t)lsksyannkek (SEQ ID NO. 165)

1948 72, 89, 96

h(k/n)(g/q)kssfy(r/k)nlilwitek (SEQ ID NO. 166)

1948 72, 89, 96

hakksfyk (SEQ ID NO. 167)

1951, 57, 59

hngklcrkkgk (SEQ ID NO. 168)

1951, 52, 55, 56, 57, 59, 72,

hyklmn(q/g)kk (SEQ ID NO. 169)

1956, 00

hdiyrdeainnrfaqgvklqgyk (SEQ ID NO. 170)

1956

kgngcfeifuk (SEQ ID NO. 171)

1956

klrliekndkyhqiek (SEQ ID NO. 172)

1956

klrliekndkyh (SEQ ID NO. 173)

1956

kehndkgsstik (SEQ ID NO. 174)

1956

kinngdyaklyiwgvh (SEQ ID NO. 175)

1956

hngklcrkgiapklqgk (SEQ ID NO. 176)

1959, 82

hetnrqvtacpyagansffmliwlvkkessypkisk (SEQ ID NO. 177)

hetnrqvtacpyagansffmliwlvkkessypk (SEQ ID NO. 178)

hptstdqqslyqnadayifvgsskynrkdk (SEQ ID NO. 179)

hptstdqqslyqnadayifvgsskynrkdkpela (SEQ ID NO. 180)

hdiyrdeainnrfaqgkvkitqgyk (SEQ ID NO. 181)

hqneqsggyaadqkstknaidgitmkvnsviekmntqftavgk (SEQ ID NO. 182)

hqneqsggyaadqkstknaidgitmkvnsviek (SEQ ID NO. 183)

hqneqsggyaadqkstknaidgitmkvnsviekmntqftavgkefnkdek (SEQ ID NO. 184)

hngklcrkigiaplqigk (SEQ ID NO. 185)

hkennetmesvk (SEQ ID NO. 186)

kfeifpkasswpnh (SEQ ID NO. 187)

hdsnvlmlyekvrsqhmna (SEQ ID NO. 188)

kvnsvikkmntqfaavgkefnh (SEQ ID NO. 189)

khngkick (SEQ ID NO. 190)

kkgtisypklksytnkgkevvlwgvh (SEQ ID NO. 191)

kgtsypklksytnkgkevvlwgvh (SEQ ID NO. 192)

klsksytnkgkevvlwgvh (SEQ ID NO. 193)

ksytnkgkevvlwgvh (SEQ ID NO. 194)

kgvtasoshk (SEQ ID NO. 195)

kgvtasoshkgrssfymlwiteknglypnisk (SEQ ID NO. 196)

kgnsypklksyvnakekevvlwgih (SEQ ID NO. 197)

kefnhlek (SEQ ID NO. 198)

hptstdqqslyqnadayvfvvgsskynkkdkpeistrpk (SEQ ID NO. 199)

hptstdqqslyqnadayvfvvgsskynkkdk (SEQ ID NO. 200)

1963, 81

1963, 81

1963, 81

1963, 81

1977, 91

1977

1977

1979, 91

1979

1979

1981

1981

1981

1981

1981

1981

1981

1981

1985, 87

1985, 87

1988

1988

1988

1988

hegkssfymliwitekagssypklknsyvk (SEQ ID NO. 201)	1991	
hegkssfymliwitekagssypk (SEQ ID NO. 202)	1991	
hkodnecmesvrmgtidydkyseesk (SEQ ID NO. 203)	1991	
kesswpnhtvik (SEQ ID NO. 204)	1991,92	
knllwiteknglypnlsksyvnnkekeivlwgvh (SEQ ID NO. 205)	1991,92, <u>96</u>	
hngkssfy(k/m)(n/-)llwt(e/g)(-/k)knglypnlsk (SEQ ID NO. 206)	1991,92, <u>96</u>	00
hngkssfyknllwitek (SEQ ID NO. 207)	1991,92, <u>96</u>	
htvtkgvtascshngkssfyknllwiteknglypnlsksyvnnkekeivlwgvh (SEQ ID NO. 208)	1995	
hlvt(k/g)gv(t/s)ascshngkssfy(k/m)(n/-)llwt(e/g)k(-n/k)glypnlsk (SEQ ID NO. 209)	1995,	00
htvtkgvtascshngkssfyknllwitek (SEQ ID NO. 210)	1995	
kyvrstklrmvgtlrmipsiqsrglfgalagfieggtgnidgwygva (SEQ ID NO. 211)	1995	
hqneqsggyaadqkstqnaingitnkvnsilekmtqfavgk (SEQ ID NO. 212)	1995	
hqneqsggyaadqkstqnaingitnkvnsilek (SEQ ID NO. 213)	1995	
hqneqsggyaadqkstqnaingitnkvnsilek (SEQ ID NO. 214)	1995	
hsgarsfymliwivkkgsypk (SEQ ID NO. 215)	<u>1996</u>	
hsgarsfymliwivkkgsypklk (SEQ ID NO. 216)	<u>1996</u>	
hsgarsfymliwivkkgsypklksytndk (SEQ ID NO. 217)	<u>1996</u>	
hsgarsfymliwivkkgsypklksytndkgk (SEQ ID NO. 218)	<u>1996</u>	
htvskgvtscshngk (SEQ ID NO. 219)	<u>1996</u>	
katswpnhtvik (SEQ ID NO. 220)	<u>1996</u>	
kqvtscshngk (SEQ ID NO. 221)	<u>1996</u>	
kgnsypklksytndkgkeivlwgvh (SEQ ID NO. 222)	<u>1996</u>	
klksytndkgkeivlwgvh (SEQ ID NO. 223)	<u>1996</u>	
ksytndkgkeivlwgvh (SEQ ID NO. 224)	<u>1996</u>	

hngkssfymllwlt(e/q)knglypnlsksy(v/a)annkek (SEQ ID NO. 225)	1997,98,99
hpitigecpkyrsak (SEQ ID NO. 226)	1997
hneqsgsgyaadqkstqnaingitnkvnsviekmntqftavgk (SEQ ID NO. 227)	1998
hneqsgsgyaadqkstqnaingitnkvnsviek (SEQ ID NO. 228)	1998
hngkssfymllwltknglypnlsksyvnnkek (SEQ ID NO. 229)	1998

-
1. Influenza H1N1 was responsible for the human pandemic (global distribution) of 1918.
 2. Abbreviation for years: eg. "96" = 1996.
 3. The first year that a given Replikin appears is indicated at the beginning of the series of years in which that Replikin has been found in this work.
 4. Overlapping Replikin sequences are listed separately.
 5. *Increase in number of new Replikin structures occurs in years of epidemics (underlined): eg. 1918 and 1977 and correlates with increased total Replikin concentration (number of Replikins per 100 amino acid residues). See Figure 7.*

Table 5

Repikin Sequences present in hemagglutinins of Influenza H2N2 viruses in years 1957-2000

Influenza H2N2 Repikins Year Detected in Influenza H2N2 strain

(Peak in Figure 8: P2 E2)

khfekvkilpk (SEQ ID NO. 230)	1957,58,59,60,61,64,65,68,	78,83,84,91
khlssvkhfekvk (SEQ ID NO. 231)	1957,58,59,60,61,	83,84,91
ha(k/q/m)(d/n)ilekthngk (SEQ ID NO. 232)	1957,58,59,60,61,64,65,68,	78,83,84,91, 95
ha(k/q/m)(d/n)ilekthngk(c(k/r) (SEQ ID NO. 233)	1957,58,59,60,61,64,65,68,	78,83,84,91, 95
hnvhlptigeckpyvksek (SEQ ID NO. 234)	1957,58,59, 65,68	
hptigeckpyvksek (SEQ ID NO. 235)	1957,58,59, 65,68,64,65,68,78,83,84,91	
khlssvkhfekvkilpk (SEQ ID NO. 236)	1957,58,59,60,61,64,65,68,	78
krqssgimktegtlencetkqtpigaintlph (SEQ ID NO. 237)	1957, 59,	83
kgsnyp(v/i)ak(g/r)syntsgemliiwq(w/i)h (SEQ ID NO. 238)	1957,58,59, 61,	83, 91, 95
htlgqsracavsgnpsffnmvwltekgsnypvak (SEQ ID NO. 239)	1957	
khfekvk (SEQ ID NO. 240)	1957, 59, 65	
kiskrgssgimktegtlencetkqtpigaintlph (SEQ ID NO. 241)	1957, 59, 65,	91
krqssgimktegtlencetkqtpigaintlph (SEQ ID NO. 242)	1957, 59, 65,	91
ktegtlencetkqtpigaintlph (SEQ ID NO. 243)	1957, 59, 65,	91
kiskrgssgimktegtlencetkqtpigaintlph (SEQ ID NO. 244)	1957, 59, 65,	91
ktegtlencetkqtpigaintlph(w/i)h (SEQ ID NO. 245)	1957, 59, 65,	91
kiskrgssgimktegtlencetkqtpigaintlph (SEQ ID NO. 246)	1957, 59, 65,	91

	k(e/g)snypvakgsynntsgemliiwgvh (SEQ ID NO. 247)	1957,	60,	65
	hpltigecpkyvksek (SEQ ID NO. 248)	1957,	60,	65
	keqtplgaikttdph (SEQ ID NO. 249)	1957,		65
	hhsndqsgyaadkestqka(f/i)dgimkvnsiek-			
	-mntqfeavgklf(n/s)nlekeninkk (SEQ ID NO. 250)	1961,	65,68,	83,84
	hsndqsgyaadkestqka(f/i)dgimkvnsiek-			
	-mntqfeavgklf(n/s)nlekeninkk (SEQ ID NO. 251)	1961,	65,68,	83,84
	hsndqsgyaadkestqka(f/i)dgimkvnsiek (SEQ ID NO. 252)	1961,	65,68,	83,84
	hdsnvmlydkvrmqirdnak (SEQ ID NO. 253)	1964,	68,76,	84,91
	hkoddecmsvknngtydypklnmeikgvk (SEQ ID NO. 254)	1964,65,68,76,		83,84,91
2	hkoddecmsvknngtydypklnmek (SEQ ID NO. 255)	1964,65,68,76,		83,84,91
	hkoddecmsvknngtydypk (SEQ ID NO. 256)	1964,65,68,76,		83,84,91
	hkoddecmsvkn (SEQ ID NO. 257)	1964,65,68,76,		83,84,91
	kgsnypvakgsynntsgemliiwgvh (SEQ ID NO. 258)		1976,78	
	hsndqsgyaadkestqkavdgimkvnsiekmntqfeavgk (SEQ ID NO. 259)		1976,	91
	krsgsglntegtlenceelkeqtplgainttdph (SEQ ID NO. 260)		1976,78,	83,84
	hpltigecpkyvksek (SEQ ID NO. 261)		1976	
	hakdilekthngklek (SEQ ID NO. 262)		1976	

1. Influenza H2N2 was responsible for the human pandemic (global distribution) of 1957.

2. Abbreviation for years: eg. "58" =1958.

3. The first year that a given Replikin appears is indicated at the beginning of the series of years in which that Replikin has been found in this work.
4. Overlapping Replikin sequences are listed separately.
5. Increase in number of new Replikin structures occurs in years of epidemics (underlined): eg. 1957 and 1965 and correlates with increased total Replikin concentration (number of Replikins per 100 amino acid residues). See Figure 8.

Table 6

H3N2 Replikin Sequences present in H3N2 hemagglutinins of Influenza viruses in each year for which amino acid sequences were available (1968-2000)

Influenza H3N2 Replikins Year Detected in Influenza H3N2 strain Influenza Replikins
(Peak in Figure 8: P3 E3

E4)

hdvyrdealnrfqikgvelksgyk (SEQ ID NO. 263)	<u>1968,72,</u>	<u>75</u>		96,97,98
htidldsemnklfertrk (SEQ ID NO. 264)	<u>1968</u>			
kfhqiek (SEQ ID NO. 265)	<u>1968,72,</u>	<u>75,</u>	<u>77</u>	96,97,98
ktmekfh(g/q)iek (SEQ ID NO. 266)	<u>1968</u>		86	98
klmr(v/l)iektmekfh (SEQ ID NO. 267)	<u>1968,72,</u>	<u>75,</u>	<u>77</u>	97,98
hgiekefsevegriqdlekyyvedtk (SEQ ID NO. 268)	<u>1968,72,</u>			98
kicmnpkh (SEQ ID NO. 269)		<u>1975</u>		
klrvikkmekfh (SEQ ID NO. 270)		<u>1975</u>		
hd(l,v)yrdealnrfqik(g/q)ve(r/k)s(q/g)yk (SEQ ID NO. 271)		<u>1975,76,77,</u>	86	
hgiekefsevegriqdlekyyvedtk (SEQ ID NO. 272)		<u>1975</u>		
kyvedtkidlwsynaellvalenqh (SEQ ID NO. 273)		<u>1975</u>		
kyvkqnsllkatgmrvpektgrlgaiagfiengwegmidgwygfrh (SEQ ID NO. 274)		<u>1975</u>		
kefsevegriqdlekyyvedtkidlwsynaellvalenqh (SEQ ID NO. 275)		<u>1975</u>		2000
hqn(s/e)(e/q)g(t/s)g(q/y)aad(l/q)k-				
-stq(a/n)a(i/l)d(q/g)l(n/t)(g/n)k(l/v)n(r/s)vi(e/c)k (SEQ ID NO. 276)		<u>1975</u>		2000
hcd(g/q)f(q,r)nekwldf(v/i)er(s/t)k (SEQ ID NO. 277)		<u>1975,76,77,78,80,81,82,83,84,85,86,88,89,90,91,92,93,94,95,96,97,98</u>		

htidldsemnkkkfertrk (SEQ ID NO. 278)	<u>1977</u>		
ksgstypvlkvtnpndnfdklyiwgvh (SEQ ID NO. 279)	<u>1977</u>		
klrwltksgntypvlhvtmnpndnfdklviwgvh (SEQ ID NO. 280)		1982	
htidldsemnkkfetrk (SEQ ID NO. 281)			1986
klrlietknekfnqtek (SEQ ID NO. 282)			<u>1987</u>
htgkssvmrsdapidfensecitpnqspndkpfqnvnkitygacpk (SEQ ID NO. 283)			1994
htgkssvmrsdapidfensecitpnqspndkpfqnvnk (SEQ ID NO. 284)			1994
hpsdtdsqtslyvrasgrvtstkrsgqtviplk (SEQ ID NO. 285)			1994
kyvedtkidlwsynaelvalenqh (SEQ ID NO. 286)			1997,98
kifertrkqlrenaedmgngcfkiyh (SEQ ID NO. 287)			1998
2 krrsiksffsrlnwlh (SEQ ID NO. 288)			1998
hptdigecpky(v/r)kstk (SEQ ID NO. 289)			<u>2000</u>
kgnsypklslksklyiinkkkeviviwgih (SEQ ID NO. 290)			<u>2000</u>
klslslks(v/y)iinkkkeviviwgih (SEQ ID NO. 291)			<u>2000</u>
klslks(v/y)iinkkkeviviwgih (SEQ ID NO. 292)			<u>2000</u>

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1. Influenza H3N2 was responsible for the human pandemic (global distribution) of 1968.
 2. Abbreviation for years: eg. "77" =1977.
 3. The first year that a given Replikin appears is indicated at the beginning of the series of years in which that Replikin has been found.
 4. Overlapping Replikin sequences are listed separately.
 5. Increase in number of new Replikin structures occurs in years of epidemics (underlined) : eg. 1975 and correlates with increased total Replikin concentration (number of Replikins per 100 amino acid residues). See Figure 8.

[0135] Both the concentration and type, i.e., composition of Replikins observed, were found to relate to the occurrence of influenza pandemics and epidemics. The concentration of Replikins in influenza viruses was examined by visually scanning the hemagglutinin amino acid sequences published in the National Library of Medicine "PubMed" data base for influenza strains isolated world wide from human and animal reservoirs year by year over the past century, i.e., 1900 to 2001. These Replikin concentrations (number of Replikins per 100 amino acids, mean $\pm$ SD) were then plotted for each strain.

[0136] The concentration of Replikins was found to directly relate to the occurrence of influenza pandemics and epidemics. The concentration of Replikins found in influenza B hemagglutinin and influenza A strain, H1N1, is shown in Figure 7, and the concentration of Replikins found in the two other common influenza virus A strains, H2N2 and H3N2 is shown in Figure 8 (H2N2, H3N2). The data in Figure 8 also demonstrate an emerging new strain of influenza virus as defined by its constituent Replikins (H3N2(R)).

[0137] Each influenza A strain has been responsible for one pandemic: in 1918, 1957, and 1968, respectively. The data in Figures 7 and 8 show that at least one Replikin per 100 amino acids is present in each of the influenza hemagglutinin proteins of all isolates of the four common influenza viruses examined, suggesting a function for Replikins in the maintenance of survival levels of replication. In the 1990s, during the decline of the H3N2 strain, there were no Replikins in many isolates of H3N2, but a high concentration of new Replikins appeared in H3N2 isolates, which define the emergence of the H3N2(R) strain.

[0138] Several properties of Replikin concentration are seen in Figure 7 and Figure 8 to be common to all four influenza virus strains. First, the concentration is cyclic over the years, with a single cycle of rise and fall occurring over a period of two to thirty years. This rise and fall is consistent with the known waxing and waning of individual influenza virus strain predominance by hemagglutinin and neuraminidase classification. Second, peak Replikin concentrations of each influenza virus strain previously shown to be responsible for a pandemic were observed to relate specifically and individually to each of the three years of the pandemics. For example, for the pandemic of 1918, where the influenza virus strain, H1N1, was shown to be responsible, a peak concentration of the Replikins in H1N1 independently occurred (P1); for the pandemic of 1957, where H2N2 emerged and was shown to be responsible, a peak concentration of the Replikins in H2N2 occurred (P2); and for the pandemic of 1968, where H3N2 emerged and was shown to be the cause of the pandemic, a peak concentration of the Replikins in H3N2 occurred (P3). Third, in the years immediately following each of the above three pandemics, the specific Replikin concentration decreased markedly, perhaps reflecting the broadly distributed immunity generated in each case. Thus, this post-pandemic decline is specific for H1N1 immediately following the pandemic (P1) for which it was responsible, and is not a general property of all strains at the time. An increase of Replikin concentration in influenza B repeatedly occurred simultaneously with the decrease in Replikin concentration in H1N1, e.g., EB1 in 1951 and EB2 in 1976, both associated with influenza B epidemics having the highest mortality. (Stuart-Harris, et al., Edward Arnold Ltd. (1985). Fourth, a secondary peak concentration, which exceeded the primary peak

increase in concentration, occurred 15 years after each of the three pandemics, and this secondary peak was accompanied by an epidemic: 15 years after the 1918 pandemic in an H1N1 'epidemic' year (E1); eight years after the 1957 pandemic in an H2N2 'epidemic' year (E2); and occurred seven years after the 1968 pandemic in an H3N2 'epidemic' year (E3). These secondary peak concentrations of specific Replikins may reflect recovery of the strain. Fifth, peaks of each strain's specific Replikin concentration frequently appear to be associated with declines in Replikin concentration of one or both other strains, suggesting competition between strains for host sites. Sixth, there is an apparent overall tendency for the Replikin concentration of each strain to decline over a period of 35 years (H2N2) to 60 years (influenza B). This decline cannot be ascribed to the influence of vaccines because it was evident in the case of influenza B from 1901 to 1964, prior to common use of influenza vaccines. In the case of influenza B, Replikin recovery from the decline is seen to occur after 1965, but Replikin concentration declined again between 1997 and 2000 (Figure 7). This correlates with the low occurrence of influenza B in recent case isolates. H1N1 Replikin concentration peaked in 1978-1979 (Figure 7) together with the reappearance and prevalence of the H1N1 strain, and then peaked in 1996 coincident with an H1N1 epidemic. (Figure 7). H1N1 Replikin concentration also declined between 1997 and 2000, and the presence of H1N1 strains decreased in isolates obtained during these years. For H2N2 Replikins, recovery from a 35 year decline has not occurred (Figure 8), and this correlates with the absence of H2N2 from recent isolates. For H3N2, the Replikin concentration of many isolates fell to zero during the period from 1996 to 2000, but other H3N2 isolates showed a significant, sharp increase in

Replikin concentration. This indicates the emergence of a substrain of H3N2, which is designated herein as H3N2(R).

[0139] Figures 7 and 8 demonstrate that frequently, a one to three year
5 stepwise increase is observed before Replikin concentration reaches a peak. This
stepwise increase proceeds the occurrence of an epidemic, which occurs
concurrently with the Replikin peak. Thus, the stepwise increase in concentration
of a particular strain is a signal that particular strain is the most likely candidate to
cause an epidemic or pandemic.

10 [0140] Currently, Replikin concentration in the H3N2(R) strain of influenza
virus is increasing (Figure 8, 1997 to 2000). Three similar previous peak increases
in H3N2 Replikin concentration are seen to have occurred in the H3N2-based
pandemic of 1968 (Figure 8), when the strain first emerged; and in the H3N2-
15 based epidemics of 1972 and 1975 (Figure 8). Each of these pandemic and
epidemics was associated with excess mortality. (Ailing, et al., Am J.
Epidemiol., 113(1):30-43 (1981). The rapid ascent in concentration of the
H3N2(R) subspecies of the H3N2 Replikins in 1997-2000, therefore, statistically
represents an early warning of an approaching severe epidemic or pandemic. An
20 H3N2 epidemic occurred in Russia in 2000 (Figure 8, E4); and the CDC report of
December 2001 states that currently, H3N2 is the most frequently isolated strain of
influenza virus world wide. (Morbidity and Mortality Weekly Reports (MMWR),
Center for Disease Control; 50(48):1084-68 (Dec.7, 2001).

25 [0141] In each case of influenza virus pandemic or epidemic new Replikins

emerge. There has been no observation of two of the same Replikins in a given hemagglutinin in a given isolate. To what degree the emergence of a new Replikin represents mutations versus transfer from another animal or avian pool is unknown. In some cases, each year one or more of the original Replikin structures is conserved, while at the same time, new Replikins emerge. For example, in influenza virus B hemagglutinin, five Replikins were constantly conserved between 1919 and 2001, whereas 26 Replikins came and went during the same period (some recurred after several years absence). The disappearance and re-emergence years later of a particular Replikin structure suggests that the Replikins return from another virus host pool rather than through de novo mutation.

[0142] In the case of H1N1 Replikins, the two Replikins present in the P1 peak associated with the 1918 pandemic were not present in the recovery B1 peak of 1933, which contains 12 new Replikins. Constantly conserved Replikins, therefore, are the best choice for vaccines, either alone or in combination. However, even recently appearing Replikins accompanying one year's increase in concentration frequently persist and increase further for an additional one or more years, culminating in a concentration peak and an epidemic, thus providing both an early warning and time to vaccinate with synthetic Replikins (see for example, H1N1 in the early 1990's, Figure 7).

[0143] The data in FIGURES 7 and 8 demonstrate a direct relationship between the presence and concentration of a particular Replikin in influenza protein sequences and the occurrence of pandemics and epidemics of influenza. Thus, analysis of the influenza virus hemagglutinin protein sequence for the

presence and concentration of Replikins provides a predictor of influenza pandemics and/or epidemics, as well as a target for influenza vaccine formulation.

[0144] Composition of Replikins in Strains of Influenza Virus B: Of a total of 26 Replikins identified in this strain (Table 3), the following ten Replikins are present in every influenza B isolate examined from 1902-2001. Overlapping Replikin sequences are listed separately. Lysines and histidines are in bold type to demonstrate homology consistent with the "3-point recognition."

kshfanlk (SEQ ID NO. 104)

kshfanlkgtk (SEQ ID NO. 105)

kshfanlkgtktrgkdpk (SEQ ID NO. 106)

hekygglnk (SEQ ID NO. 107)

hekygglnksk (SEQ ID NO. 108)

hekygglnkskpyytgehak (SEQ ID NO. 109)

hakaigncpiwvk (SEQ ID NO. 110)

hakaigncpiwvkvktpklkangtk (SEQ ID NO. 111)

hakaigncpiwkvktpklkangtkyrppak (SEQ ID NO. 112)

hakaigncpiwkvktpklkangtkyrppakllk (SEQ ID NO. 113)

[0145] Tables 3 and 4 indicate that there appears to be much greater stability of the Replikin structures in influenza B hemagglutinins compared with H1N1 Replikins. Influenza B has not been responsible for any pandemic, and it appears not to have an animal or avian reservoirs. (Stuart-Harris et al., Edward Arnold Ltd., London (1985)).

[0146] Influenza H1N1 Replikins: Only one Replikin

"hp(v/i)tigecpkyv(r/k)(s/t)(t/a)k" is present in every H1N1 isolate for which sequences are available from 1918, when the strain first appeared and caused the pandemic of that year, through 2000. (Table 4). ("(v/i)" indicates that the amino acid v or i is present in the same position in different years.) Although H1N1 contains only one persistent Replikin, H1N1 appears to be more prolific than influenza B. There are 95 different Replikin structures in 82 years on H1N1 versus only 31 different Replikins in 100 years of influenza B isolates (Table 4). An increase in the number of new Replikin structures occurs in years of epidemics (Tables 3, 4, 5 and 6) and correlates with increased total Replikin concentration (Figures 7 and 8).

[0147] Influenza H2N2 Replikins: Influenza H2N2 was responsible for the human pandemic of 1957. Three of the 20 Replikins identified in that strain for 1957 were conserved in each of the H2N2 isolates available for examination on PubMed until 1995 (Table 5).

ha(k/q/m)(d/n)ilekthngk (SEQ ID NO. 232)

ha(k/q/m)(d/n)ilekthngklc(k/r) (SEQ ID NO. 233)

kgsnyp(v/i)ak(g/r)synntsgeqmliiwq(v/i)h (SEQ ID No. 238)

[0148] However, in contrast to H1N1, only 13 additional Replikins have been found in H2N2 beginning in 1961. This paucity of appearance of new Replikins correlates with the decline in the concentration of the H2N2 Replikins and the appearance of H2N2 in isolates over the years. (Figure 8).

[0149] Influenza H3N2 Replikins: Influenza H3N2 was responsible for the human pandemic of 1968. Five Replikins which appeared in 1968 disappeared after 1977, but reappeared in the 1990s (Table 6). The only Replikin structure which persisted for 22 years was hcd(g/q)f(q/r)nekwdlf(v/i)er(s/t)k, which
5 appeared first in 1977 and persisted through 1998. The emergence of twelve new H3N2 Replikins in the mid 1990s (Table 6) correlates with the increase in Replikin concentration at the same time (Figure 8), and with the prevalence of the H3N2 strain in recent isolates together with the concurrent disappearance of all Replikins from some of these isolates (Figure 8), this suggests the emergence of
10 the new substrain H3N2(R).

[0150] Figures 1 and 2 show that influenza epidemics and pandemics correlate with the increased concentration of Replikins in influenza virus, which is due to the reappearance of at least one Replikin from one to 59 years after its
15 disappearance. Also, in the A strain only, there is an emergence of new strain-specific Replikin compositions (Tables 4-6). Increase in Replikin concentration by repetition of individual Replikins within a single protein appears not to occur in influenza virus, but is seen in other organisms.

[0151] It has been believed that changes in the activity of different influenza strains are related to sequence changes in influenza hemagglutinins, which in turn are the products of substitutions effected by one of two poorly understood processes: i) antigenic drift, thought to be due to the accumulation of a series of point mutations in the hemagglutinin molecule, or ii) antigenic shift, in which the
25 changes are so great that genetic reassortment is postulated to occur between the

viruses of human and non-human hosts. First, the present data suggests that the change in activity of different influenza strains, rather than being related to non-specific sequence changes, are based upon, or relate to the increased concentration of strain-specific Replikins and strain-specific increases in the replication associated with epidemics. In addition, the data were examined for a possible insight into which sequence changes are due to "drift" or "shift", and which are due to conservation, storage in reservoirs, and reappearance. The data show that the epidemic-related increase in Replikin concentration is not due to the duplication of existing Replikins per hemagglutinin, but is due to the reappearance of at least one Replikin composition from 1 to up to 59 years after its disappearance, plus in the A strains only, the emergence of new strain-specific Replikin compositions (Tables 3-6). Thus the increase in Replikin concentration in the influenza B epidemics of 1951 and 1977 are not associated with the emergence of new Replikin compositions in the year of the epidemic but only with the reappearance of Replikin compositions which had appeared in previous years then disappeared (Table 3). In contrast, for the A strains, in addition to the reappearance of previously disappeared virus Replikins, new compositions appear (e.g. in H1N1 in the year of the epidemic of 1996, in addition to the reappearance of 6 earlier Replikins, 10 new compositions emerged). Since the A strains only, not influenza B, have access to non-human animal and avian reservoirs, totally new compositions probably derive from non-human host reservoirs rather than from mutations of existing human Replikins which appear to bear no resemblance to the new compositions other than the basic requirements of "3-point recognition" (Tables 2-5). The more prolific nature of H1N1 compared with B, and the fact that pandemics have been produced by the three A strains only, but not by the B strain,

both may also be a function of the ability of the human A strains to receive new Replikin compositions from non-human viral reservoirs.

[0152] Some Replikins have appeared in only one year, disappeared, and not
5 reappeared to date (Tables 3-6). Other Replikins disappear from one to up to 81
years, when the identical Replikin sequence reappears. Key Replikin 'k' and 'h'
amino acids, and the spaces between them, are conserved during the constant
presence of particular Replikins over many years, as shown in Tables 23-6 for the
following strain-specific Replikins: ten of influenza B, the single Replikin of
10 H1N1, and the single Replikin of H2N3, as well as for the reappearance of
identical Replikins after an absence. Despite the marked replacement or
substitution activity of other amino acids both inside the Replikin structure and
outside it in the rest of the hemagglutinin sequences, influenza Replikin histidine
(h) appears never to be, and lysine (k) is rarely replaced. Examples of this
15 conservation are seen in the H1N1 Replikin "hp(v/i)tigecpkyv(r/k)(s/t)(t/a)k," (SEQ
ID NO. 135) constant between 1918 and 2000, in the H3N2 Replikin
"hcd(g/q)f(q,r)nekwdlf(v/i)er(s/t)k" (SEQ ID NO. 277) constant between 1975 and
1998 and in the H3N2
Replikin "hqn(s/e)(e/q)g(t/s)g(q/y)aad(l/q)kstq(a/n)a(i/l)d(q/g)l(n/t)(g/n)k,(l/v)n(r/s)
20 vi(e/c)k" (SEQ ID NO. 276) which first appeared in 1975, disappeared for 25
years, and then reappeared in 2000. While many amino acids were substituted, the
basic Replikin structure of 2 Lysines, 6 to 10 residues apart, one histidine, a
minimum of 6% lysine in not more than approximately 50 amino acids, was
conserved.

[0153] Totally random substitution would not permit the persistence of these H1N1 and H3N2 Replikins, nor from 1902 to 2001 in influenza B the persistence of 10 Replikin structures, nor the reappearance in 1993 of a 1919 18mer Replikin after an absence of 74 years. Rather than a random type of substitution, the constancy suggests an orderly controlled process, or in the least, protection of the key Replikin residues so that they are fixed or bound in some way: lysines, perhaps bound to nucleic acids, and histidines, perhaps bound to respiratory redox enzymes. The mechanisms which control this conservation are at present unknown.

10

CONSERVATION OF REPLIKIN STRUCTURES

[0154] Whether Replikin structures are conserved or are subject to extensive natural mutation was examined by scanning the protein sequences of various isolates of foot and mouth disease virus (FMDV), where mutations in proteins of these viruses have been well documented worldwide for decades. Protein sequences of FMDV isolates were visually examined for the presence of both the entire Replikin and each of the component Replikin amino acid residues observed in a particular Replikin.

20 [0155] Rather than being subject to extensive substitution over time as occurs in neighboring amino acids, the amino acids which comprise the Replikin structure are substituted little or not at all, that is the Replikin structure is conserved.

[0156] For example, in the protein VP1 of FMDV type O, the Replikin (SEQ ID NO.: 3) "hkqkivapvk" was found to be conserved in 78% of the 236 isolates reported in PubMed, and each amino acid was found to be conserved in individual isolates as follows: his, 95.6%; lys, 91.8%; gln 92.3%; lys, 84.1%; ile, 90.7%; val, 91.8%; ala, 97.3%; pro, 96.2%; ala, 75.4%; and lys, 88.4%. The high rate of conservation suggests structural and functional stability of the Replikin structure and provides constant targets for treatment.

[0157] Similarly, sequence conservation was found in different isolates of HIV for its Replikins, such as (SEQ ID NO.: 5) "kcfncgkegh" or (SEQ ID NO.: 6) "kvylawvpahk" in HIV Type 1 and (SEQ ID NO.: 7) "kcwncgkegh" in HIV Type 2 (Table 2). Further examples of sequence conservation were found in the HIV tat proteins, such as (SEQ ID NO.: 613) "hclvckqkkglgisygrkk," wherein the key lysine and histidine amino acids are conserved. (See Table 7)

[0158] Similarly, sequence conservation was observed in plants, for example in wheat, such as in wheat ubiquitin activating enzyme B (SEQ ID NOs. 614-616). The Replikins in wheat even provided a reliable target for stimulation of plant growth as described within. Other examples of conservation are seen in the constant presence of malignin in successive generations, over ten years of tissue culture of glioma cells, and by the constancy of affinity of the glioma Replikin for antimalignin antibody isolated by immunoadsorption from 8,090 human sera from the U.S., U.K., Europe and Asia (e.g., Figure 5 and U.S. Patent 6,242,578 B1).

[0159] Similarly, conservation was observed in trans-activator (Tat) proteins

in isolates of HIV. Tat (trans-activator) proteins are early RNA binding proteins regulating lentiviral transcription. These proteins are necessary components in the life cycle of all known lentiviruses, such as the human immunodeficiency viruses (HIV). Tat is a transcriptional regulator protein that acts by binding to the trans-activating response sequence (TAR) RNA element and activates transcription Initiation and/or elongation from the LTR promoter. HIV cannot replicate without tat, but the chemical basis of this has been unknown. In the HIV tat protein sequence from 89 to 102 residues, we have found a Replikin that is associated with rapid replication in other organisms. The amino acid sequence of this Replikin is "hclvcfqkkglgisygrkk." In fact, we found that this Replikin is present in every HIV tat protein. Some tat amino acids are substituted frequently, as shown in Table 8, by alternate amino acids (in small size fonts lined up below the most frequent amino acid (Table 7), the percentage of conservation for the predominant Replikin "hclvcfqkkglgisygrkk"). These substitutions have appeared for most of the individual amino acids. However, the key lysine and histidine amino acids within the Replikin sequence, which define the Replikin structure, are conserved 100% in the sequence; while substitutions are common elsewhere in other amino acids, both within and outside the Replikin, none occurs on these key histidine amino acids.

[0160] As shown in Table 7, it is not the case that lysines are not substituted in the tat protein amino acid sequence. From the left side of the table, the very first lysine in the immediate neighboring sequence, but outside the Replikin sequence, and the second lysine (k) in the sequence inside the Replikin, but "extra" in that it is not essential for the Replikin formation, are both substituted

frequently. However, the 3rd, 4th and 5th lysines, and the one histidine, in parentheses, which together set up the Replikin structure, are never substituted. Thus, these key amino acid sequences are 100% conserved. As observed in the case of the influenza virus Replikins, random substitution would not permit this
5 selective substitution and selective non-substitution to occur due to chance.

Table 7

% Replikin CONSERVATION of each constituent amino acid in the first 117 different isolates of HIV tat protein as reported in PubMed:

38 100 57 86 100 100 66 76 100 99 57 49 100 94 100 97 98 85 97 99 100 100 100%
Neighboring

Amino acids [tat Replikin]

k (c) s y [(h) (c) l v (c) f q k (k) g (l) g i s y g (r) (k) (k)]

below are the amino acid substitutions observed for each amino acid above:

h	c f	q i	l h t	a	a l y h q
r	w p	l l	i h	q	v
y	s	s	l m	r	s
i		s	m s		
s		r	n		
v					
a					
f					
p					
q					

[0161] The conservation of the Replikin structure suggests that the Replikin structure has a specific survival function for the HIV virus which must be preserved and conserved, and cannot be sacrificed to the virus 'defense' maneuver of amino acid substitution crested to avoid antibody and other 'attack.' These 'defense' functions, although also essential, cannot 'compete' with the virus survival function of HIV replication.

[0162] Further conservation was observed in different isolates of HIV for its Replikins such as "kcfncgkegh" (SEQ ID NO. 5) or "kvylawvpahk" (SEQ ID NO. 6) in HIV Type 1 and "kcwncgkegh" (SEQ ID NO. 7) in HIV Type 2.

[0163] The high rate of conservation observed in FMVD and HIV Replikins

suggests that conservation also observed in the Replikins of influenza Replikins is a general property of viral Replikins. This conservation makes them a constant and reliable target for either destruction, for example by using specific Replikins such as for influenza, FMDV or HIV vaccines as illustrated for the glioma Replikin, or stimulation.

[0164] Similarly, as provided in examples found in viruses including influenza viruses, FMDV, and HIV, where high rates of conservation in Replikins suggest that conservation is a general property of viral Replikins and thus making Replikins a constant and reliable target for destruction or stimulation, conservation of Replikin structures occurs in plants. For example, in wheat plants, Replikins are conserved and provide a reliable target for stimulation. Examples of conserved Replikins in wheat plants ubiquitin activating enzyme E include:

E3 hkdrltkkvvdiarevakvdpesyrh (SEQ ID NO. 614)

E2 hkerldrkvvdvarevakvevpsyrh (SEQ ID NO. 615)

E1 hkerldrkvvdvarevaknevpsyrh (SEQ ID NO. 616)

* * * * *

[0165] Similarly to conservation found in the HIV tat protein, the Replikin in the wheat ubiquitin activating enzyme E is conserved. As with the HIV tat protein, substitutions of amino acids (designated with an '**') adjacent to the Replikin variant forms in wheat ubiquitin activating enzyme E are common. The key k and h amino acids that form the Replikin structure, however, do not vary whereas the 'unessential' k that is only 5 amino acids (from the first k on the left) is substituted.

ANTI-REPLIKIN ANTIBODIES

[0166] An anti-Replikin antibody is an antibody against a Replikin. Data on anti-Replikin antibodies also support Replikin class unity. An anti-Replikin antibody response has been quantified by immunoadsorption of serum antimalignin antibody to immobilized malignin (see Methods in U.S. Patent #5,866,690). The abundant production of antimalignin antibody by administration to rabbits of the synthetic version of the 16-mer peptide whose sequence was derived from malignin, absent carbohydrate or other groups, has established rigorously that this peptide alone is an epitope, that is, provides a sufficient basis for this immune response (Figure 3). The 16-mer peptide produced both IgM and IgG forms of the antibody. Antimalignin antibody was found to be increased in concentration in serum in 37% of 79 cases in the U.S. and Asia of hepatitis B and C, early, in the first five years of infection, long before the usual observance of liver cancer, which develops about fifteen to twenty-five years after infection. Relevant to both infectious hepatitis and HIV infections, transformed cells may be one form of safe haven for the virus: prolonging cell life and avoiding virus eviction, so that the virus remains inaccessible to anti-viral treatment.

[0167] Because administration of Replikins stimulates the immune system to produce antibodies having a cytotoxic effect, peptide vaccines based on the particular influenza virus Replikin or group of Replikins observed to be most concentrated over a given time period provide protection against the particular strain of influenza most likely to cause an outbreak in a given influenza season., e.g., an emerging strain or re-emerging strain. For example, analysis of the influenza virus hemagglutinin amino acid sequence on a yearly or bi-yearly basis,

provides data which are useful in formulating a specifically targeted influenza vaccine for that year. It is understood that such analysis may be conducted on a region-by-region basis or at any desired time period, so that strains emerging in different areas throughout the world can be detected and specifically targeted vaccines for each region can be formulated.

INFLUENZA

[0168] Currently, vaccine formulations are changed twice yearly at international WHO and CDC meetings. Vaccine formulations are based on serological evidence of the most current preponderance of influenza virus strain in a given region of the world. However, prior to the present invention there has been no correlation of influenza virus strain specific amino acid sequence changes with occurrence of influenza epidemics or pandemics.

[0169] The observations of specific Replikins and their concentration in influenza virus proteins provides the first specific quantitative early chemical correlates of influenza pandemics and epidemics and provides for production and timely administration of influenza vaccines tailored specifically to treat the prevalent emerging or re-emerging strain of influenza virus in a particular region of the world. By analyzing the protein sequences of isolates of strains of influenza virus, such as the hemagglutinin protein sequence, for the presence, concentration and/or conservation of Replikins, influenza virus pandemics and epidemics can be predicted. Furthermore, the severity of such outbreaks of influenza can be significantly lessened by administering an influenza peptide vaccine based on the Replikin sequences found to be most abundant or shown to be on the rise in virus

isolates over a given time period, such as about one to about three years.

[0170] An influenza peptide vaccine of the invention may include a single

Replikinpeptide sequence or may include a plurality of Replikin sequences

5 observed in influenza virus strains. Preferably, the peptide vaccine is based on

Replikin sequence(s) shown to be increasing in concentration over a given time

period and conserved for at least that period of time. However, a vaccine may

include a conserved Replikin peptide(s) in combination with a new Replikin(s)

peptide or may be based on new Replikin peptide sequences. The Replikin

10 peptides can be synthesized by any method, including chemical synthesis or

recombinant gene technology, and may include non-Replikin sequences, although

vaccines based on peptides containing only Replikin sequences are preferred.

Preferably, vaccine compositions of the invention also contain a pharmaceutically
acceptable carrier and/or adjuvant.

15

[0171] The influenza vaccines of the present invention can be administered alone

or in combination with antiviral drugs, such as gancyclovir, interferon; interleukin;

M2 inhibitors, such as, amantadine, rimantadine; neuraminidase inhibitors, such as

zanamivir and oseltamivir; and the like, as well as with combinations of antiviral

20 drugs.

REPLIKIN DECOYS IN MALARIA

[0172] Analysis of the primary structure of a Plasmodium falciparum malaria

antigen located at the merozoite surface and/or within the parasitophorous vacuole

revealed that this organism, like influenza virus, also contains numerous Replikins (Table 8). However, there are several differences between the observation of Replikins in *Plasmodium falciparum* and influenza virus isolates. For example, *Plasmodium falciparum* contains several partial Replikins, referred to herein as "Replikin decoys." These decoy structures contain an abundance of lysine residues, but lack the histidine required of Replikin structures. Specifically, these decoys contain many lysines 6 to 10 residues apart in overlapping fashion, similar to the true malaria recognins but without histidine residues. It is believed that the decoy structure maximizes the chances that an anti-malarial antibody or other agent will bind to the relatively less important structure containing the lysines, i.e., the Replikin decoys, rather than binding to histidine, which is present in Replikin structure, such as Replikins in respiratory enzymes, which could result in destruction of the trypanosome. For example, an incoming antibody, with specificity for Replikin structures, might attach to the Replikin decoy structure, leaving the true Replikin structure remains untouched.

[0173] Therefore, anti-Replikin treatment of malaria requires two phases (dual treatment): i) preliminary treatment with proteolytic enzymes that cleave the Replikin decoys, permitting 'safe passage' of the specific anti-Replikin treatment; and ii) attacking malaria Replikins either with specific antibodies or by cellular immunity engendered by synthetic malaria Replikin vaccines or by organic means targeting the malaria Replikins.

REPETITION AND OVERLAPPING OF REPLIKIN STRUCTURES

[0174] Another difference seen in *Plasmodium falciparum* is a frequent repetition of individual Replikin structures within a single protein, which was not observed with influenza virus. Repetition may occur by (a) sharing of lysine residues
5 between Replikins, and (b) by repetition of a portion of a Replikin sequence within another Replikin sequence.

[0175] A third significant difference between Replikin structures observed in influenza virus isolates and *Plasmodium falciparum* is a marked overlapping of
10 Replikin structures throughout malarial proteins, e.g., there are nine overlapping Replikins in the 39 amino acid sequence of SEQ ID NO. 393 (Replikin concentration = 23.1/100 amino acids); and 15 overlapping Replikins in the 41 amino acids of SEQ ID NO. 467 (Replikin concentration = 36.6/100 amino acids). Both of these overlapping Replikin structures occur in blood stage trophozoites
15 and schizonts. In contrast, influenza virus Replikins are more scattered throughout the protein and the maximum Replikin concentration is about 7.5/100 amino acids (Figure 7); and tomato leaf curl gemini virus, which was also observed to have overlapping Replikins has only about 3.1/100 amino acids.

[0176] This mechanism of lysine multiples is also seen in the Replikins of cancer proteins such as in gastric cancer transforming protein, ktkkgnrvsptmkvth (SEQ
20 ID NO. 88), and in transforming protein P21B (K-RAS 2B) of lung, khkekmskdgkklkkkks (SEQ ID NO. 89).

[0177] The relationship of higher Replikin concentration to rapid replication is also confirmed by analysis of HIV isolates. It was found that the slow-growing low titer strain of HIV (NSI, "Bru," which is prevalent in early stage HIV infection) has a Replikin concentration of 1.1 (+/- 1.6) Replikins per 100 amino acids, whereas the rapidly-growing high titer strain of HIV (S1, "Lai", which is prevalent in late stage HIV infection) has a Replikin concentration of 6.8 (+/- 2.7) Replikins per 100 amino acid residues.

[0178] The high concentration of overlapping Replikins in malaria, influenza virus and cancer cells is consistent with the legendary high and rapid replicating ability of malaria organisms. The multitude of overlapping Replikins in malaria also provides an opportunity for the organism to flood and confuse the immune system of its host and thereby maximize the chance that the wrong antibody will be made and perpetuated, leaving key malaria antigens unharmed.

[0179] As in the case of influenza virus, for example, peptide vaccines based on the Replikin structure(s) found in the malaria organism can provide an effective means of preventing and/or treating malaria. Vaccination against malaria can be achieved by administering a composition containing one or a mixture of Replikin structures observed in *Plasmodium falciparum*. Furthermore, antibodies to malaria Replikins can be generated and administered for passive immunity or malaria detection

[0180] Table 8 provides a list of several *Plasmodium falciparum* Replikin sequences. It should be noted that this list is not meant to be complete. Different isolates of the organism may contain other Replikin structures.

Malaria Replikins

a) 1) DECOYS:

[illegible]

Hkklikalkkniesiqnkk (SEQ ID NO. 297)
 hkklikalkkniesiqnkm (SEQ ID NO. 298)
 hkklikalkk (SEQ ID NO. 299)
 hkklikalk (SEQ ID NO. 300)
 katysfvntkkkiislsqghkk (SEQ ID NO. 301)
 katysfvntkkkiislsqghk (SEQ ID NO. 302)
 katysfvntkkkiislsqgh (SEQ ID NO. 303)
 htyvkgkkapsdpqca dikeeckellkek (SEQ ID NO. 304)
 kiislsqghk (SEQ ID NO. 305)
 kkkkfepkngnvsetiklih (SEQ ID NO. 306)
 kkkkfepkngnvsetiklih (SEQ ID NO. 307)
 kcfepkngnvsetiklih (SEQ ID NO. 308)
 kngnvsetiklih (SEQ ID NO. 309)
 klhlgnkdkk (SEQ ID NO. 310)
 kvkkgivtlkkfepkngnvsetiklihlgnkdkkh (SEQ ID NO. 311)
 hliynksynpillscvkkmmmlkenvdyiqnqlfkelmnqkatysfvntkkkiislk (SEQ ID NO. 312)
 hliynksynpillscvkkmmmlkenvdyiqnqlfkelmnqkatysfvntk (SEQ ID NO. 313)
 hliynksynpillscvkkmmmlkenvdyiqnqlfkelmnqk (SEQ ID NO. 314)
 hliynksynpillscvkkmmmlkenvdyiqnqlfkelmnqk (SEQ ID NO. 315)
 hliynksynpillscvkkmmmlk (SEQ ID NO. 316)
 ksannsanngkknnaeemknlvnflqshkklikalkkniesiqnkkh (SEQ ID NO. 317)
 knnaeemknlvnflqshkklikalkkniesiqnkkh (SEQ ID NO. 318)
 knlvnflqshkklikalkkniesiqnkkh (SEQ ID NO. 319)
 kklialkkniesiqnkkh (SEQ ID NO. 320)
 kklialkkniesiqnkkh (SEQ ID NO. 321)
 kniesiqnkkh (SEQ ID NO. 322)
 kniesiqnkkh (SEQ ID NO. 323)
 knnaeemknlvnflqsh (SEQ ID NO. 324)
 kklialkkniesiqnkkqghkk (SEQ ID NO. 325)
 knnaeemknlvnflqshk (SEQ ID NO. 326)
 knnaeemknlvnflqsh (SEQ ID NO. 327)
 kklialkkniesiqnkkqghkk (SEQ ID NO. 328)
 kvkkgivtlkkfepkngnvsetiklih (SEQ ID NO. 329)
 kngnvsetiklih (SEQ ID NO. 330)
 klhlgnkdkk (SEQ ID NO. 331)

ksannsanngkknnaeemknlvnflqsh (SEQ ID NO. 332)
 kknnaeemknlvnflqsh (SEQ ID NO. 333)
 kklkalkkniesiqnkkh (SEQ ID NO. 334)
 kalkkniesiqnkkh (SEQ ID NO. 335)
 kkniesiqnkkh (SEQ ID NO. 336)
 kelmnqkatysfvntkkkslsqgh (SEQ ID NO. 337)
 ksqghkk (SEQ ID NO. 338)
 kddislsqgh (SEQ ID NO. 339)
 kdislsqgh (SEQ ID NO. 340)
 kkniesiqnkkh (SEQ ID NO. 341)
 kniesiqnkkh (SEQ ID NO. 342)
 htyvkgkapsdpqcadikeekellkek (SEQ ID NO. 343)
 htyvkgkapsdpqcadikeekellk (SEQ ID NO. 344)

b)"liver stage antigen-3" gene="LSA-3" Replikins
 henvlaalentqseeckkevidvieevk (SEQ ID NO. 345)
 kenvvttilekveettaesvttfsnileeigentitndticckleelh (SEQ ID NO. 346)
 hylqqmkekfskek (SEQ ID NO. 347)
 hylqqmkekfskeknnnvievtkaekkgvqvtnktekttk (SEQ ID NO. 348)
 hylqqmkekfskeknnnvievtkaekkgvqvtnktekttkvdknnk (SEQ ID NO. 349)
 hylqqmkekfskeknnnvievtkaekkgvqvtnktekttkvdknnkvpkdkrtqk (SEQ ID NO. 350)
 hylqqmkekfskeknnnvievtkaekkgvqvtnktekttkvdknnkvpkdkrtqk (SEQ ID NO. 351)
 hvdevmkyvqkidkevdkvskaleskndvtnvlkqngdffskvknfvkkyk (SEQ ID NO. 352)
 hvdevmkyvqkidkevdkvskaleskndvtnvlkqngdffskvknfvk (SEQ ID NO. 353)
 hvdevmkyvqkidkevdkvskaleskndvtnvlkqngdffsk (SEQ ID NO. 354)
 hvdevmkyvqkidkevdkvskaleskndvtnvlk (SEQ ID NO. 355)
 hvdevmkyvqkidkevdkvskalesk (SEQ ID NO. 356)
 hvdevmkyvqkidkevdkvsk (SEQ ID NO. 357)
 hvdevmkyvqkidkevdk (SEQ ID NO. 358)
 hvdevmkyvqkidk (SEQ ID NO. 359)
 kdevidlivqkekriekvkakkklekkveegvsglkkh (SEQ ID NO. 360)
 kvkakkklekkveegvsglkkh (SEQ ID NO. 361)
 kakkklekkveegvsglkkh (SEQ ID NO. 362)
 kddlekkveegvsglkkh (SEQ ID NO. 363)
 kklekkveegvsglkkh (SEQ ID NO. 364)
 kklekkveegvsglkkh (SEQ ID NO. 365)
 kklekkveegvsglkkh (SEQ ID NO. 366)
 kkveegvsglkkh (SEQ ID NO. 367)
 kveegvsglkkh (SEQ ID NO. 368)
 hveqnvyyvdvdpamkdqflgilncaggikemffaledvfksesdvitveeikdepvqk (SEQ ID NO. 369)
 hikgleeddleevddlkgildmilkmdmelgdmmdkesledvtiklgerveslk (SEQ ID NO. 370)
 hikgleeddleevddlkgildmilkmdmelgdmmdkesledvttk (SEQ ID NO. 371)
 hikgleeddleevddlkgildmilkmdmelgdmmdk (SEQ ID NO. 372)
 hikgleeddleevddlkgildmilk (SEQ ID NO. 373)
 hiisgdadvlssalgmdeeqmtrkkaqrpk (SEQ ID NO. 374)
 hditttldevvelkdveedkiek (SEQ ID NO. 375)
 kkleevhelk (SEQ ID NO. 376)
 kleevehelk (SEQ ID NO. 377)
 ktietdileekkkciekdh (SEQ ID NO. 378)
 kkeiekdhfek (SEQ ID NO. 379)

kfeeeaeikh (SEQ ID NO. 381)

c) 28 KDA ookinete surface antigen precursor Replikins:

hleckcnndyvltnryecepknkctsledtnk (SEQ ID NO. 392)

d) Blood stage trophozoites and schizonts Replikas:

aknnedikndnskdikndnskdikndnskdikndnnedikndnskdik (SEQ ID NO. 425)

hknmedikndnskdikndnskdikndnskdikndmedikndnsk (SEQ ID NO. 426)
 hknmedikndnskdikndnskdikndnskdikndnedik (SEQ ID NO. 427)
 hknmedikndnskdikndnskdikndnskdik (SEQ ID NO. 428)
 hknmedikndnskdikndnskdikndnsk (SEQ ID NO. 429)
 hknmedikndnskdikndnskdik (SEQ ID NO. 430)
 hknmedikndnskdikndnsk (SEQ ID NO. 431)
 hknmedikndnskdik (SEQ ID NO. 432)
 hknmedik (SEQ ID NO. 433)
 kkyddlqnkynilnklsleekneelkkyh (SEQ ID NO. 434)
 kyddlqnkynilnklsleekneelkkyh (SEQ ID NO. 435)
 kynilnklsleekneelkkyh (SEQ ID NO. 436)
 klksleekneelkkyh (SEQ ID NO. 437)
 klsleekneelkkyh (SEQ ID NO. 438)
 kneelkkyh (SEQ ID NO. 439)
 hmgnqndinenvynikpqefkeeeedismvntkk (SEQ ID NO. 440)
 kksnellkrindoffklh (SEQ ID NO. 441)
 kplykkclisqlykkckisqvwvmpvkdftfyernvlnskienniekiph (SEQ ID NO. 442)
 hinneytnknpkncllykneermynndnnikdyinsmnfck (SEQ ID NO. 443)
 hinneytnknpkncllykneermynndnnikdyinsmnfck (SEQ ID NO. 444)
 hinneytnknpkncllyk (SEQ ID NO. 445)
 knktngskgvkgeyekkketngh (SEQ ID NO. 446)
 ktngskgvkgeyekkketngh (SEQ ID NO. 447)
 kgvkggeyekkketngh (SEQ ID NO. 448)
 kgeyekkketngh (SEQ ID NO. 449)
 ksgmytnegnkscecsykkkssssnkvh (SEQ ID NO. 450)
 kscecsykkkssssnkvh (SEQ ID NO. 451)
 kkkssssnkvh (SEQ ID NO. 452)
 kkssssnkvh (SEQ ID NO. 453)
 kssssnkvh (SEQ ID NO. 454)
 himlksmytnegnkscecsykkkssssnk (SEQ ID NO. 455)
 himlksmytnegnkscecsykkk (SEQ ID NO. 456)
 himlksmytnegnkscecsykk (SEQ ID NO. 457)
 himlksmytnegnkscecsyk (SEQ ID NO. 458)
 kplaklrrektqinktkyergdviidnteiqkiiirdyhetlnvhkldh (SEQ ID NO. 459)
 krektqinktkyergdviidnteiqkiiirdyhetlnvhkldh (SEQ ID NO. 460)
 ktqinktkyergdviidnteiqkiiirdyhetlnvhkldh (SEQ ID NO. 461)
 kplaklrrektqinktkyergdviidnteiqkiiirdyhetlnvh (SEQ ID NO. 462)
 kplaklrrektqinktkyergdviidnteiqkiiirdyhetlnvh (SEQ ID NO. 463)
 klrkrrektqinktkyergdviidnteiqkiiirdyhetlnvh (SEQ ID NO. 464)
 krektqinktkyergdviidnteiqkiiirdyhetlnvh (SEQ ID NO. 465)
 ktqinktkyergdviidnteiqkiiirdyhetlnvh (SEQ ID NO. 466)
 kkdkekksdsnenrkkqkedkknnpndnklkkieytnkith (SEQ ID NO. 467)
 kdkkekksdsnenrkkqkedkknnpndnklkkieytnkith (SEQ ID NO. 468)
 kekksdsnenrkkqkedkknnpndnklkkieytnkith (SEQ ID NO. 469)
 kksdsnenrkkqkedkknnpndnklkkieytnkith (SEQ ID NO. 470)
 kdsnenrkkqkedkknnpndnklkkieytnkith (SEQ ID NO. 471)
 kksqkedkknnpndnklkkieytnkith (SEQ ID NO. 472)
 kksqkedkknnpndnklkkieytnkith (SEQ ID NO. 473)
 kksqkedkknnpndnklkkieytnkith (SEQ ID NO. 474)
 kksqkedkknnpndnklkkieytnkith (SEQ ID NO. 475)

kedkknpnndnklkkieytnkith (SEQ ID NO. 476)
 kknpnndnklkkieytnkith (SEQ ID NO. 477)
 knpnndnklkkieytnkith (SEQ ID NO. 478)
 klkkieytnkith (SEQ ID NO. 479)
 kkieytnkith (SEQ ID NO. 480)
 kieytnkith (SEQ ID NO. 481)
 hgqikiedvnnenfneeqmknkyndeekmdiskskslksdflek (SEQ ID NO. 482)
 hgqikiedvnnenfneeqmknkyndeekmdiskskslk (SEQ ID NO. 483)
 hgqikiedvnnenfneeqmknkyndeekmdisksk (SEQ ID NO. 484)
 hgqikiedvnnenfneeqmknkyndeekmdisk (SEQ ID NO. 485)
 lkyddlqnkynilnklknsleekneelkkyh (SEQ ID NO. 486)
 kyddlqnkynilnklknsleekneelkkyh (SEQ ID NO. 487)
 kynilnklknsleekneelkkyh (SEQ ID NO. 488)
 klknsleekneelkkyh (SEQ ID NO. 489)
 knsleekneelkkyh (SEQ ID NO. 490)
 kneelkkyh (SEQ ID NO. 491)
 hmgnnqdinenvynikpqefkeeeecedismvntkkeddiqenik (SEQ ID NO. 492)
 ktlnyinyannknddkdnildnenreglylcvnmknsnelkrindnffklh (SEQ ID NO. 493)
 knsnelkrindnffklh (SEQ ID NO. 494)
 krindnffklh (SEQ ID NO. 495)
 hinneytnknpkncllykneernyndnnikdyinsmfnfk (SEQ ID NO. 496)
 hinneytnknpkncllykneernyndnnikdyinsmfnk (SEQ ID NO. 497)
 hinneytnknpkncllyk (SEQ ID NO. 498)
 kpcllykckisqvwwcmpvkdftfyernnnvlnskienniekiph (SEQ ID NO. 499)
 kckisqvwwcmpvkdftfyernnnvlnskienniekiph (SEQ ID NO. 500)
 kienniekiph (SEQ ID NO. 501)
 knktngskgvkgeyekkketngh (SEQ ID NO. 502)
 ktngskgvkgeyekkketngh (SEQ ID NO. 503)
 kgvkgeyekkketngh (SEQ ID NO. 504)
 kgeyekkketngh (SEQ ID NO. 505)
 ktiekinkskswffeeldeidkplaklrkrektqinktkyergdviiidnteiqkiirdyh (SEQ ID NO. 506)
 kinkskswffeeldeidkplaklrkrektqinktkyergdviiidnteiqkiirdyh (SEQ ID NO. 507)
 kplaklrkrektqinktkyergdviiidnteiqkiirdyh (SEQ ID NO. 508)
 himlksqmytnegnkscecsykkssssnkvh (SEQ ID NO. 509)
 klrkrektqinktkyergdviiidnteiqkiirdyh (SEQ ID NO. 510)
 krektqinktkyergdviiidnteiqkiirdyh (SEQ ID NO. 511)
 ktqinktkyergdviiidnteiqkiirdyh (SEQ ID NO. 512)
 kplaklrkrektqinktkyergdviiidnteiqkiirdyhtlnvhkldh (SEQ ID NO. 513)
 klrkrektqinktkyergdviiidnteiqkiirdyhtlnvhkldh (SEQ ID NO. 514)
 krektqinktkyergdviiidnteiqkiirdyhtlnvhkldh (SEQ ID NO. 515)
 ktqinktkyergdviiidnteiqkiirdyhtlnvhkldh (SEQ ID NO. 516)
 kplaklrkrektqinktkyergdviiidnteiqkiirdyhtlnvh (SEQ ID NO. 517)
 klrkrektqinktkyergdviiidnteiqkiirdyhtlnvh (SEQ ID NO. 518)
 krektqinktkyergdviiidnteiqkiirdyhtlnvh (SEQ ID NO. 519)
 ktqinktkyergdviiidnteiqkiirdyhtlnvh (SEQ ID NO. 520)
 himlksqmytnegnkscecsykkssssnkvh (SEQ ID NO. 521)
 ksqmytnegnkscecsykkssssnkvh (SEQ ID NO. 522)
 kscecsykkssssnkvh (SEQ ID NO. 523)
 kkkssssnkvh (SEQ ID NO. 524)
 kkkssssnkvh (SEQ ID NO. 525)

kssssnkvh (SEQ ID NO. 526)
 himlksqmytnegnkscecsykkkssssnk (SEQ ID NO. 527)
 himlksqmytnegnkscecsykkk (SEQ ID NO. 528)
 himlksqmytnegnkscecsykk (SEQ ID NO. 529)
 himlksqmytnegnkscecsyk (SEQ ID NO. 530)
 hnnhniqiykdkrinfnnphkvmyhdnmsknertek (SEQ ID NO. 531)
 hnnhniqiykdkrinfnnphkvmyhdamsk (SEQ ID NO. 532)
 hnnhniqiykdkrinfnnphk (SEQ ID NO. 533)
 hkvmyhdnmsknertek (SEQ ID NO. 534)
 hkvmyhdamsk (SEQ ID NO. 535)

REPLIKINS IN STRUCTURAL PROTEINS

[0181] It has also been determined that some structural proteins include Replikin structures. Structural proteins are molecules involved in tissue and organ support, such as collagen in skin and connective tissue and in membrane structures, for example amyloid A4 precursor protein (APP) in brain. Overproduction of these proteins is associated with disease; specifically, scleroderma in the case of overproduction of collagen in skin (Table 9) and Alzheimer's Disease in the case of overproduction of APP in the brain (Table 10).

[0182] The association of scleroderma and malignancy has been a source of controversy during recent years. Several mechanisms of interrelationship have been suggested in earlier reports. Recent long-term studies suggest an increased association-ratio of scleroderma and malignancy. However, the underlying mechanisms remain elusive. (Wenzel, J. Eur. J. Dermatol. 20002 May-Jun; 12(3): 296-300).

[0183] Several proteins concerned with the excessive production of proteins in scleroderma have been found to contain Replikin structures. Thus, these provide further examples of unrecognized targets for inhibition or cessation of excessive

collagen production. Table 9 provides a list of proteins in scleroderma and the associated Replikins.

[0184] The APP protein is the source of the amyloid beta A4 protein, which in
5 excessive amounts forms plaques in the extracellular spaces in the brain,
producing toxic effects associated with nerve cell loss in Alzheimer's Disease.
Most studies to date have focused on the inability to clear the excessive deposits of
A4, but have not considered that, rather than a waste clearance problem, this may
actually be a problem of overproduction of the precursor protein APP. The high
10 concentration of the Replikins in APP (3.3 Replikins per 100 amino acids)
strongly suggest that overproduction may well be the cause of Alzheimer's
Disease (Table 10). Therefore, the Replikins contained in Table 10 can be blocked
or inhibited by the same methods as illustrated in detail for the glioma Replikin.

Table 9

Proteins overproduced in scleroderma and associated Replikins:

PMCI HUMAN:

hreictiqssggimllkdqvlreskiagvkvacitelilk (SEQ ID NO.536)

hreictiqssggimllkdqvlresk (SEQ ID NO.537)

34KD nucleolar scleroderma antigen:

hreictiqssggimllkdqvlreskiagvkvacitelikkalendqk (SEQ ID NO.538)

hreictiqssggimllkdqvlreskiagvkvacitelilk (SEQ ID NO.539)

Fibrillarin:

kkmqgenmkqpeqltlepyerdh (SEQ ID NO.540)

kmqgenmkpqqeqltlepyerdh (SEQ ID NO. 541)

SPOP HUMAN:

hemeeskknrveindvepevfkemmcfiytkapnldk (SEQ ID NO.542)

hemeeskknrveindvepevfkemmcfiytk (SEQ ID NO.543)

Centromere protein C:

khgelkvyk (SEQ ID NO.544)

klilgpqeeqgkqh (SEQ ID NO. 545)

hmrihhk (SEQ ID NO. 546)

hhssrkstfktmqssk (SEQ ID NO. 547)

hnsrkstfktmqssk (SEQ ID NO. 548)

khnilpktlandkhshkph (SEQ ID NO.549)

hnilpktlandkhshk (SEQ ID NO. 550)

hnilpktlandkhshk (SEQ ID NO. 551)

hnilpktlandk (SEQ ID NO. 552)

kntpdsklissmindhh (SEQ ID NO.553)

kntpdsklissmindh (SEQ ID NO. 554)

kdtciqspskceqkshpksvpvsckk (SEQ ID NO. 555)

kdtciqspskceqkshpksvpvsckk (SEQ ID NO. 556)

hpksvpvsckk (SEQ ID NO. 557)

hpksvpvsckk (SEQ ID NO. 558)

hpksvpvsckk (SEQ ID NO. 559)

Factor CTCBF, KU antigen:

kalqekveikqlnh (SEQ ID NO. 560)

ktlfplieakkdqvtageifgdnhedgptakclkteggah (SEQ ID NO. 561)

ktlfplieakkdqvtageifqdnb (SEQ ID NO. 562)

klcvfkierhsih (SEQ ID NO. 563)

klcvfkierh (SEQ ID NO. 564)

kgpsfplkgiteqqkegleivk (SEQ ID NO. 565)

hgpsfplkgiteqqk (SEQ ID NO. 566)

ATP synthase subunit 6:

htllkilstflk (SEQ ID NO. 567)

hllgndknllpsk (SEQ ID NO. 568)

FBRL nuclear protein:

hrhegvficrgkedalvtk (SEQ ID NO. 569)

hegvficrgkedalvtk (SEQ ID NO. 570)

hsggnrgrgrggrghqsgk (SEQ ID NO. 571)

krqnqsgknvmveph (SEQ ID NO. 572)

krqnqsgknvmvephrrh (SEQ ID NO. 573)

kkmqqenmkpqqqltlepyerdh (SEQ ID NO.574)
 kmqqenmkpqqqltlepyerdh (SEQ ID NO. 575)
HPIHs-alpha protein:
 haypedaenkeketak (SEQ ID NO. 576)
 keanvkcpqivafyeertwh (SEQ ID NO. 577)
 kvldrrvvkgqveyllkwkgfseeh (SEQ ID NO. 578)
 kgqveyllkwkgfseeh (SEQ ID NO. 579)
FM/Sel nucleolar protein:
 ksevaagvkksqplsaerlenvlfghdcsh (SEQ ID NO.580)
 ksevaagvkksqplsaerlenvlfgh (SEQ ID NO. 581)
 kaaeygkkaksetfrllhakniirpqlk (SEQ ID NO. 582)
 kaaeygkkaksetfrllhak (SEQ ID NO. 583)
 ksetfrllhak (SEQ ID NO. 584)
 hakniirpqlk (SEQ ID NO. 585)
 hmnkiaaelpk (SEQ ID NO. 586)
 hslldhllklycnvdsnk (SEQ ID NO. 587)
 hllklycnvdsnk (SEQ ID NO. 588)

Table 10

Amlyoid beta A4 precursor protein (APP) Replikins:

kakerleakh (SEQ ID NO. 589)
 kdrqhtlk (SEQ ID NO. 590)
 kdrqhtlkh (SEQ ID NO. 591)
 ketcsekstnlh (SEQ ID NO. 592)
 kteisevkmdaeefgh (SEQ ID NO. 593)
 kteisevkmdaeefghdsgfevrh (SEQ ID NO. 594)
 kkyvraeqkdrqhtlkh (SEQ ID NO. 595)
 kyvraeqkdrqhtlkh (SEQ ID NO. 596)
 kkyvraeqkdrqh (SEQ ID NO. 597)
 kyvraeqkdrqht (SEQ ID NO. 598)
 hhvfnnlkkkyvraeqk (SEQ ID NO. 599)
 hvfnmlkkkyvraeqk (SEQ ID NO. 600)
 hhvfnnlkkkyvraeqkdrqhtlkh (SEQ ID NO. 601)
 hvfnmlkkkyvraeqkdrqhtlkh (SEQ ID NO. 602)
 hahfqkakerleakh (SEQ ID NO. 603)
 hahfqkakerleak (SEQ ID NO. 604)
 hfqkakerleak (SEQ ID NO. 605)
 hqermdvcethllhwhtvaketcsekstnlh (SEQ ID NO. 606)
 hqermdvcethllhwhtvaketcsek (SEQ ID NO. 607)
 hwhtvaketcsek (SEQ ID NO. 608)
 htvaketcsek (SEQ ID NO. 609)
 hllhwhtvaketcsek (SEQ ID NO. 610)
 hmnvqngkwesdpsgtkctgik (SEQ ID NO. 611)
 hmnvqngkwesdpsgtk (SEQ ID NO. 612)

PASSIVE IMMUNITY

[0185] In another embodiment of the invention, isolated Replikin peptides may be used to generate antibodies, which may be used, for example to provide passive immunity in an individual. Passive immunity to the strain of influenza identified by the method of the invention to be the most likely cause of future influenza infections may be obtained by administering antibodies to Replikin sequences of the identified strain of influenza virus to patients in need. Similarly, passive immunity to malaria may be obtained by administering antibodies to Plasmodium falciparum Replikin(s).

[0186] Various procedures known in the art may be used for the production of antibodies to Replikin sequences. Such antibodies include but are not limited to polyclonal, monoclonal, chimeric, humanized, single chain, Fab fragments and fragments produced by an Fab expression library. Antibodies that are linked to a cytotoxic agent may also be generated. Antibodies may also be administered in combination with an antiviral agent. Furthermore, combinations of antibodies to different Replikins may be administered as an antibody cocktail.

[0187] For the production of antibodies, various host animals or plants may be immunized by injection with a Replikin peptide or a combination of Replikin peptides, including but not limited to rabbits, mice, rats, and larger mammals.

[0188] Monoclonal antibodies to Replikins may be prepared by using any technique that provides for the production of antibody molecules. These include but are not limited to the hybridoma technique originally described by Kohler and

Milstein, (Nature, 1975, 256:495-497), the human B-cell hybridoma technique (Kosbor et al., 1983, Immunology Today, 4:72), and the EBV hybridoma technique (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96). In addition, techniques developed for the production of chimeric
5 antibodies (Morrison et al., 1984, Proc. Nat. Acad. Sci USA, 81:6851-6855) or other techniques may be used. Alternatively, techniques described for the production of single chain antibodies (US 4,946,778) can be adapted to produce Replikin-specific single chain antibodies.

10 [0189] Particularly useful antibodies of the invention are those that specifically bind to Replikin sequences contained in peptides and/or polypeptides of influenza virus. For example, antibodies to any of peptides observed to be present in an emerging or re-emerging strain of influenza virus and combinations of such
antibodies are useful in the treatment and/or prevention of influenza. Similarly,
15 antibodies to any Replikins present on malaria antigens and combinations of such antibodies are useful in the prevention and treatment of malaria.

[0190] Antibody fragments which contain binding sites for a Replikin may be generated by known techniques. For example, such fragments include but are not
20 limited to F(ab')₂ fragments which can be produced by pepsin digestion of the antibody molecules and the Fab fragments that can be generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternatively, Fab expression libraries can be generated (Huse et al., 1989, Science, 246:1275-1281) to allow rapid and
easy identification of monoclonal Fab fragments with the desired specificity.

25

[0191] The fact that antimalignin antibody is increased in concentration in human malignancy regardless of cancer cell type (Figure 5), and that this antibody binds to malignant cells regardless of cell type now may be explained by the presence of the Replikin structures herein found to be present in most malignancies (Figure 1 and Table 2). Population studies have shown that antimalignin antibody increases in concentration in healthy adults with age, and more so in high-risk families, as the frequency of cancer increases. An additional two-fold or greater antibody increase which occurs in early malignancy has been independently confirmed with a sensitivity of 97% in breast cancers 1-10 mm in size. Shown to localize preferentially in malignant cells in vivo, histochemically the antibody does not bind to normal cells but selectively binds to (Figure 4a,b) and is highly cytotoxic to transformed cells in vitro (Figure 4c-f). Since in these examples the same antibody is bound by several cell types, that is, brain glioma, hematopoietic cells (leukemia), and small cell carcinoma of lung, malignant Replikin class unity is again demonstrated.

[0192] Antimalignin does not increase with benign proliferation, but specifically increases only with malignant transformation and replication in breast in vivo and returns from elevated to normal values upon elimination of malignant cells (Figure 5). Antimalignin antibody concentration has been shown to relate quantitatively to the survival of cancer patients, that is, the more antibody, the longer the survival. Taken together, these results suggest that anti-Replikin antibodies may be a part of a mechanism of control of cell transformation and replication. Augmentation of this immune response may be useful in the control of replication, either actively with synthetic Replikins as vaccines, or passively by the administration of anti-

Replikin antibodies, or by the introduction of non-immune based organic agents, such as for example, carbohydrates, lipids and the like, which are similarly designed to target the Replikin specifically.

5 [0193] In another embodiment of the invention, immune serum containing antibodies to one or more Replikins obtained from an individual exposed to one or more Replikins may be used to induce passive immunity in another individual or animal. Immune serum may be administered via i.v. to a subject in need of treatment. Passive immunity also can be achieved by injecting a recipient with
10 preformed antibodies to one or more Replikins. Passive immunization may be used to provide immediate protection to individuals who have been exposed to an infectious organism. Administration of immune serum or preformed antibodies is routine and the skilled practitioner can readily ascertain the amount of serum or antibodies needed to achieve the desired effect.

15

SYNTHETIC REPLIKIN VACCINE (ACTIVE IMMUNITY)

[0194] Synthetic Replikin vaccines, based on Replikins such as the glioma Replikin (SEQ ID NO.: 1) "kagvafbhkk" or the hepatitis C Replikin (SEQ ID NO.: 18) "hyppkpgcivpak", or HIV Replikins such as (SEQ ID NO.: 5) "kcfncgkegh" or (SEQ ID NO.: 6) "kvylawvpahk" or preferably, an influenza vaccine based on
20 conserved and/or emerging or re-emerging Replikin(s) over a given time period may be used to augment antibody concentration in order to lyse the respective virus infected cells and release virus extracellularly where chemical treatment can then be effective. Similarly, a malaria vaccine, based on Replikins observed in
25 Plasmodium falciparum malaria antigens on the merozoite surface or within the

parasitophorous vacuole, for example, can be used to generate cytotoxic antibodies to malaria.

[0195] Recognin and/or Replikin peptides may be administered to a subject to induce the immune system of the subject to produce anti-Replikin antibodies.

Generally, a 0.5 to about 2 mg dosage, preferably a 1 mg dosage of each peptide is administered to the subject to induce an immune response. Subsequent dosages may be administered if desired.

[0196] The Replikin sequence structure is associated with the function of replication. Thus, whether the Replikins of this invention are used for targeting sequences that contain Replikins for the purpose of diagnostic identification, promoting replication, or inhibiting or attacking replication, for example, the structure-function relationship of the Replikin is fundamental.

[0197] It is preferable to utilize only the specific Replikin structure when seeking to induce antibodies that will recognize and attach to the Replikin fragment and thereby cause destruction of the cell. Even though the larger protein sequence may be known in the art as having a "replication associated function," vaccines using the larger protein often have failed or proven ineffective.

[0198] Although the present inventors do not wish to be held to a single theory, the studies herein suggest that the prior art vaccines are ineffective because they are based on the use of the larger protein sequence. The larger protein sequence invariably has one or more epitopes (independent antigenic sequences that can

induce specific antibody formation); Replikin structures usually comprise one of these potential epitopes. The presence of other epitopes within the larger protein may interfere with adequate formation of antibodies to the Replikin, by "flooding" the immune system with irrelevant antigenic stimuli that may preempt the Replikin antigens, See, e.g., Webster, R.G., *J. Immunol.*, 97(2):177-183 (1966); and Webster et al., *J. Infect. Dis.*, 134:48-58, 1976; Klennerman et al, *Nature* 394:421-422 (1998) for a discussion of this well-known phenomenon of antigenic primacy whereby the first peptide epitope presented and recognized by the immune system subsequently prevails and antibodies are made to it even though other peptide epitopes are presented at the same time. This is another reason that, in a vaccine formulation, it is important to present the constant Replikin peptide to the immune system first, before presenting other epitopes from the organism so that the Replikin is not pre-empted but lodged in immunological memory.

[0199] The formation of an antibody to a non-Replikin epitope may allow binding to the cell, but not necessarily lead to cell destruction. The presence of structural "decoys" on the C-termini of malaria proteins is another aspect of this ability of other epitopes to interfere with binding of effective anti-Replikin antibodies, since the decoy epitopes have many lysine residues, but no histidine residues. Thus, decoy epitopes may bind anti-Replikin antibodies, but may keep the antibodies away from histidine-bound respiratory enzymes. Treatment may therefore be most efficacious in two stages: 1) proteases to hydrolyze decoys, then; 2) anti-Replikin antibodies or other anti-Replikin agents.

[0200] It is well known in the art that in the course of antibody production against a "foreign" protein, the protein is first hydrolyzed into smaller fragments. Usually fragments containing from about six to ten amino acids are selected for antibody formation. Thus, if hydrolysis of a protein does not result in Replikin-containing fragments, anti-Replikin antibodies will not be produced. In this regard, it is interesting that Replikins contain lysine residues located six to ten amino acids apart, since lysine residues are known to bind to membranes.

[0201] Furthermore, Replikin sequences contain at least one histidine residue.

Histidine is frequently involved in binding to redox centers. Thus, an antibody that specifically recognizes a Replikin sequence has a better chance of inactivating or destroying the cell in which the Replikin is located, as seen with anti-malignin antibody, which is perhaps the most cytotoxic anti-cancer antibody yet described, being active at picograms per cell.

[0202] One of the reasons that vaccines directed towards a particular protein antigen of a disease causing agent have not been fully effective in providing protection against the disease (such as foot and mouth vaccine which has been developed against the VP1 protein or large segments of the VP1 protein) is that the best antibodies have not been produced, that is – it is likely that the antibodies to the Replikins have not been produced. Replikins have not been produced. That is, either epitopes other than Replikins present in the larger protein fragments may interfere according to the phenomenon of antigenic primacy referred to above, and/or because the hydrolysis of larger protein sequences into smaller sequences for processing to produce antibodies results in loss of integrity of any Replikin

structure that is present, e.g., the Replikin is cut in two and/or the histidine residue is lost in the hydrolytic processing. The present studies suggest that for an effective vaccine to be produced, the Replikin sequences, and no other epitope, should be used as the vaccine. For example, a vaccine of the invention can be generated using any one of the Replikin peptides identified by the three point recognition system.

[0203] Particularly preferred peptides - for example - an influenza vaccine include peptides that have been demonstrated to be conserved over a period of one or more years, preferably about three years or more, and/or which are present in a strain of influenza virus shown to have the highest increase in concentration of Replikins relative to Replikin concentration in other influenza virus strains, e.g., an emerging strain. The increase in Replikin concentration preferably occurs over a period of at least about six months to one year, preferably at least about two years or more, and most preferably about three years or more. Among the preferred Replikin peptides for use in an influenza virus vaccine are those Replikins observed to "re- emerge" after an absence from the hemagglutinin amino acid sequence for one or more years.

[0204] The Replikin peptides of the invention, alone or in various combinations are administered to a subject, preferably by i.v. or intramuscular injection, in order to stimulate the immune system of the subject to produce antibodies to the peptide. Generally the dosage of peptides is in the range of from about 0.1 μ g to about 10 mg, preferably about 10 μ g to about 1 mg, and most preferably about 50 μ g to

about 500 ug. The skilled practitioner can readily determine the dosage and number of dosages needed to produce an effective immune response.

QUANTITATIVE MEASUREMENT EARLY RESPONSE(S) TO REPLIKIN VACCINES

[0205] The ability to measure quantitatively the early specific antibody response in days or a few weeks to a Replikin vaccine is a major practical advantage over other vaccines for which only a clinical response months or years later can be measured.

ADJUVANTS

[0206] Various adjuvants may be used to enhance the immunological response, depending on the host species, including but not limited to Freund's (complete and incomplete), mineral gels, such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, key limpet hemocyanin, dinitrophenol, and potentially useful human adjuvants such as BCG and *Corynebacterium parvum*.

REPLIKIN NUCLEOTIDE SEQUENCES

[0207] Replikin DNA or RNA may have a number of uses for the diagnosis of diseases resulting from infection with a virus, bacterium or other Replikin encoding agent. For example, Replikin nucleotide sequences may be used in hybridization assays of biopsied tissue or blood, e.g., Southern or Northern analysis, including in situ hybridization assays, to diagnose the presence of a particular organism in a tissue sample or an environmental sample, for example. The present invention also contemplates kits containing antibodies specific for particular Replikins that are present in a particular pathogen of interest, or

containing nucleic acid molecules (sense or antisense) that hybridize specifically to a particular Replikin, and optionally, various buffers and/or reagents needed for diagnosis.

5 [0208] Also within the scope of the invention are oligoribonucleotide sequences, that include antisense RNA and DNA molecules and ribozymes that function to inhibit the translation of Replikin- or recognin-containing mRNA. Both antisense RNA and DNA molecules and ribozymes may be prepared by any method known in the art. The antisense molecules can be incorporated into a wide variety of
10 vectors for delivery to a subject. The skilled practitioner can readily determine the best route of delivery, although generally i.v. or i.m. delivery is routine. The dosage amount is also readily ascertainable.

[0209] Particularly preferred antisense nucleic acid molecules are those that are
15 complementary to a Replikin sequence contained in a mRNA encoding, for example, an influenza virus polypeptide, wherein the Replikin sequence comprises from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues. More preferred are antisense nucleic acid
20 molecules that are complementary to a Replikin present in the coding strand of the gene or to the mRNA encoding the influenza virus hemagglutinin protein, wherein the antisense nucleic acid molecule is complementary to a nucleotide sequence encoding a Replikin that has been demonstrated to be conserved over a period of six months to one or more years and/or which are present in a strain of influenza
25 virus shown to have an increase in concentration of Replikins relative to Replikin

concentration in other influenza virus strains. The increase in Replikin concentration preferably occurs over a period of at least six months, preferably about one year, most preferably about two or three years or more.

5 [0210] Similarly, antisense nucleic acid molecules that are complementary to mRNA those that are complementary to a mRNA encoding bacterial Replikins comprising a Replikin sequence of from 7 to about 50 amino acids including (1) at least one lysine residue located six to ten residues from a second lysine residue; (2) at least one histidine residue; and (3) at least 6% lysine residues. More
10 preferred are antisense nucleic acid molecules that are complementary to the coding strand of the gene or to the mRNA encoding a protein of the bacteria.

DIAGNOSTIC APPLICATIONS

[0211] For organisms such as diatom plankton, foot and mouth disease virus,
15 tomato leaf curl gemini virus, hepatitis B and C, HIV, influenza virus and malignant cells, identified constituent Replikins are useful as vaccines, and also may be usefully targeted for diagnostic purposes. For example, blood collected for transfusions may be screened for contamination of organisms, such as HIV, by screening for the presence of Replikins shown to be specific for the contamination
20 organism. Also, screening for Replikin structures specific for a particular pathological organism leads to diagnostic detection of the organism in body tissue or in the environment.

REPLIKIN STIMULATION OF GROWTH

25 [0212] In another embodiment of the invention, Replikin structures are used to

increase the replication rate of cells, tissues or organs. A method is available to increase replication rates by the addition of specific Replikin structures for other cells, tissues or organs that it is desired to replicate more rapidly, together with or without appropriate stimulæ to cell division know in the art for said cells, tissues or organs to increase the rate of replication and yield. This may be accomplished, for example, by methods known in the art, by modifying or transforming a gene encoding for or associated with a protein or enzyme having a replication function in the organism with at least one Replikin structure.

[0213] In another aspect of the invention, Replikin structures are used to increase the replication of organisms. The present invention demonstrates that in influenza virus, for example, increased replication associated with epidemics is associated with increased concentration of Replikins. The increase is due to 1) the reappearance of particular Replikin structures, which were present in previous years, but which then disappeared for one or more years; and/or 2) by the appearance of new Replikin compositions. In addition, in malaria Replikins, repetition of the same Replikin in a single protein occurs.

[0214] Thus, the present invention provides methods and compositions for increasing the replication of organisms. Similarly, in the manner that Replikins of different organisms can be targeted to inhibit replication of any organism, Replikins can be used to increase the replication of any organism. For example, production of rice, maize, and wheat crops, which are critical to feeding large populations in the world, can be improved, for example, by increasing the

concentration (number of Replikins/100 amino acid residues) of any particular strain of rice.

[0215] As an example, in the *Oryza sativa* strain of rice, catalase isolated from immature seeds was observed to contain the following different Replikins within the 491 amino acid sequence of the protein:

kfpdvihafkpnprsh (SEQ ID NO. 638)

kfpdvihafk (SEQ ID NO. 639)

karyvkfhwk (SEQ ID NO. 640)

hpkvspelraiwvnylsqedeslgvkianlvk (SEQ ID NO. 641)

katihkqndfk (SEQ ID NO. 642)

haptpitprpvvgrrqkatihkqndfk (SEQ ID NO. 643)

kfrpsssfdktttnagapvwndnealtvgprgpilledyhliekvah (SEQ ID NO. 644)

kfrpsssfdktttnagapvwndnealtvgprgpilledyn (SEQ ID NO. 645)

[0216] Thus, by using recombinant gene cloning techniques well known in the art, the concentration of Replikin structures in an organism, such as a food crop plant, can be increased, which will promote increased replication of the organism. For example, inserting additional Replikin sequences like the Replikins identified above into the *Oryza sativa* catalase gene by methods well known in the art will promote this organism's replication.

[0217] Similarly, in the NBS-LRR protein of *Oryza sativa* (japonica cultivar group), the following Replikins were found:

kvkahfqkh (SEQ ID NO. 647)

kvkahfqk (SEQ ID NO. 648)

kdyeidkddlih (SEQ ID NO. 648)

hmkqcfafcafpk (SEQ ID NO. 650)

hvfwevwrsffqnvkqigsifqrkvryrgsdvtskihdlnhdldavh (SEQ ID NO. 651)

5 kqigsifqrkvryrgsdvtskihdlnhdldavh (SEQ ID NO. 652)

kqigsifqrkvryrgsdvtskihdlnh (SEQ ID NO. 653)

kqigsifqrkvryrgsdvtskih (SEQ ID NO. 654)

[0218] Further, for aspartic proteinase oryzasin I precursor protein, the following

10 Replikins were found:

khgvsagik (SEQ ID NO.655)

htvfdygmrvgfak (SEQ ID NO. 657)

hsryksgqsstyqkngk (SEQ ID NO. 658)

15 [0219] Similarly, in the MADS-box protein FDRMADS3 transcription factor of
Oryza sativa (indica cultivar-group), the following Replikins were found:

kqeamvfkqeinllqkglryygnranch (SEQ ID NO. 659)

kqeinllqkglryygnranch (SEQ ID NO. 660)

kskegmkaaneilqekiveqnglidvgmmvadqqngh (SEQ ID NO.661)

20 kaaneilqekiveqnglidvgmmvadqqngh (SEQ ID NO. 662)

[0220] Similarly, in LONI MAIZE (ATP-binding redox associated Hydrolase;
Serine protease; Multigene family; Mitochondrion), the following Replikins were
found:

25 kvlaahrygik (SEQ ID NO. 663)

- klkiamkhliprvleqh (SEQ ID NO.664)
- klkiamkh (SEQ ID NO. 665)
- ktslassiakalnrfirislggkdeadirgh (SEQ ID NO.666)
- kalnrkfirislggkdeadirgh (SEQ ID NO. 667)
- 5 kfnrlsggkdeadirgh (SEQ ID NO. 668)
- kvrlskatelvdrlhqlsilvaekitqkvegqlsksqk (SEQ ID NO. 669)
- hlqsilvaekitqkvegqlsksqk (SEQ ID NO. 670)
- kvrlskatelvdrlh (SEQ ID NO. 671)
- kvggssavesskqdtknkgepihwhskgvaaralh (SEQ ID NO. 672)
- 10 kvggssavesskqdtknkgepihwh (SEQ ID NO. 673)
- kvggssavesskqdtknkgepih (SEQ ID NO. 674)
- kqdtknkgepihwhskgvaaralh (SEQ ID NO. 675)
- kqdtknkgepih (SEQ ID NO. 676)

15 [0221] Similarly, for Glyceraldehyde 3-phosphate dehydrogenase A, a chloroplast precursor, the following Replikins are found:

- hndlraraaalnrvptstgaakavslvlpnlk (SEQ ID NO. 677)
- kvlddqkfgiikgtmttth (SEQ ID NO. 678)
- hiqagakkvltapgk (SEQ ID NO. 679)
- 20 hgrgdaspldviaindtggvkqashllk (SEQ ID NO. 680)
- kqashllk (SEQ ID NO. 710)

[0222] Further, examples of rust resistance-like protein RP1-4 (Zea mays) found include the following Replikins:

- 25 kvrvlskdysslkqlmtlrmdddiskhlqitesgleeredkvwmkeniik (SEQ ID NO. 681)

- kvrrvlskdysslkqlmtlmmdddiskh (SEQ ID NO. 682)
- hlqiiesgleeredkvwmkeniik (SEQ ID NO.683)
- hdlreniimkaddlask (SEQ ID NO. 684)
- hvnqlenvigkdealask (SEQ ID NO. 685)
- 5 kkggyelrqldlnelggsih (SEQ ID NO. 686)
- kkggyelrqldlnelggsih (SEQ ID NO. 687)
- klylksrikelilewssengmdamnilh (SEQ ID NO. 688)
- hlqlqlngmverlpnkvcnlskrylrgykdqipnigk (SEQ ID NO. 689)
- hlqlqlngmverlpnkvcnlskrylrgyk (SEQ ID NO. 690)
- 10 hlqlqlngmverlpnkvcnlsk (SEQ ID NO. 691)
- hnsnklpksvgelk (SEQ ID NO. 692)
- klpkvgelkh (SEQ ID NO. 693)
- hlsvrvesmqkhkeiik (SEQ ID NO. 694)
- khkeiik (SEQ ID NO. 695)
- 15 klrdilqesqkflvldialfkh (SEQ ID NO. 696)
- hafsgaeikdqlrmklqdtaceiakrlgqcplaakvlgsmcrrk (SEQ ID NO. 697)
- hafsgaeikdqlrmk (SEQ ID NO. 698)
- klqdtaceiakrlgqcplaakvlgsmcrrkdiaewkaadvwfeksh (SEQ ID NO. 699)
- kvlgsmcrrkdiaewkaadvwfeksh (SEQ ID NO. 700)
- 20 kdiaewkaadvwfeksh (SEQ ID NO. 701)
- kaadvwfeksh (SEQ ID NO. 702)
- hvppttislptskvfgmsdrdrvklfgktttaeasstk (SEQ ID NO. 703)
- kailteakqlrdllgph (SEQ ID NO. 704)
- kakaksgkgpllredessstattvmkpfh (SEQ ID NO. 705)
- 25 ksphrqkieswlrrikeafydaedlldeh (SEQ ID NO. 706)

ksphrgkdeswlrrlk (SEQ ID NO. 707)

hrgkleswlrrlk (SEQ ID NO. 708)

ksphrgk (SEQ ID NO. 709)

5 [0223] As discussed previously, the Replikin in wheat ubiquitin activating enzyme E (SEQ ID Nos. 614-616) is conserved. This conservation of Replikin structure provides reliable targets for stimulation of plant growth.

[0224] The close relationship of Replikins to redox enzymes is also clearly
10 indicated in this structure in wheat. Thus, this wheat ubiquitin activating enzyme E activates ubiquitin by first adenylating with ATP its carboxy-terminal glycine residue and, thereafter, linking this residue to the side chain of a cysteine residue in E1 (SEQ ID NO. 614), yielding an ubiquitin-E1 thiolester and free AMP.

15 [0225] A further example of the relationship of wheat Replikins to redox enzymes was also found in the PSABWheat Protein, Photosystem I P700 chlorophyll A apoprotein A2 (PsaB) (PSI-B) isolated from bread Chinese spring wheat Chloroplast Triticum aestivum. This protein functions as follows: PsaA and PsaB bind 9700, the primary electron donor of photosystem I (PSI), as well as the
20 electron acceptors A0, A1, and FX. PSI functions as a plastocyanin/cytochrome c6-ferredoxin oxidoreductase. Cofactor P700 is a chlorophyll A dimer, A0 is chlorophyll A, A1 is a phylloquinone and FX is a 4Fe- 4S iron-sulfur center. The subunit A psaA/S heterodimer binds the P700 chlorophyll special pair and subsequent electron acceptors. The PSI reaction center of higher plants and algae
25 is composed of one at least 11 subunits. This is an integral membrane protein of

the Chloroplast thylakoid membrane. The 4Fe-4S iron-sulfur"center" to which 'h' bind is critical; hence the significance of 'h' in Replikin structure. Next to bacterial Replikins, these wheat Replikins and plant Replikins are the most primitive evolutionary illustrations of the importance of the Replikin structure to replication and the energy source needed for replication. This basic relationship carries through algae, virus Replikins, bacteria, cancer cells, and apparently all organisms with regard to replication.

[0226] Further examples of Replikins were found in the PSAB Wheat protein,

10 which is critical for wheat growth. These include:

hlqpkwkpslswfknaesrlnhh (SEQ ID NO.617)

hlqpkwkpslswfk (SEQ ID NO. 618)

kwkpslswfknaesrlnhh (SEQ ID NO. 619)

kwkpslswfknaesrlnh (SEQ ID NO. 620)

15 kpslswfknaesrlnhh (SEQ ID NO. 621)

kpslswfknaesrlnh (SEQ ID NO. 622)

hhaialglhttlilvkgaldargsklmpdkk (SEQ ID NO. 623)

haialglhttlilvkgaldargsklmpdkk (SEQ ID NO. 624)

hhaialglhttlilvkgaldargsk (SEQ ID NO. 625)

20 haialglhttlilvkgaldargsk (SEQ ID NO. 626)

httlilvkgaldargsklmpdkk (SEQ ID NO.627)

httlilvkgaldargsklmpdk (SEQ ID NO. 628)

httlilvkgaldargsk (SEQ ID NO. 629)

[0227] A further example of the relationship of wheat Replikins to redox is provide in the PSAA_WHEAT Photosystem I 9700 chlorophyll A apoprotein A1, that include:

hhhlaiailfliaghmyrtnwgighglkdileahkgpftgqghk (SEQ ID NO. 630)

5 hhlaiailfliaghmyrtnwgighglkdileahkgpftgqghk (SEQ ID NO. 631)

hlaiaailfliaghmyrtnwgighglkdileahkgpftgqghk (SEQ ID NO. 632)

hmyrtnwgighglkdileahkgpftgqghk (SEQ ID NO. 633)

hglkdileahkgpftgqghk (SEQ ID NO. 634)

bdileahkgpftgqghk (SEQ ID NO. 635)

10 hkgpftgqghk (SEQ ID NO. 636)

kgpftgqghk (SEQ ID NO. 637)

COMPUTER SOFTWARE FOR IDENTIFYING REPLIKINS

[0228] The present invention also provides methods for identifying Replikin
15 sequences in an amino acid or nucleic acid sequence. Visual scanning of over four thousand sequences was performed in developing the present 3-point-recognition methods. However, data banks comprising nucleotide and/or amino acid sequences can also be scanned by computer for the presence of sequences meeting the 3 point recognition requirements.

20

[0229] According to another embodiment of the invention, three-point recognition methods described herein may be performed by a computer. Figure 6 is a block diagram of a computer available for use with the foregoing embodiments of the present invention. The computer may include a processor, an input/output device
25 and a memory storing executable program instructions representing the 3-point-

recognition methods of the foregoing embodiments. The memory may include a static memory, volatile memory and/or a nonvolatile memory. The static memory conventionally may be a read only memory ("ROM") provided on a magnetic, or an electrical or optical storage medium. The volatile memory conventionally may be a random access memory ("RAM") and may be integrated as a cache within the processor or provided externally from the processor as a separate integrated circuit. The non-volatile memory may be an electrical, magnetic or optical storage medium.

[0230] From a proteomic point of view the construction of a "3-point recognition" template based on the new glioma peptide sequence led directly to identification of a biology-wide class of proteins having related structures and functions. The operation of the 3-point-recognition method resembles identification by the use of a "keyword" search; but instead of using the exact spelling of the keyword "kagvafhhkk" (SEQ ID NO.: 1) as in a typical sequence homology search, or in the nucleotide specification of an amino acid, an abstraction of the keyword delimited by the "3-point-recognition" parameters is used. This delimited abstraction, although derived from a single relatively short amino acid sequence leads to identification of a class of proteins with structures that are defined by the same specifications. That particular functions, in this case transformation and replication, in addition to structures, turn out also to be shared by members of the exposed class suggests that these structures and functions are related. Thus, from this newly identified short peptide sequence, a molecular recognition 'language' has been formulated, which previously has not been described. Further, the sharing of immunological specificity by diverse members of the class, as here

demonstrated for the cancer Replikins, suggests that B cells and their product antibodies recognize Replikins by means of a similar recognition language.

OTHER USES OF THE THREE POINT RECOGNITION METHOD

5 [0231] Since "3-point-recognition" is a proteomic method that specifies a particular class of proteins, using three or more different recognition points for other peptides similarly should provide useful information concerning other proteins classes. Further, the "3-point-recognition" method is applicable to other recognins, for example to the TOLL 'innate' recognition of lipopolyssacharides of
10 organisms. The three point recognition method may also be modified to identify other useful compounds of covalently linked organic molecules, including other covalently linked amino acids, nucleotides, carbohydrates, lipids or combinations thereof. In this embodiment of the invention a sequence is screened for subsequences containing three or more desired structural characteristics. In the
15 case of screening compounds composed of covalently linked amino acids, lipids or carbohydrates the subsequence of 7 to about 50 covalently linked units should contain (1) at least one first amino acid, carbohydrate or lipid residue located seven to ten residues from a second of the first amino acid, carbohydrate or lipid residue; (2) encoding at least one second amino acid, lipid or carbohydrate residue;
20 and (3) at least 6% of the first amino acid, carbohydrate or lipid residue. In the case of screening nucleotide sequences, the subsequence of about 21 to about 150 nucleotides should contain (1) at least one codon encoding a first amino acid located within eighteen to thirty nucleotides from a second codon encoding the first amino acid residue; (2) at least one second amino acid residue; and (3)
25 encodes at least 6% of said first amino acid residue.

[0232] Several embodiments of the present invention are specifically illustrated and described herein. However, it will be appreciated that modifications and variations of the present invention are encompassed by the above teachings and within the purview of the appended claims without departing from the spirit and intended scope of the invention.

EXAMPLE 1

PROCESS FOR EXTRACTION, ISOLATION AND
IDENTIFICATION OF ReplikinS AND THE USE OF *REPLIKINS* TO
TARGET, LABEL OR DESTROY *REPLIKIN*-CONTAINING ORGANISMS

a) Algae

[0233] The following algae were collected from Bermuda water sites and either extracted on the same day or frozen at -20 degrees C and extracted the next day. The algae were homogenized in a cold room (at 0 to 5 degrees C) in 1 gram aliquots in neutral buffer, for example 100 cc. of 0.005M phosphate buffer solution, pH 7 ("phosphate buffer") for 15 minutes in a Waring blender, centrifuged at 3000 rpm, and the supernatant concentrated by preevaporation and dialyzed against phosphate buffer in the cold to produce a volume of approximately 15 ml. The volume of this extract solution was noted and an aliquot taken for protein analysis, and the remainder was fractionated to obtain the protein fraction having a pK range between 1 and 4.

[0234] The preferred method of fractionation is chromatography as follows:

The extract solution is fractionated in the cold room (4 degrees C) on a DEAE cellulose (Cellex-D) column 2.5x11.0 cm, which has been equilibrated with 0.005M phosphate buffer. Stepwise eluting solvent changes are made with the following solutions:

Solution 1 - 4.04 g. NaH_2P_04 and 0.5g NaH_2P_04 are dissolved in 15 litres of distilled water (0.005 molar, pH 7);

Solution 2 - 8.57 g. NaH_2P_04 is dissolved in 2,480 mL of distilled water;

Solution 3 - 17.1 g. of NaH_2P_04 is dissolved in 2480 ml of distilled water (0.05 molar, pH 4.7);

Solution 4 - 59.65 g. of NaH_2P_04 is dissolved in 2470 ml distilled water (0.175 molar);

Solution 5 - 101.6 g. of NaH_2P_04 is dissolved in 2455 ml distilled water (pH 4.3);

Solution 6 - 340.2 g. of NaH_2P_04 is dissolved in 2465 of distilled water (1.0 molar, pX-i 4.1);

Solution 7 - 283.63 g. of 80% phosphoric acid (H_3P_04) is made up in 2460 ml of distilled water (1.0 molar, pH 1.0).

[0235] The extract solution, in 6 to 10 ml volume, is passed onto the column and overlayed with Solution 1, and a reservoir of 300 ml of Solution 1 is attached and allowed to drip by gravity onto the column. Three ml aliquots of eluant are collected and analyzed for protein content at OD 280 until all of the protein to be removed with Solution 1 has been removed from the column. Solution 2 is then applied to the column, followed in succession by Solutions 3, 4, 5, 6 aid 7 until all

of the protein which can, be removed with each Solution is removed from the column. The eluates from Solution 7 are combined, dialyzed against phosphate buffer, the protein content determined of both dialysand and dialyzate, and both analyzed by gel electrophoresis. One or two bands of peptide or protein of molecular weight between 3,000 and 25,000 Daltons are obtained in Solution 7. For example the algae *Caulerpa mexicana*, *Laurencia obtusa*, *Cladophora prolifera*, *Sargassum natans*, *Caulerpa verticillata*, *Halimeda tuna*, and *Penicillus capitatus*, after extraction and treatment as above, all demonstrated in Solution 7 eluates sharp peptide bands in this molecular weight region with no contaminants. These Solution 7 proteins or their eluted bands are hydrolyzed, and the amino acid composition determined. The peptides so obtained, which have a lysine composition of 6% or greater are Replikin precursors. These Replikin peptide precursors are then determined for amino acid sequence and the Replikins are determined by hydrolysis and mass spectrometry as detailed in U.S. patent 6,242,578 B1. Those which fulfill the criteria defined by the "3-point-recognition" method are identified as Replikins. This procedure can also be applied to obtain yeast, bacterial and any plant Replikins.

b) Virus

[0236] Using the same extraction and column chromatography separation methods as above in a) for algae, Replikens in virus-infected cells are isolated and identified.

c) Tumor cells in vivo and in vitro tissue culture

[0237] Using the same extraction and column chromatography separation methods as above in a) for algae, Replikins in tumor cells are isolated and identified. For example, Replikin precursors of Astrocytin isolated from malignant brain tumors, Malignin (Aglyco IOB) isolated from glioblastoma tumor cells in tissue culture, MCF7 mammary carcinoma cells in tissue culture, and P3J Lymphoma cells in tissue culture each treated as above in a) yielded Replikin precursors with lysine content of 9.1%, 6.7%, 6.7%, and 6.5% respectively. Hydrolysis and mass spectrometry of Aglyco IOB as described in Example 10 U.S. 6,242,578 B1 produced the amino acid sequence, ykagvafllhkkndiide the 16-mer Replikin.

EXAMPLE 2:

[0238] As an example of diagnostic use of Replikins: Aglyco IOB or the 16-mer Replikin may be used as antigen to capture and quantify the amount of its corresponding antibody present in serum for diagnostic purposes are as shown in Figures 2,3,4 and 7 of U.S. 6,242,578 B1.

[0239] As an example of the production of agents to attach to Replikins for labeling, nutritional or destructive purposes: Injection of the 16-mer Replikin into rabbits to produce the specific antibody to the 16-mer Replikin is shown in Example 6 and Figures 9A and 9B of U.S. 6,242,578 B1.

[0240] As an example of the use of agents to label Replikins: The use of antibodies to the 16-mer Replikin to label specific cells which contain this Replikin is shown in Figure 5 and Example 6 of U.S. 6,242,578 B1.

5 [0241] As an example of the use of agents to destroy Replikins: The use of antibodies to the 16-mer Replikin to inhibit or destroy specific cells which contain this Replikin is shown in Figure 6 of U.S. 6,242,578 B1.

EXAMPLE 3

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[0242] Analysis of sequence data of isolates of influenza virus hemagglutinin protein or neuraminidase protein for the presence and concentration of Replikins is carried out by visual scanning of sequences or through use of a computer program based on the 3-point recognition system described herein. Isolates of influenza virus are obtained and the amino acid sequence of the influenza hemagglutinin and/or neuraminidase protein is obtained by any art known method, such as by sequencing the hemagglutinin or neuraminidase gene and deriving the protein sequence therefrom. Sequences are scanned for the presence of new Replikins, conservation of Replikins over time and concentration of Replikins in each isolate.

15

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Comparison of the Replikin sequences and concentrations to the amino acid sequences obtained from isolates at an earlier time, such as about six months to about three years earlier, provides data that are used to predict the emergence of strains that are most likely to be the cause of influenza in upcoming flu seasons, and that form the basis for seasonal influenza peptide vaccines or nucleic acid based vaccines. Observation of an increase in concentration, particularly a

25

stepwise increase in concentration of Replikins in a given strain of influenza virus for a period of about six months to about three years or more is a predictor of emergence of the strain as a likely cause of influenza epidemic or pandemic in the future.

5

[0243] Peptide vaccines or nucleic acid-based vaccines based on the Replikins observed in the emerging strain are generated. An emerging strain is identified as the strain of influenza virus having the highest increase in concentration of Replikin sequences within the hemagglutinin and/or neuraminidase sequence during the time period. Preferably, the peptide or nucleic acid vaccine is based on or includes any Replikin sequences that are observed to be conserved in the emerging strain. Conserved Replikins are preferably those Replikin sequences which are present in the hemagglutinin or neuraminidase protein sequence for about two years and preferably longer. The vaccines may include any combination of Replikin sequences identified in the emerging strain.

10

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[0244] For vaccine production, the Replikin peptide or peptides identified as useful for an effective vaccine are synthesized by any method, including chemical synthesis and molecular biology techniques, including cloning, expression in a host cell and purification therefrom. The peptides are preferably admixed with a pharmaceutically acceptable carrier in an amount determined to induce a therapeutic antibody reaction thereto. Generally, the dosage is about 0.1 μ g to about 10 mg.

20

[0245] The influenza vaccine is preferably administered to a patient in need thereof prior to the onset of "flu season." Influenza flu season generally occurs in late October and lasts through late April. However, the vaccine may be administered at any time during the year. Preferably, the influenza vaccine is administered once yearly, and is based on Replikin sequences observed to be present, and preferably conserved in the emerging strain of influenza virus. Another preferred Replikin for inclusion in an influenza vaccine is a Replikin demonstrated to have re-emerged in a strain of influenza after an absence of one or more years.

EXAMPLE 4

[0246] Analysis of sequence data of isolates of *Plasmodium falciparum* antigens for the presence and concentration of Replikins is carried out by visual scanning of sequences or through use of a computer program based on the 3-point recognition method described herein. Isolates of *Plasmodium falciparum* are obtained and the amino acid sequence of the protein is obtained by any art known method, such as by sequencing the gene and deriving the protein sequence therefrom. Sequences are scanned for the presence of Replikins, conservation of Replikins over time and concentration of Replikins in each isolate. This information provides data that are used to form the basis for anti-malarial peptide vaccines or nucleic acid based vaccines.

[0247] Peptide vaccines or nucleic acid-based vaccines based on the Replikins

observed in the malaria causing organism are generated. Preferably, the peptide or nucleic acid vaccine is based on or includes any Replikin sequences that are observed to be present on a surface antigen of the organism. The vaccines may include any combination of Replikin sequences identified in the malaria causing strain.

[0248] For vaccine production, the Replikin peptide or peptides identified as useful for an effective vaccine are synthesized by any method, including chemical synthesis and molecular biology techniques, including cloning, expression in a host cell and purification therefrom. The peptides are preferably admixed with a pharmaceutically acceptable carrier in an amount determined to induce a therapeutic antibody reaction thereto. Generally, the dosage is about 0.1 μ g to about 10 mg.

[0249] Then malaria vaccine is preferably administered to a patient in need thereof at any time during the year, and particularly prior to travel to a tropical environment.

[250] Another embodiment includes an antisense nucleic acid molecule complementary to the coding strand of the gene or the mRNA encoding organism for the replikins in organisms including, but not limited to, viruses, trypanosomes, bacteria, fungi, algae, amoeba, and plants, wherein said antisense nucleic acid molecules is complementary to a nucleotide sequence of a replikin containing organism.

Claims:

1. An antibody that specifically binds to a cancer-cell associated or transforming-associated peptide sequence having from 7 to about 50 amino acids and including:
 - (1) at least one lysine residue located at a first terminus of said peptide sequence and at least one lysine residue or at least one histidine residue located at a second terminus of said peptide sequence;
 - (2) a first lysine residue located six to ten residues from a second lysine residue;
 - (3) at least one histidine residue; and
 - (4) at least 6% lysine residues.
2. An antibody cocktail comprising a plurality of isolated antibodies of claim 1.
3. The antibody cocktail of claim 2, wherein the peptide sequence is a transforming-associated peptide sequence.
4. The antibody cocktail of claim 2, wherein the peptide sequence is a cancer-cell associated peptide sequence.
5. The isolated antibody of claim 1, wherein said peptide sequence is a transforming-associated peptide sequence.
6. The isolated antibody of claim 1, wherein said peptide sequence is a cancer-cell associated peptide sequence.
7. The isolated antibody of claim 6, wherein said cancer-cell associated peptide sequence is a glioma peptide sequence.
8. The isolated antibody of claim 1 wherein said peptide sequence comprises at least one peptide sequence of SEQ ID NO(s): 1 and 66-89.
9. The isolated antibody of claim 1, wherein said peptide sequence consists of one peptide sequence of SEQ ID NO(s): 1 and 66-89.
10. An isolated antibody that specifically binds to a peptide sequence of 7 to 50 amino acid residues comprising at least one of SEQ ID NO(s): 66-89.

SEQ.List.txt

SEQUENCE LISTING

<110> BOGOCH, SAMUEL
BOGOCH, ELENORE S.

<120> REPLIKIN PEPTIDES AND METHODS OF USE

<130> 09425/469765

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<141> 2002-07-09

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<151> 2002-03-26

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5

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5

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5

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SEQ.List.txt

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<213> Avian sarcoma virus

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<212> PRT

<213> Homo sapiens

<400> 50

Lys Lys Leu Arg His Asp Lys
1 5

<210> 51

<211> 7

<212> PRT

<213> Avian sarcoma virus

<400> 51

Lys Lys Leu Arg His Glu Lys
1 5

<210> 52

SEQ.List.txt

<211> 7

<212> PRT

<213> Homo sapiens

<400> 52

Lys Lys Leu Arg His Glu Lys

1 5

<210> 53

<211> 8

<212> PRT

<213> Homo sapiens

<400> 53

Lys Gln Ala His Glu Leu Ala Lys

1 5

<210> 54

<211> 8

<212> PRT

<213> Polyoma virus

<400> 54

Lys Thr His Arg Phe Ser Lys His

1 5

<210> 55

<211> 8

<212> PRT

<213> Sindbis virus

<400> 55

Lys Asn Leu His Glu Lys Ile Lys

1 5

<210> 56

<211> 9

<212> PRT

<213> Human papilloamavirus type 71

<400> 56

Lys His Arg Pro Leu Leu Gln Leu Lys

1 5

SEQ.List.txt

<210> 57
 <211> 7
 <212> PRT
 <213> Avian encephalomyelitis virus

<400> 57
 Lys Ser Pro Asn His Val Lys
 1 5

<210> 58
 <211> 8
 <212> PRT
 <213> Feline sarcoma virus

<400> 58
 Lys Asn Ile His Leu Glu Lys Lys
 1 5

<210> 59
 <211> 8
 <212> PRT
 <213> Homo sapiens

<400> 59
 Lys Asn Ile His Leu Glu Lys Lys
 1 5

<210> 60
 <211> 10
 <212> PRT
 <213> Polyoma virus

<400> 60
 Lys Pro His Leu Ala Gln Ser Leu Glu Lys
 1 5 10

<210> 61
 <211> 9
 <212> PRT
 <213> Polyoma virus

<400> 61
 Lys Gln His Arg Glu Leu Lys Asp Lys

SEQ.List.txt

1

5

<210> 62
 <211> 9
 <212> PRT
 <213> Polyoma virus

<400> 62
 Lys Gln His Arg Glu Leu Lys Asp Lys
 1 5

<210> 63
 <211> 12
 <212> PRT
 <213> Murine leukemia virus

<400> 63
 Lys Val Pro Val Leu Ile Ser Pro Thr Leu Lys His
 1 5 10

<210> 64
 <211> 13
 <212> PRT
 <213> Human T-cell lymphotropic virus type 2

<400> 64
 Lys Ser Leu Leu Leu Glu Val Asp Lys Asp Ile Ser His
 1 5 10

<210> 65
 <211> 13
 <212> PRT
 <213> Homo sapiens

<400> 65
 Lys Ala Gly Ile Thr Ile Met Val Lys Arg Glu Tyr His
 1 5 10

<210> 66
 <211> 8
 <212> PRT
 <213> Homo sapiens

SEQ.List.txt

<400> 66

Lys Ser Gly Lys His Leu Gly Lys

1

5

<210> 67

<211> 9

<212> PRT

<213> Homo sapiens

<400> 67

Lys Arg Arg Glu Gln Leu Lys His Lys

1

5

<210> 68

<211> 10

<212> PRT

<213> Homo sapiens

<400> 68

Lys Ser Phe Glu Val Ile Lys Val Ile His

1

5

10

<210> 69

<211> 8

<212> PRT

<213> Homo sapiens

<400> 69

Lys Lys Lys His Thr Val Lys Lys

1

5

<210> 70

<211> 9

<212> PRT

<213> Homo sapiens

<400> 70

Lys Ala Gln Lys Asp His Leu Ser Lys

1

5

<210> 71

<211> 10

<212> PRT

SEQ.List.txt

<213> Homo sapiens

<400> 71

His Leu Lys Arg Val Lys Asp Leu Lys Lys
1 5 10

<210> 72

<211> 11

<212> PRT

<213> Homo sapiens

<400> 72

Lys Tyr Gly Ser Pro Lys His Arg Leu Ile Lys
1 5 10

<210> 73

<211> 13

<212> PRT

<213> Papilloma virus type 11

<400> 73

Lys Leu Lys His Ile Leu Gly Lys Ala Arg Phe Ile Lys
1 5 10

<210> 74

<211> 12

<212> PRT

<213> Homo sapiens

<400> 74

Lys Gly Asp His Val Lys His Tyr Lys Ile Arg Lys
1 5 10

<210> 75

<211> 13

<212> PRT

<213> Homo sapiens

<400> 75

Lys Glu Lys Leu Arg Asp Val Met Val Asp Arg His Lys
1 5 10

<210> 76

SEQ.List.txt

<211> 15
 <212> PRT
 <213> Homo sapiens

<400> 76
 Lys Leu Gln Ala Arg Gln Gln Gln Leu Leu Lys Lys Ile Glu His
 1 5 10 15

<210> 77
 <211> 14
 <212> PRT
 <213> Homo sapiens

<400> 77
 Lys Lys Gly Asn Arg Val Ser Pro Thr Met Lys Val Thr His
 1 5 10

<210> 78
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 78
 Lys Glu Ile Pro Leu His Phe Arg Lys
 1 5

<210> 79
 <211> 8
 <212> PRT
 <213> Homo sapiens

<400> 79
 Lys Lys Lys Pro His Ile Lys Lys
 1 5

<210> 80
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 80
 Lys Thr Arg His Asp Pro Leu Ala Lys
 1 5

SEQ.List.txt

<210> 81
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 81
 Lys His His Pro Lys Asp Asn Leu Ile Lys
 1 5 10

<210> 82
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 82
 Lys His Lys Arg Lys Lys Phe Arg Gln Lys
 1 5 10

<210> 83
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 83
 Lys Ala Gly Val Ala Phe Leu His Lys Lys
 1 5 10

<210> 84
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 84
 Lys His Lys Arg Lys Lys Phe Arg Gln Lys
 1 5 10

<210> 85
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 85
 Lys Lys Lys Ser Lys Lys His Lys Asp Lys

SEQ.List.txt

1 5 10

<210> 86
 <211> 11
 <212> PRT
 <213> Homo sapiens

<400> 86
 His Lys Ser Glu Lys Pro Ala Leu Pro Arg Lys
 1 5 10

<210> 87
 <211> 14
 <212> PRT
 <213> Homo sapiens

<400> 87
 Lys Lys Lys Lys Pro Ser Arg Leu Lys Gly Asp Asn Glu Lys
 1 5 10

<210> 88
 <211> 16
 <212> PRT
 <213> Homo sapiens

<400> 88
 Lys Thr Lys Lys Gly Asn Arg Val Ser Pro Thr Met Lys Val Thr His
 1 5 10 15

<210> 89
 <211> 18
 <212> PRT
 <213> Homo sapiens

<400> 89
 Lys His Lys Glu Lys Met Ser Lys Asp Gly Lys Lys Lys Lys Lys Lys
 1 5 10 15

Ser Lys

<210> 90
 <211> 9
 <212> PRT

SEQ.List.txt

<213> Legionella sp:

<400> 90

Lys Ile His Leu Ile Ser Val Lys Lys
1 5

<210> 91

<211> 10

<212> PRT

<213> Bacillus anthracis

<400> 91

His Val Lys Lys Glu Lys Glu Lys Asn Lys
1 5 10

<210> 92

<211> 9

<212> PRT

<213> Bacillus anthracis

<400> 92

Lys His Ile Val Lys Ile Glu Val Lys
1 5

<210> 93

<211> 16

<212> PRT

<213> Bacillus anthracis

<400> 93

Lys Lys Lys Lys Ile Lys Asp Ile Tyr Gly Lys Asp Ala Leu Leu His
1 5 10 15

<210> 94

<211> 8

<212> PRT

<213> Bacillus anthracis

<400> 94

Lys Trp Glu Lys Ile Lys Gln His
1 5

<210> 95

SEQ.List.txt

<211> 18
 <212> PRT
 <213> Bacillus anthracis

<400> 95
 Lys Lys Leu Gln Ile Pro Pro Pro Ile Glu Pro Lys Lys Asp Asp Ile
 1 5 10 15

Ile His

<210> 96
 <211> 31
 <212> PRT
 <213> Bacillus anthracis

<400> 96
 His Asn Arg Tyr Ala Ser Asn Ile Val Glu Ser Ala Tyr Leu Leu Ile
 1 5 10 15

Leu Asn Glu Trp Lys Asn Asn Ile Gln Ser Asp Leu Ile Lys Lys
 20 25 30

<210> 97
 <211> 24
 <212> PRT
 <213> Bacillus anthracis

<400> 97
 His Ala Val Asp Asp Tyr Ala Gly Tyr Leu Leu Asp Lys Asn Gln Ser
 1 5 10 15

Asp Leu Val Thr Asn Ser Lys Lys
 20

<210> 98
 <211> 13
 <212> PRT
 <213> Bacillus anthracis

<400> 98
 His Ala Glu Arg Leu Lys Val Gln Lys Asn Ala Pro Lys
 1 5 10

<210> 99

SEQ.List.txt

<211> 10
 <212> PRT
 <213> Variola virus

<400> 99
 Lys His Tyr Asn Asn Ile Thr Trp Tyr Lys
 1 5 10

<210> 100
 <211> 12
 <212> PRT
 <213> Variola virus

<400> 100
 Lys Tyr Ser Gln Thr Gly Lys Glu Leu Ile Ile His
 1 5 10

<210> 101
 <211> 17
 <212> PRT
 <213> Variola virus

<400> 101
 His Tyr Asp Asp Val Arg Ile Lys Asn Asp Ile Val Val Ser Arg Cys
 1 5 10 15

Lys

<210> 102
 <211> 11
 <212> PRT
 <213> Variola virus

<400> 102
 His Arg Phe Lys Leu Ile Leu Asp Ser Lys Ile
 1 5 10

<210> 103
 <211> 11
 <212> PRT
 <213> Variola virus

<400> 103
 Lys Glu Arg Gly His Asn Tyr Tyr Phe Glu Lys

SEQ.List.txt

1	5	10
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<210> 104
 <211> 8
 <212> PRT
 <213> Influenza B virus

<400> 104
 Lys Ser His Phe Ala Asn Leu Lys
 1 5

<210> 105
 <211> 11
 <212> PRT
 <213> Influenza B virus

<400> 105
 Lys Ser His Phe Ala Asn Leu Lys Gly Thr Lys
 1 5 10

<210> 106
 <211> 19
 <212> PRT
 <213> Influenza B virus

<400> 106
 Lys Ser His Phe Ala Asn Leu Lys Gly Thr Lys Thr Arg Gly Lys Leu
 1 5 10 15

Cys Pro Lys

<210> 107
 <211> 9
 <212> PRT
 <213> Influenza B virus

<400> 107
 His Glu Lys Tyr Gly Gly Leu Asn Lys
 1 5

<210> 108
 <211> 11
 <212> PRT

SEQ.List.txt

<213> Influenza B virus

<400> 108

His Glu Lys Tyr Gly Gly Leu Asn Lys Ser Lys
1 5 10

<210> 109

<211> 20

<212> PRT

<213> Influenza B virus

<400> 109

His Glu Lys Tyr Gly Gly Leu Asn Lys Ser Lys Pro Tyr Tyr Thr Gly
1 5 10 15

Glu His Ala Lys
20

<210> 110

<211> 13

<212> PRT

<213> Influenza B virus

<400> 110

His Ala Lys Ala Ile Gly Asn Cys Pro Ile Trp Val Lys
1 5 10

<210> 111

<211> 23

<212> PRT

<213> Influenza B virus

<400> 111

His Ala Lys Ala Ile Gly Asn Cys Pro Ile Trp Val Lys Thr Pro Leu
1 5 10 15

Lys Leu Ala Asn Gly Thr Lys
20

<210> 112

<211> 29

<212> PRT

<213> Influenza B virus

SEQ.List.txt

<400> 112

His Ala Lys Ala Ile Gly Asn Cys Pro Ile Trp Val Lys Thr Pro Leu
1 5 10 15

Lys Leu Ala Asn Gly Thr Lys Tyr Arg Pro Pro Ala Lys
20 25

<210> 113

<211> 32

<212> PRT

<213> Influenza B virus

<400> 113

His Ala Lys Ala Ile Gly Asn Cys Pro Ile Trp Val Lys Thr Pro Leu
1 5 10 15

Lys Leu Ala Asn Gly Thr Lys Tyr Arg Pro Pro Ala Lys Leu Leu Lys
20 25 30

<210> 114

<211> 13

<212> PRT

<213> Influenza B virus

<400> 114

His Phe Ala Asn Leu Lys Gly Thr Lys Thr Arg Gly Lys
1 5 10

<210> 115

<211> 17

<212> PRT

<213> Influenza B virus

<400> 115

His Phe Ala Asn Leu Lys Gly Thr Lys Thr Arg Gly Lys Leu Cys Pro
1 5 10 15

Lys

<210> 116

<211> 16

<212> PRT

<213> Influenza B virus

SEQ.List.txt

<400> 116

His Ser Asp Asn Glu Ile Gln Met Val Lys Leu Tyr Gly Asp Ser Lys
1 5 10 15

<210> 117

<211> 21

<212> PRT

<213> Influenza B virus

<400> 117

His Ser Asp Asn Glu Ile Gln Asp Lys Met Val Lys Leu Tyr Gly Asp
1 5 10 15

Ser Lys Pro Gln Lys
20

<210> 118

<211> 19

<212> PRT

<213> Influenza B virus

<400> 118

His Ser Asp Asn Glu Ile Gln Met Val Lys Leu Tyr Gly Asp Ser Lys
1 5 10 15

Pro Gln Lys

<210> 119

<211> 9

<212> PRT

<213> Influenza B virus

<220>

<221> MOD_RES

<222> (2)

<223> ala or val

<400> 119

Lys Xaa Ser Ile Leu His Glu Val Lys
1 5

<210> 120

<211> 15

<212> PRT

SEQ.List.txt

<213> Influenza B virus

<400> 120

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

<210> 121

<211> 18

<212> PRT

<213> Influenza B virus

<400> 121

Lys	Cys	Thr	Gly	Thr	Ile	Pro	Ser	Ala	Lys	Ala	Ser	Ile	Leu	His	Glu
1				5					10					15	

Val Lys

<210> 122

<211> 16

<212> PRT

<213> Influenza B virus

<400> 122

Lys	Tyr	Gly	Gly	Leu	Asn	Lys	Ser	Lys	Pro	Tyr	Tyr	Thr	Gly	Glu	His
1				5					10					15	

<210> 123

<211> 26

<212> PRT

<213> Influenza B virus

<400> 123

Lys	Val	Trp	Cys	Ala	Ser	Gly	Arg	Ser	Lys	Val	Ile	Lys	Gly	Ser	Leu
1				5					10					15	

Pro	Leu	Ile	Gly	Glu	Ala	Asp	Cys	Leu	His
			20					25	

<210> 124

<211> 10

<212> PRT

<213> Influenza B virus

<400> 124

SEQ.List.txt

Lys Pro Tyr Tyr Thr Gly Glu His Ala Lys
1 5 10

<210> 125
<211> 18
<212> PRT
<213> Influenza B virus

<400> 125
Lys Cys Met Gly Thr Ile Pro Ser Ala Lys Ala Ser Ile Leu His Glu
1 5 10 15

Val Lys

<210> 126
<211> 15
<212> PRT
<213> Influenza B virus

<400> 126
His Asn Val Ile Asn Ala Glu Lys Ala Pro Gly Gly Pro Tyr Lys
1 5 10 15

<210> 127
<211> 16
<212> PRT
<213> Influenza B virus

<400> 127
His Ser Asp Asn Glu Thr Gln Met Ala Lys Leu Tyr Gly Asp Ser Lys
1 5 10 15

<210> 128
<211> 18
<212> PRT
<213> Influenza B virus

<400> 128
His Gly Val Ala Val Ala Ala Asp Leu Lys Ser Thr Gln Glu Ala Ile
1 5 10 15

Asn Lys

SEQ.List.txt

<210> 129

<211> 29

<212> PRT

<213> Influenza B virus

<400> 129

His Gly Val Ala Val Ala Ala Asp Leu Lys Ser Thr Gln Glu Ala Ile
1 5 10 15

Asn Lys Asp Thr Ile Ser Thr Gln Glu Ala Ile Asn Lys
20 25

<210> 130

<211> 21

<212> PRT

<213> Influenza B virus

<400> 130

Lys Leu Tyr Gly Asp Ser Lys Pro Gln Lys Phe Thr Ser Ser Ala Asn
1 5 10 15

Gly Val Thr Thr His
20

<210> 131

<211> 19

<212> PRT

<213> Influenza B virus

<400> 131

His Ser Asp Asn Glu Thr Gln Met Ala Lys Leu Tyr Gly Asp Ser Lys
1 5 10 15

Pro Gln Lys

<210> 132

<211> 13

<212> PRT

<213> Influenza B virus

<400> 132

His Phe Ala Asn Leu Lys Gly Thr Gln Thr Arg Gly Lys
1 5 10

SEQ.List.txt

<210> 133

<211> 12

<212> PRT

<213> Influenza B virus

<400> 133

Lys Pro Arg Ser Ala Leu Lys Cys Lys Gly Phe His
1 5 10

<210> 134

<211> 22

<212> PRT

<213> Influenza B virus

<220>

<221> MOD_RES

<222> (15)

<223> gly or ala

<400> 134

Lys Ser Lys Pro Tyr Tyr Thr Gly Glu His Ala Lys Ala Ile Xaa Asn
1 5 10 15

Cys Pro Ile Trp Val Lys
20

<210> 135

<211> 16

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (3)

<223> val or ile

<220>

<221> MOD_RES

<222> (13)

<223> arg or lys

<220>

<221> MOD_RES

<222> (14)

<223> ser or thr

SEQ.List.txt

<220>
 <221> MOD RES
 <222> (15)
 <223> thr or ala

<400> 135
 His Pro Xaa Thr Ile Gly Glu Cys Pro Lys Tyr Val Xaa Xaa Xaa Lys
 1 5 10 15

<210> 136
 <211> 21
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD RES
 <222> (10)
 <223> glu or gly

<220>
 <221> MOD RES
 <222> (13)
 <223> lys or arg

<220>
 <221> MOD RES
 <222> (14)
 <223> asn or ser

<220>
 <221> MOD RES
 <222> (17)
 <223> lys or arg

<400> 136
 His Asp Ser Asn Val Lys Asn Leu Tyr Xaa Lys Val Xaa Xaa Gln Leu
 1 5 10 15

Xaa Asn Asn Ala Lys
 20

<210> 137
 <211> 17
 <212> PRT
 <213> Influenza virus

SEQ.List.txt

<220>
 <221> MOD_RES
 <222> (10)
 <223> glu or gly

<220>
 <221> MOD_RES
 <222> (13)
 <223> lys or arg

<220>
 <221> MOD_RES
 <222> (14)
 <223> asn or ser

<400> 137
 His Asp Ser Asn Val Lys Asn Leu Tyr Xaa Lys Val Xaa Xaa Gln Leu
 1 5 10 15

Lys

<210> 138
 <211> 36
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (4)..(5)
 <223> asn or asp

<220>
 <221> MOD_RES
 <222> (6)
 <223> ala, thr or glu

<220>
 <221> MOD_RES
 <222> (12)
 <223> arg or lys

<220>
 <221> MOD_RES
 <222> (31)
 <223> glu or lys

SEQ.List.txt

<400> 138

His Lys Cys Xaa Xaa Xaa Cys Met Glu Ser Val Xaa Asn Gly Thr Tyr
1 5 10 15

Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys Leu Asn Arg Glu Xaa Ile
20 25 30

Asp Gly Val Lys
35

<210> 139

<211> 26

<212> PRT

<213> Influenza virus

<220>

<221> MOD RES

<222> (4) (5)

<223> asn or asp

<220>

<221> MOD RES

<222> (6)

<223> ala, thr or glu

<220>

<221> MOD RES

<222> (12)

<223> arg or lys

<400> 139

His Lys Cys Xaa Xaa Xaa Cys Met Glu Ser Val Xaa Asn Gly Thr Tyr
1 5 10 15

Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys
20 25

<210> 140

<211> 50

<212> PRT

<213> Influenza virus

<220>

<221> MOD RES

<222> (4)

<223> glu or gly

SEQ.List.txt

<220>

<221> MOD RES

<222> (21)

<223> asp or asn

<400> 140

His Gln Asn Xaa Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15

Gln Asn Ala Ile Xaa Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
20 25 30

Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys Glu Phe Asn Lys Leu
35 40 45

Glu Lys
50

<210> 141

<211> 33

<212> PRT

<213> Influenza virus

<220>

<221> MOD RES

<222> (4)

<223> glu or gly

<220>

<221> MOD RES

<222> (21)

<223> asp or asn

<400> 141

His Gln Asn Xaa Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15

Gln Asn Ala Ile Xaa Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
20 25 30

Lys

<210> 142

<211> 26

<212> PRT

SEQ.List.txt

<213> Influenza virus

<220>

<221> MOD_RES

<222> (4)

<223> glu or gly

<220>

<221> MOD_RES

<222> (21)

<223> asp or asn

<400> 142

His Gln Asn Xaa Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15

Gln Asn Ala Ile Xaa Gly Ile Thr Asn Lys
20 25

<210> 143

<211> 14

<212> PRT

<213> Influenza virus

<400> 143

Lys Phe Glu Ile Phe Pro Lys Thr Ser Ser Trp Pro Asn His
1 5 10

<210> 144

<211> 27

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (3)

<223> asn, ser or thr

<220>

<221> MOD_RES

<222> (9)

<223> asn or ser

<220>

<221> MOD_RES

<222> (13)

SEQ.List.txt

<223> val or thr

<400> 144

Lys Gly Xaa Ser Tyr Pro Lys Leu Xaa Lys Ser Tyr Xaa Asn Asn Lys
1 5 10 15

Gly Lys Glu Val Leu Val Leu Trp Gly Val His
20 25

<210> 145

<211> 18

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (4)

<223> val or thr

<400> 145

Lys Ser Tyr Xaa Asn Asn Lys Gly Lys Glu Val Leu Val Leu Trp Gly
1 5 10 15

Val His

<210> 146

<211> 36

<212> PRT

<213> Influenza virus

<400> 146

His Lys Cys Asn Asn Glu Cys Met Glu Ser Val Lys Asn Gly Thr Tyr
1 5 10 15

Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys Leu Asn Arg Glu Lys Ile
20 25 30

Asp Gly Val Lys
35

<210> 147

<211> 26

<212> PRT

<213> Influenza virus

SEQ.List.txt

<400> 147

His Lys Cys Asn Asn Glu Cys Met Glu Ser Val Lys Asn Gly Thr Tyr
1 5 10 15

Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys
20 25

<210> 148

<211> 20

<212> PRT

<213> Influenza virus

<400> 148

His Lys Cys Asn Asn Glu Cys Met Glu Ser Val Lys Asn Gly Thr Tyr
1 5 10 15

Asp Tyr Pro Lys
20

<210> 149

<211> 12

<212> PRT

<213> Influenza virus

<400> 149

His Lys Cys Asn Asn Glu Cys Met Glu Ser Val Lys
1 5 10

<210> 150

<211> 34

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (9)

<223> lys or arg

<220>

<221> MOD_RES

<222> (16)

<223> glu or gly

<400> 150

His Asn Gly Lys Ser Ser Phe Tyr Xaa Asn Leu Leu Trp Leu Thr Xaa

SEQ.List.txt

1 5 10 15
 Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys Ser Tyr Val Asn Asn Lys
 20 25 30

Glu Lys

<210> 151
 <211> 32
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (9)
 <223> lys or arg--

<220>
 <221> MOD_RES
 <222> (16)
 <223> glu or gly

<400> 151
 His Asn Gly Lys Ser Ser Phe Tyr Xaa Asn Leu Leu Trp Leu Thr Xaa
 1 5 10 15

Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys Ser Tyr Val Asn Asn Lys
 20 25 30

<210> 152
 <211> 26
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (9)
 <223> lys or arg

<220>
 <221> MOD_RES
 <222> (16)
 <223> glu or gly

<400> 152
 His Asn Gly Lys Ser Ser Phe Tyr Xaa Asn Leu Leu Trp Leu Thr Xaa

SEQ.List.txt

1 5 10 15
 Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys
 20 25

<210> 153
 <211> 17
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (9)
 <223> lys or arg

<220>
 <221> MOD_RES
 <222> (16)
 <223> glu or gly

<400> 153
 His Asn Gly Lys Ser Ser Phe Tyr Xaa Asn Leu Leu Trp Leu Thr Xaa
 1 5 10 15

Lys

<210> 154
 <211> 40
 <212> PRT
 <213> Influenza virus

<400> 154
 Lys Ser Ser Phe Tyr Lys Asn Leu Leu Trp Leu Thr Glu Lys Asn Gly
 1 5 10 15

Leu Tyr Pro Asn Leu Ser Lys Ser Tyr Val Asn Asn Lys Glu Lys Glu
 20 25 30

Val Leu Val Leu Trp Gly Val His
 35 40

<210> 155
 <211> 35
 <212> PRT
 <213> Influenza virus

SEQ.List.txt

<400> 155

Lys Asn Leu Leu Trp Leu Thr Glu Lys Asn Gly Leu Tyr Pro Asn Leu
 1 5 10 15
 Ser Lys Ser Tyr Val Asn Asn Lys Glu Lys Glu Val Leu Val Leu Trp
 20 25 30
 Gly Val His
 35

<210> 156

<211> 27

<212> PRT

<213> Influenza virus

<400> 156

Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys Ser Tyr Val Asn Asn Lys
 1 5 10 15
 Glu Lys Glu Val Leu Val Leu Trp Gly Val His
 20 25

<210> 157

<211> 18

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (4)

<223> val or ala

<220>

<221> MOD_RES

<222> (12)

<223> lys or not present

<220>

<221> MOD_RES

<222> (13)

<223> val or not present

<400> 157

Lys Ser Tyr Xaa Asn Asn Lys Glu Lys Glu Val Xaa Xaa Leu Trp Gly
 1 5 10 15

SEQ.List.txt

Val His

<210> 158
 <211> 12
 <212> PRT
 <213> Influenza virus

<400> 158
 Lys Glu Ser Ser Trp Pro Asn His Thr Val Thr Lys
 1 5 10

<210> 159
 <211> 44
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (4)
 <223> thr or asn

<400> 159
 His Glu Thr Xaa Lys Gly Val Thr Ala Ala Cys Pro Tyr Ala Gly Ala
 1 5 10 15

Ser Ser Phe Tyr Arg Asn Leu Leu Trp Leu Val Lys Lys Glu Asn Ser
 20 25 30

Tyr Pro Lys Leu Ser Lys Ser Tyr Val Asn Asn Lys
 35 40

<210> 160
 <211> 38
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (4)
 <223> thr or asn

<400> 160
 His Glu Thr Xaa Lys Gly Val Thr Ala Ala Cys Pro Tyr Ala Gly Ala
 1 5 10 15

SEQ.List.txt

Ser Ser Phe Tyr Arg Asn Leu Leu Trp Leu Val Lys Lys Glu Asn Ser
20 25 30

Tyr Pro Lys Leu Ser Lys
35

<210> 161

<211> 22

<212> PRT

<213> Influenza virus

<400> 161

Lys Phe Glu Ile Phe Pro Lys Thr Ser Ser Trp Pro Asn Glu Val Leu
1 5 10 15

Val Leu Trp Gly Val His
20

<210> 162

<211> 8

<212> PRT

<213> Influenza virus

<400> 162

Lys Glu Arg Ser Trp Pro Lys His
1 5

<210> 163

<211> 21

<212> PRT

<213> Influenza virus

<400> 163

Lys Leu Ser Lys Ser Tyr Val Asn Asn Lys Glu Lys Glu Val Leu Val
1 5 10 15

Leu Trp Gln Val His
20

<210> 164

<211> 15

<212> PRT

<213> Influenza virus

SEQ.List.txt

<400> 164

Lys Asn Asn Lys Glu Lys Glu Val Leu Val Leu Trp Gln Val His
 1 5 10 15

<210> 165

<211> 34

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (2)

<223> lys or asn

<220>

<221> MOD_RES

<222> (3)

<223> gly or gln

<220>

<221> MOD_RES

<222> (9)

<223> arg or lys

<220>

<221> MOD_RES

<222> (20)

<223> lys or ser

<220>

<221> MOD_RES

<222> (23)

<223> asn or thr

<400> 165

His Xaa Xaa Lys Ser Ser Phe Tyr Xaa Asn Leu Leu Trp Leu Thr Glu
 1 5 10 15

Lys Asn Gly Xaa Tyr Pro Xaa Leu Ser Lys Ser Tyr Ala Asn Asn Lys
 20 25 30

Glu Lys

<210> 166

<211> 17

SEQ.List.txt

<212> PRT
<213> Influenza virus

<220>
<221> MOD_RES
<222> (2)
<223> lys or asn

<220>
<221> MOD_RES
<222> (3)
<223> gly or gln

<220>
<221> MOD_RES
<222> (9)
<223> arg or lys

<400> 166
His Xaa Xaa Lys Ser Ser Phe Tyr Xaa Asn Leu Leu Trp Leu Thr Glu
1 5 10 15

Lys

<210> 167
<211> 9
<212> PRT
<213> Influenza virus

<400> 167
His Ala Lys Lys Ser Ser Phe Tyr Lys
1 5

<210> 168
<211> 11
<212> PRT
<213> Influenza virus

<400> 168
His Asn Gly Lys Leu Cys Arg Leu Lys Gly Lys
1 5 10

<210> 169
<211> 9
<212> PRT

SEQ.List.txt

<213> Influenza virus

<220>

<221> MOD_RES

<222> (7)

<223> gln or gly

<400> 169

His Tyr Lys Leu Asn Asn Xaa Lys Lys

1

5

<210> 170

<211> 25

<212> PRT

<213> Influenza virus

<400> 170

His Asp Ile Tyr Arg Asp Glu Ala Ile Asn Asn Arg Phe Gln Ile Gln

1

5

10

15

Gly Val Lys Leu Thr Gln Gly Tyr Lys

20

25

<210> 171

<211> 11

<212> PRT

<213> Influenza virus

<400> 171

Lys Gly Asn Gly Cys Phe Glu Ile Phe His Lys

1

5

10

<210> 172

<211> 18

<212> PRT

<213> Influenza virus

<400> 172

Lys Leu Asn Arg Leu Ile Glu Lys Thr Asn Asp Lys Tyr His Gln Ile

1

5

10

15

Glu Lys

<210> 173

SEQ.List.txt

<211> 14
 <212> PRT
 <213> Influenza virus

<400> 173
 Lys Leu Asn Arg Leu Ile Glu Lys Thr Asn Asp Lys Tyr His
 1 5 10

<210> 174
 <211> 13
 <212> PRT
 <213> Influenza virus

<400> 174
 Lys Cys His Thr Asp Lys Gly Ser Leu Ser Thr Thr Lys
 1 5 10

<210> 175
 <211> 16
 <212> PRT
 <213> Influenza virus

<400> 175
 Lys Ile Asn Asn Gly Asp Tyr Ala Lys Leu Tyr Ile Trp Gly Val His
 1 5 10 15

<210> 176
 <211> 17
 <212> PRT
 <213> Influenza virus

<400> 176
 His Asn Gly Lys Leu Cys Arg Lys Gly Ile Ala Pro Leu Gln Leu Gly
 1 5 10 15

Lys

<210> 177
 <211> 38
 <212> PRT
 <213> Influenza virus

<400> 177
 His Glu Thr Asn Arg Gln Val Thr Ala Ala Cys Pro Tyr Ala Gly Ala

SEQ.List.txt

1

5

10

15

Asn Ser Phe Phe Arg Asn Leu Ile Trp Leu Val Lys Lys Glu Ser Ser
20 25 30

Tyr Pro Lys Leu Ser Lys
35

<210> 178

<211> 35

<212> PRT

<213> Influenza virus

<400> 178

His Glu Thr Asn Arg Gln Val Thr Ala Ala Cys Pro Tyr Ala Gly Ala
1 5 10 15

Asn Ser Phe Phe Arg Asn Leu Ile Trp Leu Val Lys Lys Glu Ser Ser
20 25 30

Tyr Pro Lys
35

<210> 179

<211> 31

<212> PRT

<213> Influenza virus

<400> 179

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

Ala Tyr Ile Phe Val Gly Ser Ser Lys Tyr Asn Arg Lys Phe Lys
20 25 30

<210> 180

<211> 35

<212> PRT

<213> Influenza virus

<400> 180

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

Ala Tyr Ile Phe Val Gly Ser Ser Lys Tyr Asn Arg Lys Phe Lys Pro

SEQ.List.txt

20

25

30

Glu Ile Ala

35

<210> 181

<211> 25

<212> PRT

<213> Influenza virus

<400> 181

His Asp Ile Tyr Arg Asp Glu Ala Ile Asn Asn Arg Phe Gln Ile Gln
1 5 10 15

Gly Val Lys Ile Thr Gln Gly Tyr Lys
20 25

<210> 182

<211> 43

<212> PRT

<213> Influenza virus

<400> 182

His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15

Gln Asn Ala Ile Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
20 25 30

Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys
35 40

<210> 183

<211> 33

<212> PRT

<213> Influenza virus

<400> 183

His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15

Gln Asn Ala Ile Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
20 25 30

Lys

SEQ.List.txt

<210> 184
 <211> 50
 <212> PRT
 <213> Influenza virus

<400> 184
 His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
 1 5 10 15
 Gln Asn Ala Ile Asn Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
 20 25 30
 Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys Glu Phe Asn Lys Leu
 35 40 45
 Glu Lys
 50

<210> 185
 <211> 18
 <212> PRT
 <213> Influenza virus

<400> 185
 His Asn Gly Lys Leu Cys Arg Leu Lys Gly Ile Ala Pro Leu Gln Leu
 1 5 10 15
 Gly Lys

<210> 186
 <211> 12
 <212> PRT
 <213> Influenza virus

<400> 186
 His Lys Cys Asn Asn Glu Cys Met Glu Ser Val Lys
 1 5 10

<210> 187
 <211> 14
 <212> PRT
 <213> Influenza virus

SEQ.List.txt

<400> 187

Lys Phe Glu Ile Phe Pro Lys Ala Ser Ser Trp Pro Asn His
1 5 10

<210> 188

<211> 21

<212> PRT

<213> Influenza virus

<400> 188

His Asp Ser Asn Val Lys Asn Leu Tyr Glu Lys Val Arg Ser Gln Leu
1 5 10 15

Arg Asn Asn Ala Lys
20

<210> 189

<211> 22

<212> PRT

<213> Influenza virus

<400> 189

Lys Val Asn Ser Val Ile Lys Lys Met Asn Thr Gln Phe Ala Ala Val
1 5 10 15

Gly Lys Glu Phe Asn His
20

<210> 190

<211> 8

<212> PRT

<213> Influenza virus

<400> 190

Lys His Asn Gly Lys Leu Cys Lys
1 5

<210> 191

<211> 28

<212> PRT

<213> Influenza virus

<400> 191

Lys Lys Gly Thr Ser Tyr Pro Lys Leu Ser Lys Ser Tyr Thr His Asn

SEQ.List.txt

1

5

10

15

Lys Gly Lys Glu Val Leu Val Leu Trp Gly Val His
20 25

<210> 192

<211> 27

<212> PRT

<213> Influenza virus

<400> 192

Lys Gly Thr Ser Tyr Pro Lys Leu Ser Lys Ser Tyr Thr His Asn Lys
1 5 10 15

Gly Lys Glu Val Leu Val Leu Trp Gly Val His
20 25

<210> 193

<211> 21

<212> PRT

<213> Influenza virus

<400> 193

Lys Leu Ser Lys Ser Tyr Thr His Asn Lys Gly Lys Glu Val Leu Val
1 5 10 15

Leu Trp Gly Val His
20

<210> 194

<211> 18

<212> PRT

<213> Influenza virus

<400> 194

Lys Ser Tyr Thr His Asn Lys Gly Lys Glu Val Leu Val Leu Trp Gly
1 5 10 15

Val His

<210> 195

<211> 10

<212> PRT

<213> Influenza virus

SEQ.List.txt

<400> 195

Lys Gly Val Thr Ala Ser Cys Ser His Lys
1 5 10

<210> 196

<211> 34

<212> PRT

<213> Influenza virus

<400> 196

Lys Gly Val Thr Ala Ser Cys Ser His Lys Gly Arg Ser Ser Phe Tyr
1 5 10 15

Arg Asn Leu Leu Trp Leu Thr Glu Lys Asn Gly Leu Tyr Pro Asn Leu
20 25 30

Ser Lys

<210> 197

<211> 27

<212> PRT

<213> Influenza virus

<400> 197

Lys Gly Asn Ser Tyr Pro Lys Leu Ser Lys Ser Tyr Val Asn Asn Lys
1 5 10 15

Glu Lys Glu Val Leu Val Leu Trp Gly Ile His
20 25

<210> 198

<211> 8

<212> PRT

<213> Influenza virus

<400> 198

Lys Glu Phe Asn His Leu Glu Lys
1 5

<210> 199

<211> 39

<212> PRT

<213> Influenza virus

SEQ.List.txt

<400> 199

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

Ala Tyr Val Phe Val Gly Ser Ser Lys Tyr Asn Lys Lys Phe Lys Pro
20 25 30

Glu Ile Ala Thr Arg Pro Lys
35

<210> 200

<211> 31

<212> PRT

<213> Influenza virus

<400> 200

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

Ala Tyr Val Phe Val Gly Ser Ser Lys Tyr Asn Lys Lys Phe Lys
20 25 30

<210> 201

<211> 31

<212> PRT

<213> Influenza virus

<400> 201

His Glu Gly Lys Ser Ser Phe Tyr Arg Asn Leu Leu Trp Leu Thr Glu
1 5 10 15

Lys Glu Gly Ser Tyr Pro Lys Leu Lys Asn Ser Tyr Val Asn Lys
20 25 30

<210> 202

<211> 23

<212> PRT

<213> Influenza virus

<400> 202

His Glu Gly Lys Ser Ser Phe Tyr Arg Asn Leu Leu Trp Leu Thr Glu
1 5 10 15

Lys Glu Gly Ser Tyr Pro Lys

<210> 203
 <211> 26
 <212> PRT
 <213> Influenza virus

<400> 203
 His Lys Cys Asp Asn Glu Cys Met Glu Ser Val Arg Asn Gly Thr Tyr
 1 5 10 15
 Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys
 20 25

<210> 204
 <211> 12
 <212> PRT
 <213> Influenza virus

<400> 204
 Lys Glu Ser Ser Trp Pro Asn His Thr Val Thr Lys
 1 5 10

<210> 205
 <211> 35
 <212> PRT
 <213> Influenza virus

<400> 205
 Lys Asn Leu Leu Trp Leu Thr Glu Lys Asn Gly Leu Tyr Pro Asn Leu
 1 5 10 15
 Ser Lys Ser Tyr Val Asn Asn Lys Glu Lys Glu Ile Leu Val Leu Trp
 20 25 30

Gly Val His
 35

<210> 206
 <211> 27
 <212> PRT
 <213> Influenza virus

<220>

SEQ.List.txt

<221> MOD_RES
<222> (9)
<223> lys or met

<220>
<221> MOD_RES
<222> (10)
<223> asn or not present

<220>
<221> MOD_RES
<222> (16)
<223> glu or gly

<220>
<221> MOD_RES
<222> (17)
<223> not present or lys

<400> 206
His Asn Gly Lys Ser Ser Phe Tyr Xaa Xaa Leu Leu Trp Leu Thr Xaa
1 5 10 15

Xaa Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys
20 25

<210> 207
<211> 17
<212> PRT
<213> Influenza virus

<400> 207
His Asn Gly Lys Ser Ser Phe Tyr Lys Asn Leu Leu Trp Leu Thr Glu
1 5 10 15

Lys

<210> 208
<211> 55
<212> PRT
<213> Influenza virus

<400> 208
His Thr Val Thr Lys Gly Val Thr Ala Ser Cys Ser His Asn Gly Lys
1 5 10 15

SEQ.List.txt

Ser Ser Phe Tyr Lys Asn Leu Leu Trp Leu Thr Glu Lys Asn Gly Leu
20 25 30

Tyr Pro Asn Leu Ser Lys Ser Tyr Val Asn Asn Lys Glu Lys Glu Val
35 40 45

Leu Val Leu Trp Gly Val His
50 55

<210> 209
<211> 38
<212> PRT
<213> Influenza virus

<220>
<221> MOD_RES
<222> (5)
<223> lys or gly

<220>
<221> MOD_RES
<222> (8)
<223> thr or ser

<220>
<221> MOD_RES
<222> (21)
<223> lys or met

<220>
<221> MOD_RES
<222> (22)
<223> asn or not present

<220>
<221> MOD_RES
<222> (28)
<223> glu or gly

<220>
<221> MOD_RES
<222> (30)
<223> asn present or not or lys

<400> 209
His Thr Val Thr Xaa Gly Val Xaa Ala Ser Cys Ser His Asn Gly Lys
1 5 10 15

SEQ.List.txt

Ser Ser Phe Tyr Xaa Xaa Leu Leu Trp Leu Thr Xaa Lys Xaa Gly Leu
 20 25 30

Tyr Pro Asn Leu Ser Lys
 35

<210> 210
 <211> 29
 <212> PRT
 <213> Influenza virus

<400> 210
 His Thr Val Thr Lys Gly Val Thr Ala Ser Cys Ser His Asn Gly Lys
 1 5 10 15

Ser Ser Phe Tyr Lys Asn Leu Leu Trp Leu Thr Glu Lys
 20 25

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

<400> 211
 Lys Tyr Val Arg Ser Thr Lys Leu Arg Met Val Thr Gly Leu Arg Asn
 1 5 10 15

Ile Pro Ser Ile Gln Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe
 20 25 30

Ile Glu Gly Gly Trp Thr Gly Met Ile Asp Gly Trp Tyr Gly Tyr His
 35 40 45

<210> 212
 <211> 43
 <212> PRT
 <213> Influenza virus

<400> 212
 His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
 1 5 10 15

Gln Asn Ala Ile Asn Gly Ile Thr Asn Lys Val Asn Ser Ile Ile Glu
 20 25 30

SEQ.List.txt

Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys
35 40

<210> 213
<211> 33
<212> PRT
<213> Influenza virus

<400> 213
His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15
Gln Asn Ala Ile Asn Gly Ile Thr Asn Lys Val Asn Ser Ile Ile Glu
20 25 30

Lys

<210> 214
<211> 26
<212> PRT
<213> Influenza virus

<400> 214
His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
1 5 10 15
Gln Asn Ala Ile Asn Gly Ile Thr Asn Lys
20 25

<210> 215
<211> 23
<212> PRT
<213> Influenza virus

<400> 215
His Ser Gly Ala Arg Ser Phe Tyr Arg Asn Leu Leu Trp Ile Val Lys
1 5 10 15
Lys Gly Asn Ser Tyr Pro Lys
20

<210> 216
<211> 26

SEQ.List.txt

<212> PRT

<213> Influenza virus

<400> 216

His Ser Gly Ala Arg Ser Phe Tyr Arg Asn Leu Leu Trp Ile Val Lys
1 5 10 15

Lys Gly Asn Ser Tyr Pro Lys Leu Asn Lys
20 25

<210> 217

<211> 32

<212> PRT

<213> Influenza virus

<400> 217

His Ser Gly Ala Arg Ser Phe Tyr Arg Asn Leu Leu Trp Ile Val Lys
1 5 10 15

Lys Gly Asn Ser Tyr Pro Lys Leu Asn Lys Ser Tyr Thr Asn Asp Lys
20 25 30

<210> 218

<211> 34

<212> PRT

<213> Influenza virus

<400> 218

His Ser Gly Ala Arg Ser Phe Tyr Arg Asn Leu Leu Trp Ile Val Lys
1 5 10 15

Lys Gly Asn Ser Tyr Pro Lys Leu Asn Lys Ser Tyr Thr Asn Asp Lys
20 25 30

Gly Lys

<210> 219

<211> 16

<212> PRT

<213> Influenza virus

<400> 219

His Thr Val Ser Lys Gly Val Thr Thr Ser Cys Ser His Asn Gly Lys
1 5 10 15

SEQ.List.txt

<210> 220
 <211> 12
 <212> PRT
 <213> Influenza virus

<400> 220
 Lys Ala Thr Ser Trp Pro Asn His Glu Thr Thr Lys
 1 5 10

<210> 221
 <211> 12
 <212> PRT
 <213> Influenza virus

<400> 221
 Lys Gln Val Thr Thr Ser Cys Ser His Asn Gln Lys
 1 5 10

<210> 222
 <211> 27
 <212> PRT
 <213> Influenza virus

<400> 222
 Lys Gly Asn Ser Tyr Pro Lys Leu Asn Lys Ser Tyr Thr Asn Asp Lys
 1 5 10 15
 Gly Lys Glu Val Leu Val Ile Trp Gly Val His
 20 25

<210> 223
 <211> 21
 <212> PRT
 <213> Influenza virus

<400> 223
 Lys Leu Asn Lys Ser Tyr Thr Asn Asp Lys Gly Lys Glu Val Leu Val
 1 5 10 15
 Ile Trp Gly Val His
 20

<210> 224

SEQ.List.txt

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

<400> 224
 Lys Ser Tyr Thr Asn Asp Lys Gly Lys Glu Val Leu Val Ile Trp Gly
 1 5 10 15
 Val His

<210> 225
 <211> 35
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD RES
 <222> (16)
 <223> glu or gln

<220>
 <221> MOD RES
 <222> (29)
 <223> val or ala

<400> 225
 His Asn Gln Lys Ser Ser Phe Tyr Arg Asn Leu Leu Trp Leu Thr Xaa
 1 5 10 15
 Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys Ser Tyr Xaa Ala Asn Asn
 20 25 30
 Lys Glu Lys
 35

<210> 226
 <211> 16
 <212> PRT
 <213> Influenza virus

<400> 226
 His Pro Ile Thr Ile Gly Glu Cys Pro Lys Tyr Val Arg Ser Ala Lys
 1 5 10 15

<210> 227

SEQ.List.txt

<211> 43
 <212> PRT
 <213> Influenza virus

<400> 227

His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
 1 5 10 15

Gln Asn Ala Ile Asn Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
 20 25 30

Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys
 35 40

<210> 228
 <211> 33
 <212> PRT
 <213> Influenza virus

<400> 228

His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr
 1 5 10 15

Gln Asn Ala Ile Asn Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
 20 25 30

Lys

<210> 229
 <211> 34
 <212> PRT
 <213> Influenza virus

<400> 229

His Asn Gly Lys Ser Ser Phe Tyr Arg Asn Leu Leu Trp Leu Thr Glu
 1 5 10 15

Lys Asn Gly Leu Tyr Pro Asn Leu Ser Lys Ser Tyr Val Asn Asn Lys
 20 25 30

Glu Lys

<210> 230
 <211> 11
 <212> PRT

SEQ.List.txt

<213> Influenza virus

<400> 230

Lys His Phe Glu Lys Val Lys Ile Leu Pro Lys
1 5 10

<210> 231

<211> 14

<212> PRT

<213> Influenza virus

<400> 231

Lys His Leu Leu Ser Ser Val Lys His Phe Glu Lys Val Lys
1 5 10

<210> 232

<211> 13

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (3)

<223> lys, gln or met

<220>

<221> MOD_RES

<222> (4)

<223> asp or asn

<400> 232

His Ala Xaa Xaa Ile Leu Glu Lys Thr His Asn Gly Lys
1 5 10

<210> 233

<211> 16

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (3)

<223> lys, gln or met

<220>

SEQ:List.txt

<221> MOD_RES

<222> (4)

<223> asp or asn

<220>

<221> MOD_RES

<222> (16)

<223> lys or arg

<400> 233

His Ala Xaa Xaa Ile Leu Glu Lys Thr His Asn Gly Lys Leu Cys Xaa
1 5 10 15

<210> 234

<211> 19

<212> PRT

<213> Influenza virus

<400> 234

His Asn Val His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val Lys
1 5 10 15

Ser Glu Lys

<210> 235

<211> 16

<212> PRT

<213> Influenza virus

<400> 235

His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val Lys Ser Glu Lys
1 5 10 15

<210> 236

<211> 18

<212> PRT

<213> Influenza virus

<400> 236

Lys His Leu Leu Ser Ser Val Lys His Phe Glu Lys Val Lys Ile Leu
1 5 10 15

Pro Lys

SEQ.List.txt

<210> 237
 <211> 38
 <212> PRT
 <213> Influenza virus

<400> 237
 Lys Arg Gln Ser Ser Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn
 1 5 10 15
 Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu
 20 25 30
 Pro Phe His Asn Val His
 35

<210> 238
 <211> 27
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (7)
 <223> val or ile

<220>
 <221> MOD_RES
 <222> (10)
 <223> gly or arg

<220>
 <221> MOD_RES
 <222> (26)
 <223> val or ile

<400> 238
 Lys Gly Ser Asn Tyr Pro Xaa Ala Lys Xaa Ser Tyr Asn Asn Thr Ser
 1 5 10 15

Gly Glu Gln Met Leu Ile Ile Trp Gln Xaa His
 20 25

<210> 239
 <211> 36
 <212> PRT
 <213> Influenza virus

SEQ.List.txt

<400> 239

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

Ser Phe Phe Arg Asn Met Val Trp Leu Thr Glu Lys Gly Ser Asn Tyr
20 25 30

Pro Val Ala Lys
35

<210> 240

<211> 7

<212> PRT

<213> Influenza virus

<400> 240

Lys His Phe Glu Lys Val Lys
1 5

<210> 241

<211> 38

<212> PRT

<213> Influenza virus

<400> 241

Lys Ile Ser Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr
1 5 10 15

Leu Glu Asn Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn
20 25 30

Thr Thr Leu Pro Phe His
35

<210> 242

<211> 35

<212> PRT

<213> Influenza virus

<400> 242

Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn
1 5 10 15

Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu

SEQ.List.txt

20 25 30

Pro Phe His
35

<210> 243
<211> 27
<212> PRT
<213> Influenza virus

<400> 243
Lys Thr Glu Gly Thr Leu Glu Asn Cys Glu Thr Lys Cys Gln Thr Pro
1 5 10 15
Leu Gly Ala Ile Asn Thr Thr Leu Pro Phe His
20 25

<210> 244
<211> 38
<212> PRT
<213> Influenza virus

<400> 244
Lys Ile Ser Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr
1 5 10 15
Leu Glu Asn Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn
20 25 30
Thr Thr Leu Pro Phe His
35

<210> 245
<211> 30
<212> PRT
<213> Influenza virus

<220>
<221> MOD RES
<222> (29)
<223> val or ile

<400> 245
Lys Thr Glu Gly Thr Leu Glu Asn Cys Glu Thr Lys Cys Gln Thr Pro
1 5 10 15

SEQ.List.txt

Leu Gly Ala Ile Asn Thr Thr Leu Pro Phe His Asn Xaa His
 20 25 30

<210> 246
 <211> 38
 <212> PRT
 <213> Influenza virus

<400> 246
 Lys Ile Ser Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr
 1 5 10 15

Leu Glu Asn Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn
 20 25 30

Thr Thr Leu Pro Phe His
 35

<210> 247
 <211> 27
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (2)
 <223> glu or gly

<400> 247
 Lys Xaa Ser Asn Tyr Pro Val Ala Lys Gly Ser Tyr Asn Asn Thr Ser
 1 5 10 15

Gly Glu Gln Met Leu Ile Ile Trp Gly Val His
 20 25

<210> 248
 <211> 16
 <212> PRT
 <213> Influenza virus

<400> 248
 His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val Lys Ser Glu Lys
 1 5 10 15

SEQ.List.txt

<210> 249
 <211> 16
 <212> PRT
 <213> Influenza virus

<400> 249
 Lys Cys Gln Thr Pro Leu Gly Ala Ile Lys Thr Thr Leu Pro Phe His
 1 5 10 15

<210> 250
 <211> 58
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (21)
 <223> phe or ile

<220>
 <221> MOD_RES
 <222> (47)
 <223> asn or ser

<400> 250
 His His Ser Asn Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser
 1 5 10 15
 Thr Gln Lys Ala Xaa Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile
 20 25 30
 Glu Lys Met Asn Thr Gln Phe Glu Ala Val Gly Lys Leu Phe Xaa Asn
 35 40 45
 Leu Glu Lys Leu Glu Asn Leu Asn Lys Lys
 50 55

<210> 251
 <211> 57
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (20)

SEQ.List.txt

<223> phe or ile

<220>

<221> MOD RES

<222> (46)

<223> asn or ser

<400> 251

His Ser Asn Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr
1 5 10 15

Gln Lys Ala Xaa Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
20 25 30

Lys Met Asn Thr Gln Phe Glu Ala Val Gly Lys Leu Phe Xaa Asn Leu
35 40 45

Glu Lys Leu Glu Asn Leu Asn Lys Lys
50 55

<210> 252

<211> 26

<212> PRT

<213> Influenza virus

<220>

<221> MOD RES

<222> (20)

<223> phe or ile

<400> 252

His Ser Asn Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr
1 5 10 15

Gln Lys Ala Xaa Asp Gly Ile Thr Asn Lys
20 25

<210> 253

<211> 21

<212> PRT

<213> Influenza virus

<400> 253

His Asp Ser Asn Val Arg Asn Leu Tyr Asp Lys Val Arg Met Gln Leu
1 5 10 15

SEQ.List.txt

Arg Asp Asn Ala Lys
20

<210> 254
<211> 30
<212> PRT
<213> Influenza virus

<400> 254
His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly Thr Tyr
1 5 10 15
Asp Tyr Pro Lys Leu Asn Arg Asn Glu Ile Lys Gly Val Lys
20 25 30

<210> 255
<211> 27
<212> PRT
<213> Influenza virus

<400> 255
His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly Thr Tyr
1 5 10 15
Asp Tyr Pro Lys Leu Asn Arg Asn Glu Ile Lys
20 25

<210> 256
<211> 20
<212> PRT
<213> Influenza virus

<400> 256
His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly Thr Tyr
1 5 10 15
Asp Tyr Pro Lys
20

<210> 257
<211> 12
<212> PRT
<213> Influenza virus

SEQ.List.txt

<400> 257

His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys
1 5 10

<210> 258

<211> 27

<212> PRT

<213> Influenza virus

<400> 258

Lys Gly Ser Asn Tyr Pro Val Ala Lys Gly Ser Tyr Asn Asn Thr Asn
1 5 10 15

Gly Glu Gln Ile Leu Ile Ile Trp Gly Val His
20 25

<210> 259

<211> 43

<212> PRT

<213> Influenza virus

<400> 259

His Ser Asn Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr
1 5 10 15

Gln Lys Ala Val Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu
20 25 30

Lys Met Asn Thr Gln Phe Glu Ala Val Gly Lys
35 40

<210> 260

<211> 35

<212> PRT

<213> Influenza virus

<400> 260

Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn
1 5 10 15

Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu
20 25 30

Pro Phe His
35

SEQ.List.txt

<210> 261
 <211> 16
 <212> PRT
 <213> Influenza virus

<400> 261
 His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val Lys Ser Glu Lys
 1 5 10 15

<210> 262
 <211> 16
 <212> PRT
 <213> Influenza virus

<400> 262
 His Ala Lys Asp Ile Leu Glu Lys Thr His Asn Gly Lys Leu Cys Lys
 1 5 10 15

<210> 263
 <211> 25
 <212> PRT
 <213> Influenza virus

<400> 263
 His Asp Val Tyr Arg Asp Glu Ala Leu Asn Asn Arg Phe Gln Ile Lys
 1 5 10 15

Gly Val Glu Leu Lys Ser Gly Tyr Lys
 20 25

<210> 264
 <211> 19
 <212> PRT
 <213> Influenza virus

<400> 264
 His Thr Ile Asp Leu Thr Asp Ser Glu Met Asn Lys Leu Phe Glu Arg
 1 5 10 15

Thr Arg Lys

<210> 265

SEQ.List.txt

<211> 7
 <212> PRT
 <213> Influenza virus

<400> 265
 Lys Phe His Gln Ile Glu Lys
 1 5

<210> 266
 <211> 11
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (8)
 <223> gly or gln

<400> 266
 Lys Thr Asn Glu Lys Phe His Xaa Ile Glu Lys
 1 5 10

<210> 267
 <211> 14
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (5)
 <223> val or leu

<400> 267
 Lys Leu Asn Arg Xaa Ile Glu Lys Thr Asn Glu Lys Phe His
 1 5 10

<210> 268
 <211> 25
 <212> PRT
 <213> Influenza virus

<400> 268
 His Gln Ile Glu Lys Glu Phe Ser Glu Val Glu Gly Arg Ile Gln Asp
 1 5 10 15

SEQ.List.txt

Leu Glu Lys Tyr Val Glu Asp Thr Lys
20 25

<210> 269
<211> 8
<212> PRT
<213> Influenza virus

<400> 269
Lys Ile Cys Asn Asn Pro His Lys
1 5

<210> 270
<211> 14
<212> PRT
<213> Influenza virus

<400> 270
Lys Leu Asn Arg Val Ile Lys Lys Thr Asn Glu Lys Phe His
1 5 10

<210> 271
<211> 24
<212> PRT
<213> Influenza virus

<220>
<221> MOD_RES
<222> (3)
<223> ile or val

<220>
<221> MOD_RES
<222> (17)
<223> gly or gln

<220>
<221> MOD_RES
<222> (20)
<223> arg or lys

<220>
<221> MOD_RES
<222> (22)
<223> gln or gly

SEQ.List.txt

<400> 271

His Asp Xaa Tyr Arg Asp Glu Ala Leu Asn Asn Arg Phe Gln Ile Lys
1 5 10 15

Xaa Val Glu Xaa Ser Xaa Tyr Lys
20

<210> 272

<211> 25

<212> PRT

<213> Influenza virus

<400> 272

His Gln Ile Glu Lys Glu Phe Ser Glu Val Glu Gly Arg Ile Gln Asp
1 5 10 15

Leu Glu Lys Tyr Val Glu Asp Thr Lys
20 25

<210> 273

<211> 25

<212> PRT

<213> Influenza virus

<400> 273

Lys Tyr Val Glu Asp Thr Lys Ile Asp Leu Trp Ser Tyr Asn Ala Glu
1 5 10 15

Leu Leu Val Ala Leu Glu Asn Gln His
20 25

<210> 274

<211> 49

<212> PRT

<213> Influenza virus

<400> 274

Lys Tyr Val Lys Gln Asn Ser Leu Lys Leu Ala Thr Gly Met Arg Asn
1 5 10 15

Val Pro Glu Lys Gln Thr Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe
20 25 30

Ile Glu Asn Gly Trp Glu Gly Met Ile Asp Gly Trp Tyr Gly Phe Arg

His

<210> 275
<211> 39
<212> PRT
<213> Influenza virus

<400> 275
Lys Glu Phe Ser Glu Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr
1 5 10 15
Val Glu Asp Thr Lys Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu
20 25 30

Val Ala Leu Glu Asn Gln His
35

<210> 276
<211> 33
<212> PRT
<213> Influenza virus

<220>
<221> MOD_RES
<222> (4)
<223> ser or glu

<220>
<221> MOD_RES
<222> (5)
<223> glu or gln

<220>
<221> MOD_RES
<222> (7)
<223> thr or ser

<220>
<221> MOD_RES
<222> (9)
<223> gln or tyr

<220>
<221> MOD_RES

SEQ.List.txt

<222> (13)
<223> leu or gln

<220>
<221> MOD RES
<222> (18)
<223> ala or asn

<220>
<221> MOD RES
<222> (20)
<223> ile or leu

<220>
<221> MOD RES
<222> (22)
<223> gln or gly

<220>
<221> MOD RES
<222> (24)
<223> asn or thr

<220>
<221> MOD RES
<222> (25)
<223> gly or asn

<220>
<221> MOD RES
<222> (27)
<223> leu or val

<220>
<221> MOD RES
<222> (29)
<223> arg or ser

<220>
<221> MOD RES
<222> (32)
<223> glu or cys

<400> 276
His Gln Asn Xaa Xaa Gly Xaa Gly Xaa Ala Ala Asp Xaa Lys Ser Thr
1 5 10 15

Gln Xaa Ala Xaa Asp Xaa Ile Xaa Xaa Lys Xaa Asn Xaa Val Ile Xaa

Lys

<210> 277
 <211> 18
 <212> PRT
 <213> Influenza virus

<220>
 <221> MOD_RES
 <222> (4)
 <223> gly or gln

<220>
 <221> MOD_RES
 <222> (6)
 <223> gln or arg

<220>
 <221> MOD_RES
 <222> (14)
 <223> val or ile

<220>
 <221> MOD_RES
 <222> (17)
 <223> ser or thr

<400> 277
 His Cys Asp Xaa Phe Xaa Asn Glu Lys Trp Asp Leu Phe Xaa Glu Arg
 1 5 10 15

Xaa Lys

<210> 278
 <211> 20
 <212> PRT
 <213> Influenza virus

<400> 278
 His Thr Ile Asp Leu Thr Asp Ser Glu Met Asn Lys Lys Leu Phe Glu
 1 5 10 15

Arg Thr Arg Lys
 20

SEQ.List.txt

<210> 279
 <211> 28
 <212> PRT
 <213> Influenza virus

<400> 279
 Lys Ser Gly Ser Thr Tyr Pro Val Leu Lys Val Thr Met Pro Asn Asn
 1 5 10 15
 Asp Asn Phe Asp Lys Leu Tyr Ile Trp Gly Val His
 20 25

<210> 280
 <211> 34
 <212> PRT
 <213> Influenza virus

<400> 280
 Lys Leu Asn Trp Leu Thr Lys Ser Gly Asn Thr Tyr Pro Val Leu Asn
 1 5 10 15
 Val Thr Met Pro Asn Asn Asp Asn Phe Asp Lys Leu Val Ile Trp Gly
 20 25 30

Val His

<210> 281
 <211> 19
 <212> PRT
 <213> Influenza virus

<400> 281
 His Thr Ile Asp Leu Thr Asp Ser Glu Met Asn Lys Leu Phe Glu Lys
 1 5 10 15
 Thr Arg Lys

<210> 282
 <211> 18
 <212> PRT
 <213> Influenza virus

<400> 282

SEQ.List.txt

Lys Leu Asn Arg Leu Ile Glu Lys Thr Asn Glu Lys Phe His Gln Thr
 1 5 10 15

Glu Lys

<210> 283

<211> 47

<212> PRT

<213> Influenza virus

<400> 283

His Thr Gly Lys Ser Ser Val Met Arg Ser Asp Ala Pro Ile Asp Phe
 1 5 10 15

Cys Asn Ser Glu Cys Ile Thr Pro Asn Gln Ser Ile Pro Asn Asp Lys
 20 25 30

Pro Phe Gln Asn Val Asn Lys Ile Thr Tyr Gly Ala Cys Pro Lys
 35 40 45

<210> 284

<211> 39

<212> PRT

<213> Influenza virus

<400> 284

His Thr Gly Lys Ser Ser Val Met Arg Ser Asp Ala Pro Ile Asp Phe
 1 5 10 15

Cys Asn Ser Glu Cys Ile Thr Pro Asn Gln Ser Ile Pro Asn Asp Lys
 20 25 30

Pro Phe Gln Asn Val Asn Lys
 35

<210> 285

<211> 33

<212> PRT

<213> Influenza virus

<400> 285

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

Gly Arg Val Thr Val Ser Thr Lys Arg Ser Gln Gln Thr Val Ile Pro

Lys

<210> 286
<211> 25
<212> PRT
<213> Influenza virus

<400> 286
Lys Tyr Val Glu Asp Thr Lys Ile Asp Leu Trp Ser Tyr Asn Ala Glu
1 5 10 15

Leu Leu Val Ala Leu Glu Asn Gln His
20 25

<210> 287
<211> 26
<212> PRT
<213> Influenza virus

<400> 287
Lys Leu Phe Glu Arg Thr Arg Lys Gln Leu Arg Glu Asn Ala Glu Asp
1 5 10 15

Met Gly Asn Gly Cys Phe Lys Ile Tyr His
20 25

<210> 288
<211> 16
<212> PRT
<213> Influenza virus

<400> 288
Lys Arg Arg Ser Ile Lys Ser Phe Phe Ser Arg Leu Asn Trp Leu His
1 5 10 15

<210> 289
<211> 16
<212> PRT
<213> Influenza virus

<220>
<221> MOD_RES

SEQ.List.txt

<222> (12)

<223> val or arg

<400> 289

His Pro Val Thr Ile Gly Glu Cys Pro Lys Tyr Xaa Lys Ser Thr Lys
1 5 10 15

<210> 290

<211> 30

<212> PRT

<213> Influenza virus

<400> 290

Lys Gly Asn Ser Tyr Pro Lys Leu Ser Lys Leu Ser Lys Ser Tyr Ile
1 5 10 15

Ile Asn Lys Lys Lys Glu Val Leu Val Ile Trp Gly Ile His
20 25 30

<210> 291

<211> 24

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (9)

<223> val or tyr

<400> 291

Lys Leu Ser Lys Leu Ser Lys Ser Xaa Ile Ile Asn Lys Lys Lys Glu
1 5 10 15

Val Leu Val Ile Trp Gly Ile His
20

<210> 292

<211> 21

<212> PRT

<213> Influenza virus

<220>

<221> MOD_RES

<222> (6)

<223> val or tyr

SEQ.List.txt

<400> 292

Lys Leu Ser Lys Ser Xaa Ile Ile Asn Lys Lys Lys Glu Val Leu Val
1 5 10 15

Ile Trp Gly Ile His
20

<210> 293

<211> 46

<212> PRT

<213> Plasmodium falciparum

<400> 293

Lys Glu Glu Glu Glu Lys Glu Lys Glu Lys Glu Lys Glu Lys Glu Glu
1 5 10 15

Lys Glu Lys Glu Glu Lys Glu Lys Glu Glu Lys Glu Lys Glu Lys Glu
20 25 30

Glu Lys Glu Lys Glu Lys Glu Glu Lys Glu Glu Glu Lys Lys
35 40 45

<210> 294

<211> 48

<212> PRT

<213> Plasmodium falciparum

<400> 294

Lys Glu Glu Glu Glu Lys Glu Lys Glu Lys Glu Lys Glu Lys Glu Glu
1 5 10 15

Lys Glu Lys Glu Glu Lys Glu Lys Glu Glu Lys Glu Lys Glu Lys Glu
20 25 30

Glu Lys Glu Lys Glu Lys Glu Glu Lys Glu Glu Glu Lys Lys Glu Lys
35 40 45

<210> 295

<211> 47

<212> PRT

<213> Plasmodium falciparum

<400> 295

Lys Glu Glu Glu Glu Lys Glu Lys Glu Lys Glu Lys Glu Lys Glu Glu

SEQ.List.txt

1 5 10 15
 Lys Glu Lys Glu Glu Lys Glu Lys Glu Lys Glu Glu Lys Glu Lys Glu
 20 25 30
 Glu Lys Glu Lys Glu Glu Lys Glu Glu Lys Glu Glu Glu Lys Lys
 35 40 45

<210> 296
 <211> 10
 <212> PRT
 <213> Plasmodium falciparum

<400> 296
 Lys Glu Glu Glu Glu Lys Glu Lys Glu Lys
 1 5 10

<210> 297
 <211> 19
 <212> PRT
 <213> Plasmodium falciparum

<400> 297
 His Lys Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln
 1 5 10 15

Asn Lys Lys

<210> 298
 <211> 19
 <212> PRT
 <213> Plasmodium falciparum

<400> 298
 His Lys Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln
 1 5 10 15

Asn Lys Met

<210> 299
 <211> 10
 <212> PRT
 <213> Plasmodium falciparum

SEQ-List.txt

<400> 299

His Lys Lys Leu Ile Lys Ala Leu Lys Lys
1 5 10

<210> 300

<211> 9

<212> PRT

<213> Plasmodium falciparum

<400> 300

His Lys Lys Leu Ile Lys Ala Leu Lys
1 5

<210> 301

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 301

Lys Ala Thr Tyr Ser Phe Val Asn Thr Lys Lys Lys Ile Ile Ser Leu
1 5 10 15

Lys Ser Gln Gly His Lys Lys
20

<210> 302

<211> 22

<212> PRT

<213> Plasmodium falciparum

<400> 302

Lys Ala Thr Tyr Ser Phe Val Asn Thr Lys Lys Lys Ile Ile Ser Leu
1 5 10 15

Lys Ser Gln Gly His Lys
20

<210> 303

<211> 21

<212> PRT

<213> Plasmodium falciparum

<400> 303

Lys Ala Thr Tyr Ser Phe Val Asn Thr Lys Lys Lys Ile Ile Ser Leu

SEQ.List.txt

1	5	10	15
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Lys Ser Gln Gly His
20

<210> 304
 <211> 29
 <212> PRT
 <213> Plasmodium falciparum

<400> 304
 His Thr Tyr Val Lys Gly Lys Lys Ala Pro Ser Asp Pro Gln Cys Ala
 1 5 10 15

Asp Ile Lys Glu Glu Cys Lys Glu Leu Leu Lys Glu Lys
 20 25

<210> 305
 <211> 11
 <212> PRT
 <213> Plasmodium falciparum

<400> 305
 Lys Ile Ile Ser Leu Lys Ser Gln Gly His Lys
 1 5 10

<210> 306
 <211> 21
 <212> PRT
 <213> Plasmodium falciparum

<400> 306
 Lys Lys Lys Lys Phe Glu Pro Leu Lys Asn Gly Asn Val Ser Glu Thr
 1 5 10 15

Ile Lys Leu Ile His
 20

<210> 307
 <211> 20
 <212> PRT
 <213> Plasmodium falciparum

<400> 307

SEQ.List.txt

Lys Lys Lys Phe Glu Pro Leu Lys Asn Gly Asn Val Ser Glu Thr Ile
1 5 10 15

Lys Leu Ile His
20

<210> 308
<211> 19
<212> PRT
<213> Plasmodium falciparum

<400> 308
Lys Lys Phe Glu Pro Leu Lys Asn Gly Asn Val Ser Glu Thr Ile Lys
1 5 10 15

Leu Ile His

<210> 309
<211> 13
<212> PRT
<213> Plasmodium falciparum

<400> 309
Lys Asn Gly Asn Val Ser Glu Thr Ile Lys Leu Ile His
1 5 10

<210> 310
<211> 11
<212> PRT
<213> Plasmodium falciparum

<400> 310
Lys Leu Ile His Leu Gly Asn Lys Asp Lys Lys
1 5 10

<210> 311
<211> 36
<212> PRT
<213> Plasmodium falciparum

<400> 311
Lys Val Lys Lys Ile Gly Val Thr Leu Lys Lys Phe Glu Pro Leu Lys
1 5 10 15

SEQ-List.txt

Asn Gly Asn Val Ser Glu Thr Ile Lys Leu Ile His Leu Gly Asn Lys
 20 25 30

Asp Lys Lys His
 35

<210> 312

<211> 59

<212> PRT

<213> Plasmodium falciparum

<400> 312

His Leu Ile Tyr Lys Asn Lys Ser Tyr Asn Pro Leu Leu Leu Ser Cys
 1 5 10 15

Val Lys Lys Met Asn Met Leu Lys Glu Asn Val Asp Tyr Ile Gln Asn
 20 25 30

Gln Asn Leu Phe Lys Glu Leu Met Asn Gln Lys Ala Thr Tyr Ser Phe
 35 40 45

Val Asn Thr Lys Lys Lys Ile Ile Ser Leu Lys
 50 55

<210> 313

<211> 52

<212> PRT

<213> Plasmodium falciparum

<400> 313

His Leu Ile Tyr Lys Asn Lys Ser Tyr Asn Pro Leu Leu Leu Ser Cys
 1 5 10 15

Val Lys Lys Met Asn Met Leu Lys Glu Asn Val Asp Tyr Ile Gln Asn
 20 25 30

Gln Asn Leu Phe Lys Glu Leu Met Asn Gln Lys Ala Thr Tyr Ser Phe
 35 40 45

Val Asn Thr Lys
 50

<210> 314

<211> 43

<212> PRT

SEQ.List.txt

<213> Plasmodium falciparum

<400> 314

His Leu Ile Tyr Lys Asn Lys Ser Tyr Asn Pro Leu Leu Leu Ser Cys
1 5 10 15

Val Lys Lys Met Asn Met Leu Lys Glu Asn Val Asp Tyr Ile Gln Asn
20 25 30

Gln Asn Leu Phe Lys Glu Leu Met Asn Gln Lys
35 40

<210> 315

<211> 38

<212> PRT

<213> Plasmodium falciparum

<400> 315

His Leu Ile Tyr Lys Asn Lys Ser Tyr Asn Pro Leu Leu Leu Ser Cys
1 5 10 15

Val Lys Lys Met Asn Met Leu Lys Glu Asn Val Asp Tyr Ile Gln Lys
20 25 30

Asn Gln Asn Leu Phe Lys
35

<210> 316

<211> 24

<212> PRT

<213> Plasmodium falciparum

<400> 316

His Leu Ile Tyr Lys Asn Lys Ser Tyr Asn Pro Leu Leu Leu Ser Cys
1 5 10 15

Val Lys Lys Met Asn Met Leu Lys
20

<210> 317

<211> 47

<212> PRT

<213> Plasmodium falciparum

<400> 317

SEQ.List.txt

Lys Ser Ala Asn Asn Ser Ala Asn Asn Gly Lys Lys Asn Asn Ala Glu
1 5 10 15

Glu Met Lys Asn Leu Val Asn Phe Leu Gln Ser His Lys Lys Leu Ile
20 25 30

Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
35 40 45

<210> 318

<211> 37

<212> PRT

<213> Plasmodium falciparum

<400> 318

Lys Lys Asn Asn Ala Glu Glu Met Lys Asn Leu Val Asn Phe Leu Gln
1 5 10 15

Ser His Lys Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile
20 25 30

Gln Asn Lys Lys His
35

<210> 319

<211> 29

<212> PRT

<213> Plasmodium falciparum

<400> 319

Lys Asn Leu Val Asn Phe Leu Gln Ser His Lys Lys Leu Ile Lys Ala
1 5 10 15

Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
20 25

<210> 320

<211> 19

<212> PRT

<213> Plasmodium falciparum

<400> 320

Lys Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn
1 5 10 15

SEQ.List.txt

Lys Lys His

<210> 321
 <211> 18
 <212> PRT
 <213> Plasmodium falciparum

<400> 321

Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys
 1 5 10 15

Lys His

<210> 322
 <211> 12
 <212> PRT
 <213> Plasmodium falciparum

<400> 322

Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
 1 5 10

<210> 323
 <211> 11
 <212> PRT
 <213> Plasmodium falciparum

<400> 323

Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
 1 5 10

<210> 324
 <211> 17
 <212> PRT
 <213> Plasmodium falciparum

<400> 324

Lys Asn Asn Ala Glu Glu Met Lys Asn Leu Val Asn Phe Leu Gln Ser
 1 5 10 15

His

<210> 325

SEQ.List.txt

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 325

Lys Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn
1 5 10 15

Lys Lys Gln Gly His Lys Lys
20

<210> 326

<211> 19

<212> PRT

<213> Plasmodium falciparum

<400> 326

Lys Lys Asn Asn Ala Glu Glu Met Lys Asn Leu Val Asn Phe Leu Gln
1 5 10 15

Ser His Lys

<210> 327

<211> 17

<212> PRT

<213> Plasmodium falciparum

<400> 327

Lys Asn Asn Ala Glu Glu Met Lys Asn Leu Val Asn Phe Leu Gln Ser
1 5 10 15

His

<210> 328

<211> 22

<212> PRT

<213> Plasmodium falciparum

<400> 328

Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys
1 5 10 15

Lys Gln Gly His Lys Lys
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SEQ.List.txt

<210> 329
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<400> 329
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 1 5 10 15
 Asn Gly Asn Val Ser Glu Thr Ile Lys Leu Ile His
 20 25

<210> 330
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<400> 330
 Lys Asn Gly Asn Val Ser Glu Thr Ile Lys Leu Ile His
 1 5 10

<210> 331
 <211> 11
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<400> 331
 Lys Leu Ile His Leu Gly Asn Lys Asp Lys Lys
 1 5 10

<210> 332
 <211> 28
 <212> PRT
 <213> Plasmodium falciparum

<400> 332
 Lys Ser Ala Asn Asn Ser Ala Asn Asn Gly Lys Lys Asn Asn Ala Glu
 1 5 10 15
 Glu Met Lys Asn Leu Val Asn Phe Leu Gln Ser His
 20 25

<210> 333

SEQ.List.txt

<211> 18

<212> PRT

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<400> 333

Lys Lys Asn Asn Ala Glu Glu Met Lys Asn Leu Val Asn Phe Leu Gln
1 5 10 15

Ser His

<210> 334

<211> 19

<212> PRT

<213> Plasmodium falciparum

<400> 334

Lys Lys Leu Ile Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn
1 5 10 15

Lys Lys His

<210> 335

<211> 15

<212> PRT

<213> Plasmodium falciparum

<400> 335

Lys Ala Leu Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
1 5 10 15

<210> 336

<211> 12

<212> PRT

<213> Plasmodium falciparum

<400> 336

Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
1 5 10

<210> 337

<211> 27

<212> PRT

<213> Plasmodium falciparum

SEQ.List.txt

<400> 337

Lys Glu Leu Met Asn Gln Lys Ala Thr Tyr Ser Phe Val Asn Thr Lys
1 5 10 15

Lys Lys Ile Ile Ser Leu Lys Ser Gln Gly His
20 25

<210> 338

<211> 7

<212> PRT

<213> Plasmodium falciparum

<400> 338

Lys Ser Gln Gly His Lys Lys
1 5

<210> 339

<211> 12

<212> PRT

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<400> 339

Lys Lys Lys Ile Ile Ser Leu Lys Ser Gln Gly His
1 5 10

<210> 340

<211> 11

<212> PRT

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<400> 340

Lys Lys Ile Ile Ser Leu Lys Ser Gln Gly His
1 5 10

<210> 341

<211> 12

<212> PRT

<213> Plasmodium falciparum

<400> 341

Lys Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
1 5 10

SEQ.List.txt

<210> 342

<211> 11

<212> PRT

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<400> 342

Lys Asn Ile Glu Ser Ile Gln Asn Lys Lys His
1 5 10

<210> 343

<211> 29

<212> PRT

<213> Plasmodium falciparum

<400> 343

His Thr Tyr Val Lys Gly Lys Lys Ala Pro Ser Asp Pro Gln Cys Ala
1 5 10 15

Asp Ile Lys Glu Glu Cys Lys Glu Leu Leu Lys Glu Lys
20 25

<210> 344

<211> 27

<212> PRT

<213> Plasmodium falciparum

<400> 344

His Thr Tyr Val Lys Gly Lys Lys Ala Pro Ser Asp Pro Gln Cys Ala
1 5 10 15

Asp Ile Lys Glu Glu Cys Lys Glu Leu Leu Lys
20 25

<210> 345

<211> 29

<212> PRT

<213> Plasmodium falciparum

<400> 345

His Glu Asn Val Leu Ser Ala Ala Leu Glu Asn Thr Gln Ser Glu Glu
1 5 10 15

Glu Lys Lys Glu Val Ile Asp Val Ile Glu Glu Val Lys
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SEQ.List.txt

<210> 346

<211> 48

<212> PRT

<213> Plasmodium falciparum

<400> 346

Lys Glu Asn Val Val Thr Thr Ile Leu Glu Lys Val Glu Glu Thr Thr
1 5 10 15

Ala Glu Ser Val Thr Thr Phe Ser Asn Ile Leu Glu Glu Ile Gln Glu
20 25 30

Asn Thr Ile Thr Asn Asp Thr Ile Glu Glu Lys Leu Glu Glu Leu His
35 40 45

<210> 347

<211> 14

<212> PRT

<213> Plasmodium falciparum

<400> 347

His Tyr Leu Gln Gln Met Lys Glu Lys Phe Ser Lys Glu Lys
1 5 10

<210> 348

<211> 42

<212> PRT

<213> Plasmodium falciparum

<400> 348

His Tyr Leu Gln Gln Met Lys Glu Lys Phe Ser Lys Glu Lys Asn Asn
1 5 10 15

Asn Val Ile Glu Val Thr Asn Lys Ala Glu Lys Lys Gly Asn Val Gln
20 25 30

Val Thr Asn Lys Thr Glu Lys Thr Thr Lys
35 40

<210> 349

<211> 48

<212> PRT

<213> Plasmodium falciparum

SEQ.List.txt

<400> 349

His Tyr Leu Gln Gln Met Lys Glu Lys Phe Ser Lys Glu Lys Asn Asn
1 5 10 15

Asn Val Ile Glu Val Thr Asn Lys Ala Glu Lys Lys Gly Asn Val Gln
20 25 30

Val Thr Asn Lys Thr Glu Lys Thr Thr Lys Val Asp Lys Asn Asn Lys
35 40 45

<210> 350

<211> 57

<212> PRT

<213> Plasmodium falciparum

<400> 350

His Tyr Leu Gln Gln Met Lys Glu Lys Phe Ser Lys Glu Lys Asn Asn
1 5 10 15

Asn Val Ile Glu Val Thr Asn Lys Ala Glu Lys Lys Gly Asn Val Gln
20 25 30

Val Thr Asn Lys Thr Glu Lys Thr Thr Lys Val Asp Lys Asn Asn Lys
35 40 45

Val Pro Lys Lys Arg Arg Thr Gln Lys
50 55

<210> 351

<211> 59

<212> PRT

<213> Plasmodium falciparum

<400> 351

His Tyr Leu Gln Gln Met Lys Glu Lys Phe Ser Lys Glu Lys Asn Asn
1 5 10 15

Asn Val Ile Glu Val Thr Asn Lys Ala Glu Lys Lys Gly Asn Val Gln
20 25 30

Val Thr Asn Lys Thr Glu Lys Thr Thr Lys Val Asp Lys Asn Asn Lys
35 40 45

Val Pro Lys Lys Arg Arg Thr Gln Lys Ser Lys
50 55

SEQ.List.txt

<210> 352

<211> 52

<212> PRT

<213> Plasmodium falciparum

<400> 352

His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
1 5 10 15

Asp Lys Glu Val Ser Lys Ala Leu Glu Ser Lys Asn Asp Val Thr Asn
20 25 30

Val Leu Lys Gln Asn Gln Asp Phe Phe Ser Lys Val Lys Asn Phe Val
35 40 45

Lys Lys Tyr Lys
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<210> 353

<211> 50

<212> PRT

<213> Plasmodium falciparum

<400> 353

His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
1 5 10 15

Asp Lys Glu Val Ser Lys Ala Leu Glu Ser Lys Asn Asp Val Thr Asn
20 25 30

Val Leu Lys Gln Asn Gln Asp Phe Phe Ser Lys Val Lys Asn Phe Val
35 40 45

Lys Lys
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<210> 354

<211> 43

<212> PRT

<213> Plasmodium falciparum

<400> 354

His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
1 5 10 15

SEQ.List.txt

Asp Lys Glu Val Ser Lys Ala Leu Glu Ser Lys Asn Asp Val Thr Asn
20 25 30

Val Leu Lys Gln Asn Gln Asp Phe Phe Ser Lys
35 40

<210> 355
<211> 35
<212> PRT
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<400> 355
His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
1 5 10 15

Asp Lys Glu Val Ser Lys Ala Leu Glu Ser Lys Asn Asp Val Thr Asn
20 25 30

Val Leu Lys
35

<210> 356
<211> 27
<212> PRT
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<400> 356
His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
1 5 10 15

Asp Lys Glu Val Ser Lys Ala Leu Glu Ser Lys
20 25

<210> 357
<211> 22
<212> PRT
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<400> 357
His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
1 5 10 15

Asp Lys Glu Val Ser Lys
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SEQ.List.txt

<210> 358
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 <212> PRT
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<400> 358
 His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys Glu Val
 1 5 10 15

Asp Lys

<210> 359
 <211> 14
 <212> PRT
 <213> Plasmodium falciparum

<400> 359
 His Val Asp Glu Val Met Lys Tyr Val Gln Lys Ile Asp Lys
 1 5 10

<210> 360
 <211> 39
 <212> PRT
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<400> 360
 Lys Asp Glu Val Ile Asp Leu Ile Val Gln Lys Glu Lys Arg Ile Glu
 1 5 10 15

Lys Val Lys Ala Lys Lys Lys Lys Leu Glu Lys Lys Val Glu Glu Gly
 20 25 30

Val Ser Gly Leu Lys Lys His
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<210> 361
 <211> 23
 <212> PRT
 <213> Plasmodium falciparum

<400> 361
 Lys Val Lys Ala Lys Lys Lys Lys Leu Glu Lys Lys Val Glu Glu Gly
 1 5 10 15

SEQ.List.txt

Val Ser Gly Leu Lys Lys His
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<210> 362
<211> 21
<212> PRT
<213> Plasmodium falciparum

<400> 362
Lys Ala Lys Lys Lys Lys Leu Glu Lys Lys Val Glu Glu Gly Val Ser
1 5 10 15
Gly Leu Lys Lys His
20

<210> 363
<211> 19
<212> PRT
<213> Plasmodium falciparum

<400> 363
Lys Lys Lys Lys Leu Glu Lys Lys Val Glu Glu Gly Val Ser Gly Leu
1 5 10 15
Lys Lys His

<210> 364
<211> 18
<212> PRT
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<400> 364
Lys Lys Lys Leu Glu Lys Lys Val Glu Glu Gly Val Ser Gly Leu Lys
1 5 10 15
Lys His

<210> 365
<211> 17
<212> PRT
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<400> 365
Lys Lys Leu Glu Lys Lys Val Glu Glu Gly Val Ser Gly Leu Lys Lys

SEQ.List.txt

1	5	10	15
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His

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 1 5 10 15

<210> 367
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<400> 367
 Lys Lys Val Glu Glu Gly Val Ser Gly Leu Lys Lys His
 1 5 10

<210> 368
 <211> 12
 <212> PRT
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<400> 368
 Lys Val Glu Glu Gly Val Ser Gly Leu Lys Lys His
 1 5 10

<210> 369
 <211> 59
 <212> PRT
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<400> 369
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 1 5 10 15

Asp Gln Phe Leu Gly Ile Leu Asn Glu Ala Gly Gly Leu Lys Glu Met
 20 25 30

Phe Phe Asn Leu Glu Asp Val Phe Lys Ser Glu Ser Asp Val Ile Thr

SEQ.List.txt

35

40

45

Val Glu Glu Ile Lys Asp Glu Pro Val Gln Lys
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<210> 370

<211> 53

<212> PRT

<213> Plasmodium falciparum

<400> 370

His Ile Lys Gly Leu Glu Glu Asp Asp Leu Glu Glu Val Asp Asp Leu
1 5 10 15

Lys Gly Ser Ile Leu Asp Met Leu Lys Gly Asp Met Glu Leu Gly Asp
20 25 30

Met Asp Lys Glu Ser Leu Glu Asp Val Thr Thr Lys Leu Gly Glu Arg
35 40 45

Val Glu Ser Leu Lys
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<210> 371

<211> 44

<212> PRT

<213> Plasmodium falciparum

<400> 371

His Ile Lys Gly Leu Glu Glu Asp Asp Leu Glu Glu Val Asp Asp Leu
1 5 10 15

Lys Gly Ser Ile Leu Asp Met Leu Lys Gly Asp Met Glu Leu Gly Asp
20 25 30

Met Asp Lys Glu Ser Leu Glu Asp Val Thr Thr Lys
35 40

<210> 372

<211> 35

<212> PRT

<213> Plasmodium falciparum

<400> 372

His Ile Lys Gly Leu Glu Glu Asp Asp Leu Glu Glu Val Asp Asp Leu

SEQ.List.txt

1 5 10 15
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 Met Asp Lys
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<210> 373
 <211> 25
 <212> PRT
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<400> 373
 His Ile Lys Gly Leu Glu Glu Asp Asp Leu Glu Glu Val Asp Asp Leu
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 Lys Gly Ser Ile Leu Asp Met Leu Lys
 20 25

<210> 374
 <211> 31
 <212> PRT
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<400> 374
 His Ile Ile Ser Gly Asp Ala Asp Val Leu Ser Ser Ala Leu Gly Met
 1 5 10 15
 Asp Glu Glu Gln Met Lys Thr Arg Lys Lys Ala Gln Arg Pro Lys
 20 25 30

<210> 375
 <211> 23
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<400> 375
 His Asp Ile Thr Thr Thr Leu Asp Glu Val Val Glu Leu Lys Asp Val
 1 5 10 15
 Glu Glu Asp Lys Ile Glu Lys
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SEQ.List.txt

<210> 376

<211> 10

<212> PRT

<213> Plasmodium falciparum

<400> 376

Lys Lys Leu Glu Glu Val His Glu Leu Lys
1 5 10

<210> 377

<211> 9

<212> PRT

<213> Plasmodium falciparum

<400> 377

Lys Leu Glu Glu Val His Glu Leu Lys
1 5

<210> 378

<211> 19

<212> PRT

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<400> 378

Lys Thr Ile Glu Thr Asp Ile Leu Glu Glu Lys Lys Lys Glu Ile Glu
1 5 10 15

Lys Asp His

<210> 379

<211> 11

<212> PRT

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<400> 379

Lys Lys Glu Ile Glu Lys Asp His Phe Glu Lys
1 5 10

<210> 380

<211> 6

<212> PRT

<213> Plasmodium falciparum

<400> 380

SEQ.List.txt

Lys Asp His Phe Glu Lys
1 5

<210> 381
<211> 11
<212> PRT
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<400> 381
Lys Phe Glu Glu Glu Ala Glu Glu Ile Lys His
1 5 10

<210> 382
<211> 47
<212> PRT
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<400> 382
Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
1 5 10 15

Cys Ile Lys His Lys Ser Asp His Asn His Lys Ser Asp His Asn His
20 25 30

Lys Ser Asp Pro Asn His Lys Lys Lys Asn Asn Asn Asn Asn Lys
35 40 45

<210> 383
<211> 40
<212> PRT
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<400> 383
Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
1 5 10 15

Cys Ile Lys His Lys Ser Asp His Asn His Lys Ser Asp His Asn His
20 25 30

Lys Ser Asp Pro Asn His Lys Lys
35 40

<210> 384
<211> 39

SEQ.List.txt

<212> PRT

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<400> 384

Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
1 5 10 15

Cys Ile Lys His Lys Ser Asp His Asn His Lys Ser Asp His Asn His
20 25 30

Lys Ser Asp Pro Asn His Lys
35

<210> 385

<211> 33

<212> PRT

<213> Plasmodium falciparum

<400> 385

Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
1 5 10 15

Cys Ile Lys His Lys Ser Asp His Asn His Lys Ser Asp His Asn His
20 25 30

Lys

<210> 386

<211> 27

<212> PRT

<213> Plasmodium falciparum

<400> 386

Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
1 5 10 15

Cys Ile Lys His Lys Ser Asp His Asn His Lys
20 25

<210> 387

<211> 21

<212> PRT

<213> Plasmodium falciparum

<400> 387

SEQ.List.txt

Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
 1 5 10 15

Cys Ile Lys His Lys
 20

<210> 388

<211> 16

<212> PRT

<213> Plasmodium falciparum

<400> 388

Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys Lys
 1 5 10 15

<210> 389

<211> 15

<212> PRT

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<400> 389

Lys Asp Gly Asp Thr Lys Cys Thr Leu Glu Cys Ala Gln Gly Lys
 1 5 10 15

<210> 390

<211> 23

<212> PRT

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<400> 390

Lys Cys Ile Gln Ala Glu Cys Asn Tyr Lys Glu Cys Gly Glu Gln Lys
 1 5 10 15

Cys Val Trp Asp Gly Ile His
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<210> 391

<211> 14

<212> PRT

<213> Plasmodium falciparum

<400> 391

Lys Glu Cys Gly Glu Gln Lys Cys Val Trp Asp Gly Ile His
 1 5 10

SEQ.List.txt

<210> 392
 <211> 32
 <212> PRT
 <213> Plasmodium falciparum

<400> 392
 His Ile Glu Cys Lys Cys Asn Asn Asp Tyr Val Leu Thr Asn Arg Tyr
 1 5 10 15
 Glu Cys Glu Pro Lys Asn Lys Cys Thr Ser Leu Glu Asp Thr Asn Lys
 20 25 30

<210> 393
 <211> 39
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<400> 393
 Lys Ser Asp His Asn His Lys Ser Asp His Asn His Lys Ser Asp His
 1 5 10 15
 Asn His Lys Ser Asp His Asn His Lys Ser Asp Pro Asn His Lys Lys
 20 25 30
 Lys Asn Asn Asn Asn Asn Lys
 35

<210> 394
 <211> 33
 <212> PRT
 <213> Plasmodium falciparum

<400> 394
 Lys Ser Asp His Asn His Lys Ser Asp His Asn His Lys Ser Asp His
 1 5 10 15
 Asn His Lys Ser Asp Pro Asn His Lys Lys Lys Asn Asn Asn Asn Asn
 20 25 30
 Lys

<210> 395
 <211> 27

SEQ.List.txt

<212> PRT

<213> Plasmodium falciparum

<400> 395

Lys Ser Asp His Asn His Lys Ser Asp His Asn His Lys Ser Asp Pro
1 5 10 15

Asn His Lys Lys Lys Asn Asn Asn Asn Asn Lys
20 25

<210> 396

<211> 21

<212> PRT

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<400> 396

Lys Ser Asp His Asn His Lys Ser Asp Pro Asn His Lys Lys Lys Asn
1 5 10 15

Asn Asn Asn Asn Lys
20

<210> 397

<211> 18

<212> PRT

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<400> 397

Lys Lys Lys Asn Asn Asn Asn Asn Lys Asp Asn Lys Ser Asp Pro Asn
1 5 10 15

His Lys

<210> 398

<211> 17

<212> PRT

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<400> 398

Lys Lys Asn Asn Asn Asn Asn Lys Asp Asn Lys Ser Asp Pro Asn His
1 5 10 15

Lys

SEQ.List.txt

<210> 399

<211> 16

<212> PRT

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<400> 399

Lys Asn Asn Asn Asn Asn Lys Asp Asn Lys Ser Asp Pro Asn His Lys
1 5 10 15

<210> 400

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<400> 400

Lys Asp Asn Lys Ser Asp Pro Asn His Lys
1 5 10

<210> 401

<211> 7

<212> PRT

<213> Plasmodium falciparum

<400> 401

Lys Ser Asp Pro Asn His Lys
1 5

<210> 402

<211> 35

<212> PRT

<213> Plasmodium falciparum

<400> 402

His Ser Leu Tyr Ala Leu Gln Gln Asn Glu Glu Tyr Gln Lys Val Lys
1 5 10 15

Asn Glu Lys Asp Gln Asn Glu Ile Lys Lys Ile Lys Gln Leu Ile Glu
20 25 30

Lys Asn Lys
35

<210> 403

<211> 28

SEQ.List.txt

<212> PRT

<213> Plasmodium falciparum

<400> 403

His Ser Leu Tyr Ala Leu Gln Gln Asn Glu Glu Tyr Gln Lys Val Lys
1 5 10 15

Asn Glu Lys Asp Gln Asn Glu Ile Lys Lys Ile Lys
20 25

<210> 404

<211> 26

<212> PRT

<213> Plasmodium falciparum

<400> 404

His Ser Leu Tyr Ala Leu Gln Gln Asn Glu Glu Tyr Gln Lys Val Lys
1 5 10 15

Asn Glu Lys Asp Gln Asn Glu Ile Lys Lys
20 25

<210> 405

<211> 25

<212> PRT

<213> Plasmodium falciparum

<400> 405

His Ser Leu Tyr Ala Leu Gln Gln Asn Glu Glu Tyr Gln Lys Val Lys
1 5 10 15

Asn Glu Lys Asp Gln Asn Glu Ile Lys
20 25

<210> 406

<211> 11

<212> PRT

<213> Plasmodium falciparum

<400> 406

His Lys Leu Glu Asn Leu Glu Glu Met Asp Lys
1 5 10

<210> 407

SEQ.List.txt

<211> 11
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<400> 407
 Lys His Phe Asp Asp Asn Thr Asn Glu Gln Lys
 1 5 10

<210> 408
 <211> 8
 <212> PRT
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<400> 408
 Lys Lys Glu Asp Asp Glu Lys His
 1 5

<210> 409
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<400> 409
 Lys Glu Glu Asn Asn Lys Lys Glu Asp Asp Glu Lys His
 1 5 10

<210> 410
 <211> 21
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<400> 410
 Lys Thr Ser Ser Gly Ile Leu Asn Lys Glu Glu Asn Asn Lys Lys Glu
 1 5 10 15

Asp Asp Glu Lys His
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<210> 411
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 <212> PRT
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<400> 411

SEQ.List.txt

Lys Asn Ile His Ile Lys Lys
1 5

<210> 412

<211> 13

<212> PRT

<213> Plasmodium falciparum

<400> 412

His Ile Lys Lys Lys Glu Gly Ile Asp Ile Gly Tyr Lys
1 5 10

<210> 413

<211> 21

<212> PRT

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<400> 413

Lys Lys Met Trp Thr Cys Lys Leu Trp Asp Asn Lys Gly Asn Glu Ile
1 5 10 15

Thr Lys Asn Ile His
20

<210> 414

<211> 30

<212> PRT

<213> Plasmodium falciparum

<400> 414

Lys Lys Gly Ile Gln Trp Asn Leu Leu Lys Lys Met Trp Thr Cys Lys
1 5 10 15

Leu Trp Asp Asn Lys Gly Asn Glu Ile Thr Lys Asn Ile His
20 25 30

<210> 415

<211> 50

<212> PRT

<213> Plasmodium falciparum

<400> 415

Lys Glu Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys Glu
1 5 10 15

SEQ.List.txt

Asp Lys Lys Asn Pro Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys
20 25 30

Ile Thr His Phe Phe Lys Ala Lys Asn Asn Lys Gln Gln Asn Asn Val
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Thr His
50

<210> 416

<211> 48

<212> PRT

<213> Plasmodium falciparum

<400> 416

Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys Glu Asp Lys
1 5 10 15

Lys Asn Pro Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr
20 25 30

His Phe Phe Lys Ala Lys Asn Asn Lys Gln Gln Asn Asn Val Thr His
35 40 45

<210> 417

<211> 47

<212> PRT

<213> Plasmodium falciparum

<400> 417

Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys Glu Asp Lys Lys
1 5 10 15

Asn Pro Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr His
20 25 30

Phe Phe Lys Ala Lys Asn Asn Lys Gln Gln Asn Asn Val Thr His
35 40 45

<210> 418

<211> 39

<212> PRT

<213> Plasmodium falciparum

SEQ.List.txt

<400> 418

Lys Lys Gln Lys Glu Asp Lys Lys Asn Pro Asn Lys Leu Lys Lys Ile
1 5 10 15

Glu Tyr Thr Asn Lys Ile Thr His Phe Phe Lys Ala Lys Asn Asn Lys
20 25 30

Gln Gln Asn Asn Val Thr His ..
35

<210> 419

<211> 38

<212> PRT

<213> Plasmodium falciparum

<400> 419

Lys Gln Lys Glu Asp Lys Lys Asn Pro Asn Lys Leu Lys Lys Ile Glu
1 5 10 15

Tyr Thr Asn Lys Ile Thr His Phe Phe Lys Ala Lys Asn Asn Lys Gln
20 25 30

Gln Asn Asn Val Thr His
35

<210> 420

<211> 36

<212> PRT

<213> Plasmodium falciparum

<400> 420

Lys Glu Asp Lys Lys Asn Pro Asn Lys Leu Lys Lys Ile Glu Tyr Thr
1 5 10 15

Asn Lys Ile Thr His Phe Phe Lys Ala Lys Asn Asn Lys Gln Gln Asn
20 25 30

Asn Val Thr His
35

<210> 421

<211> 32

<212> PRT

<213> Plasmodium falciparum

SEQ.List.txt

<400> 421

Lys Asn Pro Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr
1 5 10 15

His Phe Phe Lys Ala Lys Asn Asn Lys Gln Gln Asn Asn Val Thr His
20 25 30

<210> 422

<211> 26

<212> PRT

<213> Plasmodium falciparum

<400> 422

Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr His Phe Phe Lys Ala Lys
1 5 10 15

Asn Asn Lys Gln Gln Asn Asn Val Thr His
20 25

<210> 423

<211> 25

<212> PRT

<213> Plasmodium falciparum

<400> 423

Lys Ile Glu Tyr Thr Asn Lys Ile Thr His Phe Phe Lys Ala Lys Asn
1 5 10 15

Asn Lys Gln Gln Asn Asn Val Thr His
20 25

<210> 424

<211> 19

<212> PRT

<213> Plasmodium falciparum

<400> 424

Lys Ile Thr His Phe Phe Lys Ala Lys Asn Asn Lys Gln Gln Asn Asn
1 5 10 15

Val Thr His

<210> 425

<211> 48

SEQ.List.txt

<212> PRT

<213> Plasmodium falciparum

<400> 425

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
20 25 30

Asn Asp Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
35 40 45

<210> 426

<211> 45

<212> PRT

<213> Plasmodium falciparum

<400> 426

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
20 25 30

Asn Asp Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys
35 40 45

<210> 427

<211> 40

<212> PRT

<213> Plasmodium falciparum

<400> 427

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
20 25 30

Asn Asp Asn Asn Glu Asp Ile Lys
35 40

<210> 428

<211> 32

SEQ.List.txt

<212> PRT

<213> Plasmodium falciparum

<400> 428

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
20 25 30

<210> 429

<211> 29

<212> PRT

<213> Plasmodium falciparum

<400> 429

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys Asp Ile Lys Asn Asp Asn Ser Lys
20 25

<210> 430

<211> 24

<212> PRT

<213> Plasmodium falciparum

<400> 430

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys Asp Ile Lys
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<210> 431

<211> 21

<212> PRT

<213> Plasmodium falciparum

<400> 431

His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
1 5 10 15

Asn Asp Asn Ser Lys
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SEQ.List.txt

<210> 432
 <211> 16
 <212> PRT
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<400> 432
 His Lys Asn Asn Glu Asp Ile Lys Asn Asp Asn Ser Lys Asp Ile Lys
 1 5 10 15

<210> 433
 <211> 8
 <212> PRT
 <213> Plasmodium falciparum

<400> 433
 His Lys Asn Asn Glu Asp Ile Lys
 1 5

<210> 434
 <211> 31
 <212> PRT
 <213> Plasmodium falciparum

<400> 434
 Lys Lys Tyr Asp Asp Leu Gln Asn Lys Tyr Asn Ile Leu Asn Lys Leu
 1 5 10 15
 Lys Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr His
 20 25 30

<210> 435
 <211> 30
 <212> PRT
 <213> Plasmodium falciparum

<400> 435
 Lys Tyr Asp Asp Leu Gln Asn Lys Tyr Asn Ile Leu Asn Lys Leu Lys
 1 5 10 15
 Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr His
 20 25 30

SEQ.List.txt

<210> 436

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 436

Lys Tyr Asn Ile Leu Asn Lys Leu Lys Asn Ser Leu Glu Glu Lys Asn
1 5 10 15

Glu Glu Leu Lys Lys Tyr His
20

<210> 437

<211> 17

<212> PRT

<213> Plasmodium falciparum

<400> 437

Lys Leu Lys Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr
1 5 10 15

His

<210> 438

<211> 15

<212> PRT

<213> Plasmodium falciparum

<400> 438

Lys Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr His
1 5 10 15

<210> 439

<211> 9

<212> PRT

<213> Plasmodium falciparum

<400> 439

Lys Asn Glu Glu Leu Lys Lys Tyr His
1 5

<210> 440

<211> 35

<212> PRT

SEQ.List.txt

<213> Plasmodium falciparum

<400> 440

His Met Gly Asn Asn Gln Asp Ile Asn Glu Asn Val Tyr Asn Ile Lys
1 5 10 15

Pro Gln Glu Phe Lys Glu Glu Glu Glu Glu Asp Ile Ser Met Val Asn
20 25 30

Thr Lys Lys
35

<210> 441

<211> 17

<212> PRT

<213> Plasmodium falciparum

<400> 441

Lys Asn Ser Asn Glu Leu Lys Arg Ile Asn Asp Asn Phe Phe Lys Leu
1 5 10 15

His

<210> 442

<211> 55

<212> PRT

<213> Plasmodium falciparum

<400> 442

Lys Pro Cys Leu Tyr Lys Lys Cys Lys Ile Ser Gln Cys Leu Tyr Lys
1 5 10 15

Lys Cys Lys Ile Ser Gln Val Trp Trp Cys Met Pro Val Lys Asp Thr
20 25 30

Phe Asn Thr Tyr Glu Arg Asn Asn Val Leu Asn Ser Lys Ile Glu Asn
35 40 45

Asn Ile Glu Lys Ile Pro His
50 55

<210> 443

<211> 40

<212> PRT

<213> Plasmodium falciparum

SEQ.List.txt

<400> 443

His Ile Asn Asn Glu Tyr Thr Asn Lys Asn Pro Lys Asn Cys Leu Leu
1 5 10 15

Tyr Lys Asn Glu Glu Arg Asn Tyr Asn Asp Asn Asn Ile Lys Asp Tyr
20 25 30

Ile Asn Ser Met Asn Phe Lys Lys
35 40

<210> 444

<211> 39

<212> PRT

<213> Plasmodium falciparum

<400> 444

His Ile Asn Asn Glu Tyr Thr Asn Lys Asn Pro Lys Asn Cys Leu Leu
1 5 10 15

Tyr Lys Asn Glu Glu Arg Asn Tyr Asn Asp Asn Asn Ile Lys Asp Tyr
20 25 30

Ile Asn Ser Met Asn Phe Lys
35

<210> 445

<211> 18

<212> PRT

<213> Plasmodium falciparum

<400> 445

His Ile Asn Asn Glu Tyr Thr Asn Lys Asn Pro Lys Asn Cys Leu Leu
1 5 10 15

Tyr Lys

<210> 446

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 446

Lys Asn Lys Thr Asn Gln Ser Lys Gly Val Lys Gly Glu Tyr Glu Lys
1 5 10 15

SEQ.List.txt

Lys Lys Glu Thr Asn Gly His
20

<210> 447
<211> 21
<212> PRT
<213> Plasmodium falciparum

<400> 447
Lys Thr Asn Gln Ser Lys Gly Val Lys Gly Glu Tyr Glu Lys Lys Lys
1 5 10 15

Glu Thr Asn Gly His
20

<210> 448
<211> 16
<212> PRT
<213> Plasmodium falciparum

<400> 448
Lys Gly Val Lys Gly Glu Tyr Glu Lys Lys Lys Glu Thr Asn Gly His
1 5 10 15

<210> 449
<211> 13
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<213> Plasmodium falciparum

<400> 449
Lys Gly Glu Tyr Glu Lys Lys Lys Glu Thr Asn Gly His
1 5 10

<210> 450
<211> 28
<212> PRT
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<400> 450
Lys Ser Gly Met Tyr Thr Asn Glu Gly Asn Lys Ser Cys Glu Cys Ser
1 5 10 15

Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys Val His

<210> 451
<211> 18
<212> PRT
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<400> 451
Lys Ser Cys Glu Cys Ser Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys
1 5 10 15
Val His

<210> 452
<211> 11
<212> PRT
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<400> 452
Lys Lys Lys Ser Ser Ser Ser Asn Lys Val His
1 5 10

<210> 453
<211> 10
<212> PRT
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<400> 453
Lys Lys Ser Ser Ser Ser Asn Lys Val His
1 5 10

<210> 454
<211> 9
<212> PRT
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<400> 454
Lys Ser Ser Ser Ser Asn Lys Val His
1 5

<210> 455
<211> 30
<212> PRT

SEQ.List.txt

<213> Plasmodium falciparum

<400> 455

His Ile Met Leu Lys Ser Gly Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys
20 25 30

<210> 456

<211> 24

<212> PRT

<213> Plasmodium falciparum

<400> 456

His Ile Met Leu Lys Ser Gly Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys Lys
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<210> 457

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 457

His Ile Met Leu Lys Ser Gly Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys
20

<210> 458

<211> 22

<212> PRT

<213> Plasmodium falciparum

<400> 458

His Ile Met Leu Lys Ser Gly Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys
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SEQ.List.txt

<210> 459

<211> 50

<212> PRT

<213> Plasmodium falciparum

<400> 459

Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys
1 5 10 15

Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln
20 25 30

Lys Ile Ile Ile Arg Asp Tyr His Glu Thr Leu Asn Val His Lys Leu
35 40 45

Asp His
50

<210> 460

<211> 43

<212> PRT

<213> Plasmodium falciparum

<400> 460

Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp
1 5 10 15

Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Ile Arg Asp Tyr
20 25 30

His Glu Thr Leu Asn Val His Lys Leu Asp His
35 40

<210> 461

<211> 40

<212> PRT

<213> Plasmodium falciparum

<400> 461

Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile
1 5 10 15

Asp Asn Thr Glu Ile Gln Lys Ile Ile Ile Arg Asp Tyr His Glu Thr
20 25 30

SEQ.List.txt

Leu Asn Val His Lys Leu Asp His
35 40

<210> 462

<211> 46

<212> PRT

<213> Plasmodium falciparum

<400> 462

Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys
1 5 10 15

Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln
20 25 30

Lys Ile Ile Ile Arg Asp Tyr His Glu Thr Leu Asn Val His
35 40 45

<210> 463

<211> 40

<212> PRT

<213> Plasmodium falciparum

<400> 463

Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys
1 5 10 15

Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln
20 25 30

Lys Ile Ile Ile Arg Asp Tyr His
35 40

<210> 464

<211> 36

<212> PRT

<213> Plasmodium falciparum

<400> 464

Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu
1 5 10 15

Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Ile
20 25 30

SEQ.List.txt

Arg Asp Tyr His
35

<210> 465
<211> 33
<212> PRT
<213> Plasmodium falciparum

<400> 465
Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp
1 5 10 15
Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Ile Arg Asp Tyr
20 25 30

His

<210> 466
<211> 30
<212> PRT
<213> Plasmodium falciparum

<400> 466
Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile
1 5 10 15
Asp Asn Thr Glu Ile Gln Lys Ile Ile Ile Arg Asp Tyr His
20 25 30

<210> 467
<211> 41
<212> PRT
<213> Plasmodium falciparum

<400> 467
Lys Lys Asp Lys Glu Lys Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys
1 5 10 15
Lys Gln Lys Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys
20 25 30
Ile Glu Tyr Thr Asn Lys Ile Thr His
35 40

SEQ.List.txt

<210> 468

<211> 40

<212> PRT

<213> Plasmodium falciparum

<400> 468

Lys Asp Lys Glu Lys Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys
1 5 10 15

Gln Lys Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile
20 25 30

Glu Tyr Thr Asn Lys Ile Thr His
35 40

<210> 469

<211> 38

<212> PRT

<213> Plasmodium falciparum

<400> 469

Lys Glu Lys Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys
1 5 10 15

Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu Tyr
20 25 30

Thr Asn Lys Ile Thr His
35

<210> 470

<211> 36

<212> PRT

<213> Plasmodium falciparum

<400> 470

Lys Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys Glu Asp
1 5 10 15

Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn
20 25 30

Lys Ile Thr His
35

SEQ.List.txt

<210> 471

<211> 35

<212> PRT

<213> Plasmodium falciparum

<400> 471

Lys Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys Glu Asp Lys
1 5 10 15

Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys
20 25 30

Ile Thr His
35

<210> 472

<211> 34

<212> PRT

<213> Plasmodium falciparum

<400> 472

Lys Asp Ser Asn Glu Asn Arg Lys Lys Lys Gln Lys Glu Asp Lys Lys
1 5 10 15

Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys Ile
20 25 30

Thr His

<210> 473

<211> 27

<212> PRT

<213> Plasmodium falciparum

<400> 473

Lys Lys Lys Gln Lys Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu
1 5 10 15

Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr His
20 25

<210> 474

<211> 26

<212> PRT

<213> Plasmodium falciparum

SEQ.List.txt

<400> 474

Lys Lys Gln Lys Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys
1 5 10 15

Lys Ile Glu Tyr Thr Asn Lys Ile Thr His
20 25

<210> 475

<211> 25

<212> PRT

<213> Plasmodium falciparum

<400> 475

Lys Gln Lys Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys
1 5 10 15

Ile Glu Tyr Thr Asn Lys Ile Thr His
20 25

<210> 476

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 476

Lys Glu Asp Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu
1 5 10 15

Tyr Thr Asn Lys Ile Thr His
20

<210> 477

<211> 20

<212> PRT

<213> Plasmodium falciparum

<400> 477

Lys Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn
1 5 10 15

Lys Ile Thr His
20

SEQ.List.txt

<210> 478

<211> 19

<212> PRT

<213> Plasmodium falciparum

<400> 478

Lys Asn Pro Asn Asp Asn Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys
1 5 10 15

Ile Thr His

<210> 479

<211> 13

<212> PRT

<213> Plasmodium falciparum

<400> 479

Lys Leu Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr His
1 5 10

<210> 480

<211> 11

<212> PRT

<213> Plasmodium falciparum

<400> 480

Lys Lys Ile Glu Tyr Thr Asn Lys Ile Thr His
1 5 10

<210> 481

<211> 10

<212> PRT

<213> Plasmodium falciparum

<400> 481

Lys Ile Glu Tyr Thr Asn Lys Ile Thr His
1 5 10

<210> 482

<211> 44

<212> PRT

<213> Plasmodium falciparum

<400> 482

SEQ.List.txt

His Gly Gln Ile Lys Ile Glu Asp Val Asn Asn Glu Asn Phe Asn Asn
 1 5 10 15

Glu Gln Met Lys Asn Lys Tyr Asn Asp Glu Glu Lys Met Asp Ile Ser
 20 25 30

Lys Ser Lys Ser Leu Lys Ser Asp Phe Leu Glu Lys
 35 40

<210> 483

<211> 38

<212> PRT

<213> Plasmodium falciparum

<400> 483

His Gly Gln Ile Lys Ile Glu Asp Val Asn Asn Glu Asn Phe Asn Asn
 1 5 10 15

Glu Gln Met Lys Asn Lys Tyr Asn Asp Glu Glu Lys Met Asp Ile Ser
 20 25 30

Lys Ser Lys Ser Leu Lys
 35

<210> 484

<211> 35

<212> PRT

<213> Plasmodium falciparum

<400> 484

His Gly Gln Ile Lys Ile Glu Asp Val Asn Asn Glu Asn Phe Asn Asn
 1 5 10 15

Glu Gln Met Lys Asn Lys Tyr Asn Asp Glu Glu Lys Met Asp Ile Ser
 20 25 30

Lys Ser Lys
 35

<210> 485

<211> 33

<212> PRT

<213> Plasmodium falciparum

<400> 485

SEQ.List.txt

His Gly Gln Ile Lys Ile Glu Asp Val Asn Asn Glu Asn Phe Asn Asn
1 5 10 15

Glu Gln Met Lys Asn Lys Tyr Asn Asp Glu Glu Lys Met Asp Ile Ser
20 25 30

Lys

<210> 486

<211> 31

<212> PRT

<213> Plasmodium falciparum

<400> 486

Lys Lys Tyr Asp Asp Leu Gln Asn Lys Tyr Asn Ile Leu Asn Lys Leu
1 5 10 15

Lys Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr His
20 25 30

<210> 487

<211> 30

<212> PRT

<213> Plasmodium falciparum

<400> 487

Lys Tyr Asp Asp Leu Gln Asn Lys Tyr Asn Ile Leu Asn Lys Leu Lys
1 5 10 15

Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr His
20 25 30

<210> 488

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 488

Lys Tyr Asn Ile Leu Asn Lys Leu Lys Asn Ser Leu Glu Glu Lys Asn
1 5 10 15

Glu Glu Leu Lys Lys Tyr His
20

SEQ.List.txt

<210> 489

<211> 17

<212> PRT

<213> Plasmodium falciparum

<400> 489

Lys Leu Lys Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr
1 5 10 15

His

<210> 490

<211> 15

<212> PRT

<213> Plasmodium falciparum

<400> 490

Lys Asn Ser Leu Glu Glu Lys Asn Glu Glu Leu Lys Lys Tyr His
1 5 10 15

<210> 491

<211> 9

<212> PRT

<213> Plasmodium falciparum

<400> 491

Lys Asn Glu Glu Leu Lys Lys Tyr His
1 5

<210> 492

<211> 44

<212> PRT

<213> Plasmodium falciparum

<400> 492

His Met Gly Asn Asn Gln Asp Ile Asn Glu Asn Val Tyr Asn Ile Lys
1 5 10 15

Pro Gln Glu Phe Lys Glu Glu Glu Glu Glu Asp Ile Ser Met Val Asn
20 25 30

Thr Lys Lys Cys Asp Asp Ile Gln Glu Asn Ile Lys
35 40

SEQ.List.txt

<210> 493

<211> 50

<212> PRT

<213> Plasmodium falciparum

<400> 493

Lys Thr Asn Leu Tyr Asn Ile Tyr Asn Asn Lys Asn Asp Asp Lys Asp
1 5 10 15

Asn Ile Leu Asp Asn Glu Asn Arg Glu Gly Leu Tyr Leu Cys Asp Val
20 25 30

Met Lys Asn Ser Asn Glu Leu Lys Arg Ile Asn Asp Asn Phe Phe Lys
35 40 45

Leu His
50

<210> 494

<211> 17

<212> PRT

<213> Plasmodium falciparum

<400> 494

Lys Asn Ser Asn Glu Leu Lys Arg Ile Asn Asp Asn Phe Phe Lys Leu
1 5 10 15

His

<210> 495

<211> 11

<212> PRT

<213> Plasmodium falciparum

<400> 495

Lys Arg Ile Asn Asp Asn Phe Phe Lys Leu His
1 5 10

<210> 496

<211> 40

<212> PRT

<213> Plasmodium falciparum

<400> 496

His Ile Asn Asn Glu Tyr Thr Asn Lys Asn Pro Lys Asn Cys Leu Leu

SEQ.List.txt

1 5 10 15
Tyr Lys Asn Glu Glu Arg Asn Tyr Asn Asp Asn Asn Ile Lys Asp Tyr
 20 25 30
Ile Asn Ser Met Asn Phe Lys Lys
 35 40

<210> 497
<211> 39
<212> PRT
<213> Plasmodium falciparum

<400> 497
His Ile Asn Asn Glu Tyr Thr Asn Lys Asn Pro Lys Asn Cys Leu Leu
1 5 10 15
Tyr Lys Asn Glu Glu Arg Asn Tyr Asn Asp Asn Asn Ile Lys Asp Tyr
 20 25 30
Ile Asn Ser Met Asn Phe Lys
 35

<210> 498
<211> 18
<212> PRT
<213> Plasmodium falciparum

<400> 498
His Ile Asn Asn Glu Tyr Thr Asn Lys Asn Pro Lys Asn Cys Leu Leu
1 5 10 15
Tyr Lys

<210> 499
<211> 45
<212> PRT
<213> Plasmodium falciparum

<400> 499
Lys Pro Cys Leu Tyr Lys Lys Cys Lys Ile Ser Gln Val Trp Trp Cys
1 5 10 15
Met Pro Val Lys Asp Thr Phe Asn Thr Tyr Glu Arg Asn Asn Val Leu
 20 25 30

SEQ.List.txt

Asn Ser Lys Ile Glu Asn Asn Ile Glu Lys Ile Pro His
 35 40 45

<210> 500
 <211> 39
 <212> PRT
 <213> Plasmodium falciparum

<400> 500
 Lys Cys Lys Ile Ser Gln Val Trp Trp Cys Met Pro Val Lys Asp Thr
 1 5 10 15
 Phe Asn Thr Tyr Glu Arg Asn Asn Val Leu Asn Ser Lys Ile Glu Asn
 20 25 30

Asn Ile Glu Lys Ile Pro His
 35

<210> 501
 <211> 11
 <212> PRT
 <213> Plasmodium falciparum

<400> 501
 Lys Ile Glu Asn Asn Ile Glu Lys Ile Pro His
 1 5 10

<210> 502
 <211> 23
 <212> PRT
 <213> Plasmodium falciparum

<400> 502
 Lys Asn Lys Thr Asn Gly Ser Lys Gly Val Lys Gly Glu Tyr Glu Lys
 1 5 10 15

Lys Lys Glu Thr Asn Gly His
 20

<210> 503
 <211> 21
 <212> PRT
 <213> Plasmodium falciparum

SEQ.List.txt

<400> 503

Lys Thr Asn Gly Ser Lys Gly Val Lys Gly Glu Tyr Glu Lys Lys Lys
1 5 10 15

Glu Thr Asn Gly His
20

<210> 504

<211> 16

<212> PRT

<213> Plasmodium falciparum

<400> 504

Lys Gly Val Lys Gly Glu Tyr Glu Lys Lys Lys Glu Thr Asn Gly His
1 5 10 15

<210> 505

<211> 13

<212> PRT

<213> Plasmodium falciparum

<400> 505

Lys Gly Glu Tyr Glu Lys Lys Lys Glu Thr Asn Gly His
1 5 10

<210> 506

<211> 60

<212> PRT

<213> Plasmodium falciparum

<400> 506

Lys Thr Ile Glu Lys Ile Asn Lys Ser Lys Ser Trp Phe Phe Glu Glu
1 5 10 15

Leu Asp Glu Ile Asp Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys
20 25 30

Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp
35 40 45

Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His
50 55 60

SEQ.List.txt

<210> 507

<211> 56

<212> PRT

<213> Plasmodium falciparum

<400> 507

Lys Ile Asn Lys Ser Lys Ser Trp Phe Phe Glu Glu Leu Asp Glu Ile
1 5 10 15

Asp Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn
20 25 30

Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile
35 40 45

Gln Lys Ile Ile Arg Asp Tyr His
50 55

<210> 508

<211> 39

<212> PRT

<213> Plasmodium falciparum

<400> 508

Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys
1 5 10 15

Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln
20 25 30

Lys Ile Ile Arg Asp Tyr His
35

<210> 509

<211> 32

<212> PRT

<213> Plasmodium falciparum

<400> 509

His Ile Met Leu Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys Val His
20 25 30

SEQ.List.txt

<210> 510
 <211> 35
 <212> PRT
 <213> Plasmodium falciparum

<400> 510
 Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu
 1 5 10 15
 Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg
 20 25 30
 Asp Tyr His
 35

<210> 511
 <211> 32
 <212> PRT
 <213> Plasmodium falciparum

<400> 511
 Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp
 1 5 10 15
 Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His
 20 25 30

<210> 512
 <211> 29
 <212> PRT
 <213> Plasmodium falciparum

<400> 512
 Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile
 1 5 10 15
 Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His
 20 25

<210> 513
 <211> 48
 <212> PRT
 <213> Plasmodium falciparum

<400> 513

SEQ.List.txt

Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys
1 5 10 15

Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln
20 25 30

Lys Ile Ile Arg Asp Tyr His Thr Leu Asn Val His Lys Leu Asp His
35 40 45

<210> 514

<211> 44

<212> PRT

<213> Plasmodium falciparum

<400> 514

Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu
1 5 10 15

Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg
20 25 30

Asp Tyr His Thr Leu Asn Val His Lys Leu Asp His
35 40

<210> 515

<211> 41

<212> PRT

<213> Plasmodium falciparum

<400> 515

Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp
1 5 10 15

Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His
20 25 30

Thr Leu Asn Val His Lys Leu Asp His
35 40

<210> 516

<211> 38

<212> PRT

<213> Plasmodium falciparum

<400> 516

SEQ.List.txt

Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile
1 5 10 15

Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His Thr Leu Asn
20 25 30

Val His Lys Leu Asp His
35

<210> 517

<211> 44

<212> PRT

<213> Plasmodium falciparum

<400> 517

Lys Pro Leu Ala Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys
1 5 10 15

Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln
20 25 30

Lys Ile Ile Arg Asp Tyr His Thr Leu Asn Val His
35 40

<210> 518

<211> 40

<212> PRT

<213> Plasmodium falciparum

<400> 518

Lys Leu Arg Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu
1 5 10 15

Arg Gly Asp Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg
20 25 30

Asp Tyr His Thr Leu Asn Val His
35 40

<210> 519

<211> 37

<212> PRT

<213> Plasmodium falciparum

<400> 519

SEQ.List.txt

Lys Arg Glu Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp
1 5 10 15

Val Ile Ile Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His
20 25 30

Thr Leu Asn Val His
35

<210> 520

<211> 34

<212> PRT

<213> Plasmodium falciparum

<400> 520

Lys Thr Gln Ile Asn Lys Thr Lys Tyr Glu Arg Gly Asp Val Ile Ile
1 5 10 15

Asp Asn Thr Glu Ile Gln Lys Ile Ile Arg Asp Tyr His Thr Leu Asn
20 25 30

Val His

<210> 521

<211> 32

<212> PRT

<213> Plasmodium falciparum

<400> 521

His Ile Met Leu Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys Val His
20 25 30

<210> 522

<211> 28

<212> PRT

<213> Plasmodium falciparum

<400> 522

Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser Cys Glu Cys Ser
1 5 10 15

Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys Val His

<210> 523
<211> 18
<212> PRT
<213> Plasmodium falciparum

<400> 523
Lys Ser Cys Glu Cys Ser Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys
1 5 10 15

Val His

<210> 524
<211> 11
<212> PRT
<213> Plasmodium falciparum

<400> 524
Lys Lys Lys Ser Ser Ser Ser Asn Lys Val His
1 5 10

<210> 525
<211> 10
<212> PRT
<213> Plasmodium falciparum

<400> 525
Lys Lys Ser Ser Ser Ser Asn Lys Val His
1 5 10

<210> 526
<211> 9
<212> PRT
<213> Plasmodium falciparum

<400> 526
Lys Ser Ser Ser Ser Asn Lys Val His
1 5

<210> 527
<211> 30
<212> PRT

SEQ.List.txt

<213> Plasmodium falciparum

<400> 527

His Ile Met Leu Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys Lys Ser Ser Ser Ser Asn Lys
20 25 30

<210> 528

<211> 24

<212> PRT

<213> Plasmodium falciparum

<400> 528

His Ile Met Leu Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys Lys
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<210> 529

<211> 23

<212> PRT

<213> Plasmodium falciparum

<400> 529

His Ile Met Leu Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys Lys
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<210> 530

<211> 22

<212> PRT

<213> Plasmodium falciparum

<400> 530

His Ile Met Leu Lys Ser Gln Met Tyr Thr Asn Glu Gly Asn Lys Ser
1 5 10 15

Cys Glu Cys Ser Tyr Lys
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SEQ.List.txt

<210> 531
 <211> 36
 <212> PRT
 <213> Plasmodium falciparum

<400> 531
 His Asn Asn His Asn Ile Gln Ile Tyr Lys Asp Lys Arg Ile Asn Phe
 1 5 10 15
 Met Asn Pro His Lys Val Met Tyr His Asp Asn Met Ser Lys Asn Glu
 20 25 30
 Arg Thr Glu Lys
 35

<210> 532
 <211> 30
 <212> PRT
 <213> Plasmodium falciparum

<400> 532
 His Asn Asn His Asn Ile Gln Ile Tyr Lys Asp Lys Arg Ile Asn Phe
 1 5 10 15
 Met Asn Pro His Lys Val Met Tyr His Asp Asn Met Ser Lys
 20 25 30

<210> 533
 <211> 21
 <212> PRT
 <213> Plasmodium falciparum

<400> 533
 His Asn Asn His Asn Ile Gln Ile Tyr Lys Asp Lys Arg Ile Asn Phe
 1 5 10 15
 Met Asn Pro His Lys
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<210> 534
 <211> 17
 <212> PRT
 <213> Plasmodium falciparum

SEQ.List.txt

<400> 534

His Lys Val Met Tyr His Asp Asn Met Ser Lys Asn Glu Arg Thr Glu
1 5 10 15

Lys

<210> 535

<211> 11

<212> PRT

<213> Plasmodium falciparum

<400> 535

His Lys Val Met Tyr His Asp Asn Met Ser Lys
1 5 10

<210> 536

<211> 40

<212> PRT

<213> Homo sapiens

<400> 536

His Arg Glu Ile Cys Thr Ile Gln Ser Ser Gly Gly Ile Met Leu Leu
1 5 10 15

Lys Asp Gln Val Leu Arg Cys Ser Lys Ile Ala Gly Val Lys Val Ala
20 25 30

Glu Ile Thr Glu Leu Ile Leu Lys
35 40

<210> 537

<211> 25

<212> PRT

<213> Homo sapiens

<400> 537

His Arg Glu Ile Cys Thr Ile Gln Ser Ser Gly Gly Ile Met Leu Leu
1 5 10 15

Lys Asp Gln Val Leu Arg Cys Ser Lys
20 25

<210> 538

<211> 47

SEQ.List.txt

<212> PRT

<213> Homo sapiens

<400> 538

His Arg Glu Ile Cys Thr Ile Gln Ser Ser Gly Gly Ile Met Leu Leu
1 5 10 15

Lys Asp Gln Val Leu Arg Cys Ser Lys Ile Ala Gly Val Lys Val Ala
20 25 30

Glu Ile Thr Glu Leu Ile Leu Lys Ala Leu Glu Asn Asp Gln Lys
35 40 45

<210> 539

<211> 40

<212> PRT

<213> Homo sapiens

<400> 539

His Arg Glu Ile Cys Thr Ile Gln Ala Ala Gly Gly Ile Met Leu Leu
1 5 10 15

Lys Asp Gln Val Leu Arg Cys Ser Lys Ile Ala Gly Val Lys Val Ala
20 25 30

Glu Ile Thr Glu Leu Ile Leu Lys
35 40

<210> 540

<211> 23

<212> PRT

<213> Homo sapiens

<400> 540

Lys Lys Met Gln Gln Glu Asn Met Lys Pro Gln Glu Gln Leu Thr Leu
1 5 10 15

Glu Pro Tyr Glu Arg Asp His
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<210> 541

<211> 22

<212> PRT

<213> Homo sapiens

SEQ.List.txt

<400> 541

Lys Met Gln Gln Glu Asn Met Lys Pro Gln Glu Gln Leu Thr Leu Glu
1 5 10 15

Pro Tyr Glu Arg Asp His
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<210> 542

<211> 38

<212> PRT

<213> Homo sapiens

<400> 542

His Glu Met Glu Glu Ser Lys Lys Asn Arg Val Glu Ile Asn Asp Val
1 5 10 15

Glu Pro Glu Val Phe Lys Glu Met Met Cys Phe Ile Tyr Thr Gly Lys
20 25 30

Ala Pro Asn Leu Asp Lys
35

<210> 543

<211> 32

<212> PRT

<213> Homo sapiens

<400> 543

His Glu Met Glu Glu Ser Lys Lys Asn Arg Val Glu Ile Asn Asp Val
1 5 10 15

Glu Pro Glu Val Phe Lys Glu Met Met Cys Phe Ile Tyr Thr Gly Lys
20 25 30

<210> 544

<211> 9

<212> PRT

<213> Homo sapiens

<400> 544

Lys His Gly Glu Leu Lys Val Tyr Lys
1 5

<210> 545

SEQ.List.txt

<211> 14
 <212> PRT
 <213> Homo sapiens

<400> 545
 Lys Leu Ile Leu Gly Pro Gln Glu Glu Lys Gly Lys Gln His
 1 5 10

<210> 546
 <211> 7
 <212> PRT
 <213> Homo sapiens

<400> 546
 Lys Asn Arg Ile His His Lys
 1 5

<210> 547
 <211> 17
 <212> PRT
 <213> Homo sapiens

<400> 547
 His His Asn Ser Ser Arg Lys Ser Thr Lys Lys Thr Asn Gln Ser Ser
 1 5 10 15
 Lys

<210> 548
 <211> 16
 <212> PRT
 <213> Homo sapiens

<400> 548
 His Asn Ser Ser Arg Lys Ser Thr Lys Lys Thr Asn Gln Ser Ser Lys
 1 5 10 15

<210> 549
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 549

SEQ.List.txt

Lys His His Asn Ile Leu Pro Lys Thr Leu Ala Asn Asp Lys His Ser
1 5 10 15

His Lys Pro His
20

<210> 550
<211> 17
<212> PRT
<213> Homo sapiens

<400> 550
His His Asn Ile Leu Pro Lys Thr Leu Ala Asn Asp Lys His Ser His
1 5 10 15

Lys

<210> 551
<211> 16
<212> PRT
<213> Homo sapiens

<400> 551
His Asn Ile Leu Pro Lys Thr Leu Ala Asn Asp Lys His Ser His Lys
1 5 10 15

<210> 552
<211> 12
<212> PRT
<213> Homo sapiens

<400> 552
His Asn Ile Leu Pro Lys Thr Leu Ala Asn Asp Lys
1 5 10

<210> 553
<211> 18
<212> PRT
<213> Homo sapiens

<400> 553
Lys Asn Thr Pro Asp Ser Lys Lys Ile Ser Ser Arg Asn Ile Asn Asp
1 5 10 15

SEQ.List.txt

His His

<210> 554
 <211> 17
 <212> PRT
 <213> Homo sapiens

<400> 554
 Lys Asn Thr Pro Asp Ser Lys Lys Ile Ser Ser Arg Asn Ile Asn Asp
 1 5 10 15

His

<210> 555
 <211> 27
 <212> PRT
 <213> Homo sapiens

<400> 555
 Lys Asp Thr Cys Ile Gln Ser Pro Ser Lys Glu Cys Gln Lys Ser His
 1 5 10 15

Pro Lys Ser Val Pro Val Ser Ser Lys Lys
 20 25

<210> 556
 <211> 26
 <212> PRT
 <213> Homo sapiens

<400> 556
 Lys Asp Thr Cys Ile Gln Ser Pro Ser Lys Glu Cys Gln Lys Ser His
 1 5 10 15

Pro Lys Ser Val Pro Val Ser Ser Lys Lys
 20 25

<210> 557
 <211> 12
 <212> PRT
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SEQ.List.txt

<400> 557

His Pro Lys Ser Val Pro Val Ser Ser Lys Lys Lys ,
1 5 10

<210> 558.

<211> 11

<212> PRT

<213> Homo sapiens

<400> 558

His Pro Lys Ser Val Pro Val Ser Ser Lys Lys
1 5 10

<210> 559

<211> 10

<212> PRT

<213> Homo sapiens

<400> 559

His Pro Lys Ser Val Pro Val Ser Ser Lys
1 5 10

<210> 560

<211> 14

<212> PRT

<213> Homo sapiens

<400> 560

Lys Ala Leu Gln Glu Lys Val Glu Ile Lys Gln Leu Asn His
1 5 10

<210> 561

<211> 42

<212> PRT

<213> Homo sapiens

<400> 561

Lys Thr Leu Phe Pro Leu Ile Glu Ala Lys Lys Lys Asp Gln Val Thr
1 5 10 15

Ala Gln Glu Ile Phe Gln Asp Asn His Glu Asp Gly Pro Thr Ala Lys
20 25 30

SEQ.List.txt

Lys Leu Lys Thr Glu Gln Gly Gly Ala His
35 40

<210> 562
<211> 25
<212> PRT
<213> Homo sapiens

<400> 562
Lys Thr Leu Phe Pro Leu Ile Glu Ala Lys Lys Lys Asp Gln Val Thr
1 5 10 15
Ala Gln Glu Ile Phe Gln Asp Asn His
20 25

<210> 563
<211> 14
<212> PRT
<213> Homo sapiens

<400> 563
Lys Leu Cys Val Phe Lys Lys Ile Glu Arg His Ser Ile His
1 5 10

<210> 564
<211> 11
<212> PRT
<213> Homo sapiens

<400> 564
Lys Leu Cys Val Phe Lys Lys Ile Glu Arg His
1 5 10

<210> 565
<211> 22
<212> PRT
<213> Homo sapiens

<400> 565
His Gly Pro Ser Phe Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys Glu
1 5 10 15

Gly Leu Glu Ile Val Lys
20

SEQ.List.txt

<210> 566

<211> 15

<212> PRT

<213> Homo sapiens

<400> 566

His Gly Pro Ser Phe Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys
1 5 10 15

<210> 567

<211> 13

<212> PRT

<213> Homo sapiens

<400> 567

His Thr Leu Leu Lys Ile Leu Ser Thr Phe Leu Phe Lys
1 5 10

<210> 568

<211> 14

<212> PRT

<213> Homo sapiens

<400> 568

His Leu Leu Gly Asn Asn Asp Lys Asn Leu Leu Pro Ser Lys
1 5 10

<210> 569

<211> 19

<212> PRT

<213> Homo sapiens

<400> 569

His Arg His Glu Gly Val Phe Ile Cys Arg Gly Lys Glu Asp Ala Leu
1 5 10 15

Val Thr Lys

<210> 570

<211> 17

<212> PRT

SEQ.List.txt

<213> Homo sapiens

<400> 570

His Glu Gly Val Phe Ile Cys Arg Gly Lys Glu Asp Ala Leu Val Thr
 1 5 10 15

Lys

<210> 571

<211> 20

<212> PRT

<213> Homo sapiens

<400> 571

His Ser Gly Gly Asn Arg Gly Arg Gly Arg Gly Gly Lys Arg Gly Asn
 1 5 10 15

Gln Ser Gly Lys
 20

<210> 572

<211> 15

<212> PRT

<213> Homo sapiens

<400> 572

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

<210> 573

<211> 17

<212> PRT

<213> Homo sapiens

<400> 573

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

His

<210> 574

<211> 23

SEQ.List.txt

<212> PRT

<213> Homo sapiens

<400> 574

Lys Lys Met Gln Gln Glu Asn Met Lys Pro Gln Glu Gln Leu Thr Leu
1 5 10 15

Glu Pro Tyr Glu Arg Asp His
20

<210> 575

<211> 22

<212> PRT

<213> Homo sapiens

<400> 575

Lys Met Gln Gln Glu Asn Met Lys Pro Gln Glu Gln Leu Thr Leu Glu
1 5 10 15

Pro Tyr Glu Arg Asp His
20

<210> 576

<211> 16

<212> PRT

<213> Homo sapiens

<400> 576

His Ala Tyr Pro Glu Asp Ala Glu Asn Lys Glu Lys Glu Thr Ala Lys
1 5 10 15

<210> 577

<211> 22

<212> PRT

<213> Homo sapiens

<400> 577

Lys Glu Ala Asn Val Lys Cys Pro Gln Ile Val Ile Ala Phe Tyr Glu
1 5 10 15

Glu Arg Leu Thr Trp His
20

<210> 578

SEQ.List.txt

<211> 25
 <212> PRT
 <213> Homo sapiens

<400> 578
 Lys Val Leu Asp Arg Arg Val Val Lys Gly Gln Val Glu Tyr Leu Leu
 1 5 10 15
 Lys Trp Lys Gly Phe Ser Glu Glu His
 20 25

<210> 579
 <211> 17
 <212> PRT
 <213> Homo sapiens

<400> 579
 Lys Gly Gln Val Glu Tyr Leu Leu Lys Trp Lys Gly Phe Ser Glu Glu
 1 5 10 15
 His

<210> 580
 <211> 32
 <212> PRT
 <213> Homo sapiens

<400> 580
 Lys Ser Glu Val Ala Ala Gly Val Lys Lys Ser Gly Pro Leu Pro Ser
 1 5 10 15
 Ala Glu Arg Leu Glu Asn Val Leu Phe Gly Pro His Asp Cys Ser His
 20 25 30

<210> 581
 <211> 28
 <212> PRT
 <213> Homo sapiens

<400> 581
 Lys Ser Glu Val Ala Ala Gly Val Lys Lys Ser Gly Pro Leu Pro Ser
 1 5 10 15
 Ala Glu Arg Leu Glu Asn Val Leu Phe Gly Pro His
 20 25

SEQ.List.txt

<210> 582
 <211> 28
 <212> PRT
 <213> Homo sapiens

<400> 582
 Lys Ala Ala Glu Tyr Gly Lys Lys Ala Lys Ser Glu Thr Phe Arg Leu
 1 5 10 15
 Leu His Ala Lys Asn Ile Ile Arg Pro Gln Leu Lys
 20 25

<210> 583
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 583
 Lys Ala Ala Glu Tyr Gly Lys Lys Ala Lys Ser Glu Thr Phe Arg Leu
 1 5 10 15
 Leu His Ala Lys
 20

<210> 584
 <211> 11
 <212> PRT
 <213> Homo sapiens

<400> 584
 Lys Ser Glu Thr Phe Arg Leu Leu His Ala Lys
 1 5 10

<210> 585
 <211> 11
 <212> PRT
 <213> Homo sapiens

<400> 585
 His Ala Lys Asn Ile Ile Arg Pro Gln Leu Lys
 1 5 10

SEQ.List.txt

<210> 586
 <211> 12
 <212> PRT
 <213> Homo sapiens

<400> 586
 His Met Met Leu Lys Ile Ala Glu Glu Leu Pro Lys
 1 5 10

<210> 587
 <211> 17
 <212> PRT
 <213> Homo sapiens

<400> 587
 His Ser Leu Asp His Leu Leu Lys Leu Tyr Cys Asn Val Asp Ser Asn
 1 5 10 15

Lys

<210> 588
 <211> 13
 <212> PRT
 <213> Homo sapiens

<400> 588
 His Leu Leu Lys Leu Tyr Cys Asn Val Asp Ser Asn Lys
 1 5 10

<210> 589
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 589
 Lys Ala Lys Glu Arg Leu Glu Ala Lys His
 1 5 10

<210> 590
 <211> 8
 <212> PRT
 <213> Homo sapiens

SEQ.List.txt

<400> 590

Lys Asp Arg Gln His Thr Leu Lys
1 5

<210> 591

<211> 9

<212> PRT

<213> Homo sapiens

<400> 591

Lys Asp Arg Gln His Thr Leu Lys His
1 5

<210> 592

<211> 12

<212> PRT

<213> Homo sapiens

<400> 592

Lys Glu Thr Cys Ser Glu Lys Ser Thr Asn Leu His
1 5 10

<210> 593

<211> 16

<212> PRT

<213> Homo sapiens

<400> 593

Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe Gly His
1 5 10 15

<210> 594

<211> 24

<212> PRT

<213> Homo sapiens

<400> 594

Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe Gly His
1 5 10 15

Asp Ser Gly Phe Glu Val Arg His
20

SEQ.List.txt

<210> 595
 <211> 17
 <212> PRT
 <213> Homo sapiens

<400> 595
 Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys
 1 5 10 15

His

<210> 596
 <211> 16
 <212> PRT
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<400> 596
 Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His
 1 5 10 15

<210> 597
 <211> 13
 <212> PRT
 <213> Homo sapiens

<400> 597
 Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
 1 5 10

<210> 598
 <211> 13
 <212> PRT
 <213> Homo sapiens

<400> 598
 Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr
 1 5 10

<210> 599
 <211> 16
 <212> PRT
 <213> Homo sapiens

SEQ.List.txt

<400> 599

His His Val Phe Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys
1 5 10 15

<210> 600

<211> 15

<212> PRT

<213> Homo sapiens

<400> 600

His Val Phe Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys
1 5 10 15

<210> 601

<211> 24

<212> PRT

<213> Homo sapiens

<400> 601

His His Val Phe Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys
1 5 10 15

Asp Arg Gln His Thr Leu Lys His
20

<210> 602

<211> 23

<212> PRT

<213> Homo sapiens

<400> 602

His Val Phe Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp
1 5 10 15

Arg Gln His Thr Leu Lys His
20

<210> 603

<211> 15

<212> PRT

<213> Homo sapiens

<400> 603

His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys His

SEQ.List.txt

1 5 10 15

<210> 604
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 <212> PRT
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<400> 604
 His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys
 1 5 10

<210> 605
 <211> 12
 <212> PRT
 <213> Homo sapiens

<400> 605
 His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala Lys
 1 5 10

<210> 606
 <211> 30
 <212> PRT
 <213> Homo sapiens

<400> 606
 His Gln Glu Arg Met Asp Val Cys Glu Thr His Leu His Trp His Thr
 1 5 10 15

Val Ala Lys Glu Thr Cys Ser Glu Lys Ser Thr Asn Leu His
 20 25 30

<210> 607
 <211> 25
 <212> PRT
 <213> Homo sapiens

<400> 607
 His Gln Glu Arg Met Asp Val Cys Glu Thr His Leu His Trp His Thr
 1 5 10 15

Val Ala Lys Glu Thr Cys Ser Glu Lys
 20 25

SEQ.List.txt

<210> 608
 <211> 13
 <212> PRT
 <213> Homo sapiens

<400> 608
 His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu Lys
 1 5 10

<210> 609
 <211> 11
 <212> PRT
 <213> Homo sapiens

<400> 609
 His Thr Val Ala Lys Glu Thr Cys Ser Glu Lys
 1 5 10

<210> 610
 <211> 15
 <212> PRT
 <213> Homo sapiens

<400> 610
 His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu Lys
 1 5 10 15

<210> 611
 <211> 23
 <212> PRT
 <213> Homo sapiens

<400> 611
 His Met Asn Val Gln Asn Gly Lys Trp Glu Ser Asp Pro Ser Gly Thr
 1 5 10 15

Lys Thr Cys Ile Gly Thr Lys
 20

<210> 612
 <211> 17
 <212> PRT
 <213> Homo sapiens

SEQ.List.txt

<400> 612

His Met Asn Val Gln Asn Gly Lys Trp Glu Ser Asp Pro Ser Gly Thr
1 5 10 15

Lys

<210> 613

<211> 19

<212> PRT

<213> Human immunodeficiency virus

<400> 613

His Cys Leu Val Cys Phe Gln Lys Lys Gly Leu Gly Ile Ser Tyr Gly
1 5 10 15

Arg Lys Lys

<210> 614

<211> 27

<212> PRT

<213> Triticum aestivum

<400> 614

His Lys Asp Arg Leu Thr Lys Lys Val Val Asp Ile Ala Arg Glu Val
1 5 10 15

Ala Lys Val Asp Val Pro Glu Tyr Arg Arg His
20 25

<210> 615

<211> 27

<212> PRT

<213> Triticum aestivum

<400> 615

His Lys Glu Arg Leu Asp Arg Lys Val Val Asp Val Ala Arg Glu Val
1 5 10 15

Ala Lys Val Glu Val Pro Ser Tyr Arg Arg His
20 25

SEQ.List.txt

<210> 616
 <211> 27
 <212> PRT
 <213> Triticum aestivum

<400> 616
 His Lys Glu Arg Leu Asp Arg Lys Val Val Asp Val Ala Arg Glu Val
 1 5 10 15
 Ala Lys Met Glu Val Pro Ser Tyr Arg Arg His
 20 25

<210> 617
 <211> 23
 <212> PRT
 <213> Triticum aestivum

<400> 617
 His Leu Gln Pro Lys Trp Lys Pro Ser Leu Ser Trp Phe Lys Asn Ala
 1 5 10 15
 Glu Ser Arg Leu Asn His His
 20

<210> 618
 <211> 14
 <212> PRT
 <213> Triticum aestivum

<400> 618
 His Leu Gln Pro Lys Trp Lys Pro Ser Leu Ser Trp Phe Lys
 1 5 10

<210> 619
 <211> 19
 <212> PRT
 <213> Triticum aestivum

<400> 619
 Lys Trp Lys Pro Ser Leu Ser Trp Phe Lys Asn Ala Glu Ser Arg Leu
 1 5 10 15
 Asn His His

SEQ.List.txt

<210> 620
 <211> 18
 <212> PRT
 <213> Triticum aestivum

<400> 620
 Lys Trp Lys Pro Ser Leu Ser Trp Phe Lys Asn Ala Glu Ser Arg Leu
 1 5 10 15

Asn His

<210> 621
 <211> 17
 <212> PRT
 <213> Triticum aestivum

<400> 621
 Lys Pro Ser Leu Ser Trp Phe Lys Asn Ala Glu Ser Arg Leu Asn His
 1 5 10 15

His

<210> 622
 <211> 16
 <212> PRT
 <213> Triticum aestivum

<400> 622
 Lys Pro Ser Leu Ser Trp Phe Lys Asn Ala Glu Ser Arg Leu Asn His
 1 5 10 15

<210> 623
 <211> 32
 <212> PRT
 <213> Triticum aestivum

<400> 623
 His His Ala Ile Ala Leu Gly Leu His Thr Thr Thr Leu Ile Leu Val
 1 5 10 15

Lys Gly Ala Leu Asp Ala Arg Gly Ser Lys Leu Met Pro Asp Lys Lys
 20 25 30

SEQ.List.txt

<210> 624
 <211> 31
 <212> PRT
 <213> Triticum aestivum

<400> 624
 His Ala Ile Ala Leu Gly Leu His Thr Thr Thr Leu Ile Leu Val Lys
 1 5 10 15
 Gly Ala Leu Asp Ala Arg Gly Ser Lys Leu Met Pro Asp Lys Lys
 20 25 30

<210> 625
 <211> 26
 <212> PRT
 <213> Triticum aestivum

<400> 625
 His His Ala Ile Ala Leu Gly Leu His Thr Thr Thr Leu Ile Leu Val
 1 5 10 15
 Lys Gly Ala Leu Asp Ala Arg Gly Ser Lys
 20 25

<210> 626
 <211> 25
 <212> PRT
 <213> Triticum aestivum

<400> 626
 His Ala Ile Ala Leu Gly Leu His Thr Thr Thr Leu Ile Leu Val Lys
 1 5 10 15
 Gly Ala Leu Asp Ala Arg Gly Ser Lys
 20 25

<210> 627
 <211> 24
 <212> PRT
 <213> Triticum aestivum

<400> 627
 His Thr Thr Thr Leu Ile Leu Val Lys Gly Ala Leu Asp Ala Arg Gly

SEQ.List.txt

1 5 10 15
 Ser Lys Leu Met Pro Asp Lys Lys
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<210> 628
 <211> 23
 <212> PRT
 <213> Triticum aestivum

<400> 628
 His Thr Thr Thr Leu Ile Leu Val Lys Gly Ala Leu Asp Ala Arg Gly
 1 5 10 15

Ser Lys Leu Met Pro Asp Lys
 20

<210> 629
 <211> 18
 <212> PRT
 <213> Triticum aestivum

<400> 629
 His Thr Thr Thr Leu Ile Leu Val Lys Gly Ala Leu Asp Ala Arg Gly
 1 5 10 15

Ser Lys

<210> 630
 <211> 44
 <212> PRT
 <213> Triticum aestivum

<400> 630
 His His His Leu Ala Ile Ala Ile Leu Phe Leu Ile Ala Gly His Met
 1 5 10 15

Tyr Arg Thr Asn Trp Gly Ile Gly His Gly Leu Lys Asp Ile Leu Glu
 20 25 30

Ala His Lys Gly Pro Phe Thr Gly Gln Gly His Lys
 35 40

SEQ.List.txt

<210> 631
 <211> 43
 <212> PRT
 <213> Triticum aestivum

<400> 631

His His Leu Ala Ile Ala Ile Leu Phe Leu Ile Ala Gly His Met Tyr
 1 5 10 15
 Arg Thr Asn Trp Gly Ile Gly His Gly Leu Lys Asp Ile Leu Glu Ala
 20 25 30
 His Lys Gly Pro Phe Thr Gly Gln Gly His Lys
 35 40

<210> 632
 <211> 42
 <212> PRT
 <213> Triticum aestivum

<400> 632

His Leu Ala Ile Ala Ile Leu Phe Leu Ile Ala Gly His Met Tyr Arg
 1 5 10 15
 Thr Asn Trp Gly Ile Gly His Gly Leu Lys Asp Ile Leu Glu Ala His
 20 25 30
 Lys Gly Pro Phe Thr Gly Gln Gly His Lys
 35 40

<210> 633
 <211> 30
 <212> PRT
 <213> Triticum aestivum

<400> 633

His Met Tyr Arg Thr Asn Trp Gly Ile Gly His Gly Leu Lys Asp Ile
 1 5 10 15
 Leu Glu Ala His Lys Gly Pro Phe Thr Gly Gln Gly His Lys
 20 25 30

<210> 634
 <211> 20
 <212> PRT

SEQ.List.txt

<213> Triticum aestivum

<400> 634

His Gly Leu Lys Asp Ile Leu Glu Ala His Lys Gly Pro Phe Thr Gly
1 5 10 15

Gln Gly His Lys
20

<210> 635

<211> 17

<212> PRT

<213> Triticum aestivum

<400> 635

Lys Asp Ile Leu Glu Ala His Lys Gly Pro Phe Thr Gly Gln Gly His
1 5 10 15

Lys

<210> 636

<211> 11

<212> PRT

<213> Triticum aestivum

<400> 636

His Lys Gly Pro Phe Thr Gly Gln Gly His Lys
1 5 10

<210> 637

<211> 10

<212> PRT

<213> Triticum aestivum

<400> 637

Lys Gly Pro Phe Thr Gly Gln Gly His Lys
1 5 10

<210> 638

<211> 16

<212> PRT

<213> Oryza sativa

SEQ.List.txt

<400> 638

Lys Phe Pro Asp Val Ile His Ala Phe Lys Pro Asn Pro Arg Ser His
1 5 10 15

<210> 639

<211> 10

<212> PRT

<213> Oryza sativa

<400> 639

Lys Phe Pro Asp Val Ile His Ala Phe Lys
1 5 10

<210> 640

<211> 10

<212> PRT

<213> Oryza sativa

<400> 640

Lys Ala Arg Tyr Val Lys Phe His Trp Lys
1 5 10

<210> 641

<211> 33

<212> PRT

<213> Oryza sativa

<400> 641

His Pro Lys Val Ser Pro Glu Leu Arg Ala Ile Trp Val Asn Tyr Leu
1 5 10 15

Ser Gln Cys Asp Glu Ser Leu Gly Val Lys Ile Ala Asn Leu Asn Val
20 25 30

Lys

<210> 642

<211> 45

<212> PRT

<213> Oryza sativa

<400> 642

His Arg Asp Glu Glu Val Asp Tyr Tyr Pro Ser Arg His Ala Pro Leu

SEQ.List.txt

1 5 10 15
 Arg His Ala Pro Pro Thr Pro Ile Thr Pro Arg Pro Val Val Gly Arg
 20 25 30
 Arg Gln Lys Ala Thr Ile His Lys Gln Asn Asp Phe Lys
 35 40 45

<210> 643
 <211> 11
 <212> PRT
 <213> Oryza sativa

<400> 643
 Lys Ala Thr Ile His Lys Gln Asn Asp Phe Lys
 1 5 10

<210> 644
 <211> 27
 <212> PRT
 <213> Oryza sativa

<400> 644
 His Ala Pro Pro Thr Pro Ile Pro Arg Pro Val Val Gly Arg Arg Gln
 1 5 10 15
 Lys Ala Thr Ile His Lys Gln Asn Asp Phe Lys
 20 25

<210> 645
 <211> 49
 <212> PRT
 <213> Oryza sativa

<400> 645
 Lys Phe Arg Pro Ser Ser Ser Phe Asp Thr Lys Thr Thr Thr Thr Asn
 1 5 10 15
 Ala Gly Ala Pro Val Trp Asn Asp Asn Glu Ala Leu Thr Val Gly Pro
 20 25 30
 Arg Gly Pro Ile Leu Leu Glu Asp Tyr His Leu Ile Glu Lys Val Ala
 35 40 45

His

SEQ.List.txt

<210> 646
 <211> 42
 <212> PRT
 <213> Oryza sativa

<400> 646
 Lys Phe Arg Pro Ser Ser Ser Phe Asp Thr Lys Thr Thr Thr Thr Asn
 1 5 10 15
 Ala Gly Ala Pro Val Trp Asn Asp Asn Glu Ala Leu Thr Val Gly Pro
 20 25 30
 Arg Gly Pro Ile Leu Leu Glu Asp Tyr His
 35 40

<210> 647
 <211> 9
 <212> PRT
 <213> Oryza sativa

<400> 647
 Lys Val Lys Ala His Phe Gln Lys His
 1 5

<210> 648
 <211> 8
 <212> PRT
 <213> Oryza sativa

<400> 648
 Lys Val Lys Ala His Phe Gln Lys
 1 5

<210> 649
 <211> 12
 <212> PRT
 <213> Oryza sativa

<400> 649
 Lys Asp Tyr Glu Ile Asp Lys Asp Asp Leu Ile His
 1 5 10

SEQ.List.txt

<210> 650
 <211> 20
 <212> PRT
 <213> Oryza sativa

<400> 650
 His Met Lys Gln Cys Phe Ala Phe Cys Ala Val Phe Pro Lys Asp Tyr
 1 5 10 15
 Glu Ile Asp Lys
 20

<210> 651
 <211> 14
 <212> PRT
 <213> Oryza sativa

<400> 651
 His Met Lys Gln Cys Phe Ala Phe Cys Ala Val Phe Pro Lys
 1 5 10

<210> 652
 <211> 49
 <212> PRT
 <213> Oryza sativa

<400> 652
 His Val Phe Trp Glu Leu Val Trp Arg Ser Phe Phe Gln Asn Val Lys
 1 5 10 15
 Gln Ile Gly Ser Ile Phe Gln Arg Lys Val Tyr Arg Tyr Gly Gln Ser
 20 25 30
 Asp Val Thr Thr Ser Lys Ile His Asp Leu Met His Asp Leu Ala Val
 35 40 45
 His

<210> 653
 <211> 34
 <212> PRT
 <213> Oryza sativa

SEQ.List.txt

<400> 653

Lys Gln Ile Gly Ser Ile Phe Gln Arg Lys Val Tyr Arg Tyr Gly Gln
1 5 10 15

Ser Asp Val Thr Thr Ser Lys Ile His Asp Leu Met His Asp Leu Ala
20 25 30

Val His

<210> 654

<211> 29

<212> PRT

<213> Oryza sativa

<400> 654

Lys Gln Ile Gly Ser Ile Phe Gln Arg Lys Val Tyr Arg Tyr Gly Gln
1 5 10 15

Ser Asp Val Thr Thr Ser Lys Ile His Asp Leu Met His
20 25

<210> 655

<211> 25

<212> PRT

<213> Oryza sativa

<400> 655

Lys Gln Ile Gly Ser Ile Phe Gln Arg Lys Val Tyr Arg Tyr Gly Gln
1 5 10 15

Ser Asp Val Thr Thr Ser Lys Ile His
20 25

<210> 656

<211> 9

<212> PRT

<213> Oryza sativa

<400> 656

Lys His Gly Val Ser Ala Gly Ile Lys
1 5

<210> 657

SEQ.List.txt

<211> 15
 <212> PRT
 <213> Oryza sativa

<400> 657
 His Thr Val Phe Asp Tyr Gly Lys Met Arg Val Gly Phe Ala Lys
 1 5 10 15

<210> 658
 <211> 17
 <212> PRT
 <213> Oryza sativa

<400> 658
 His Ser Arg Tyr Lys Ser Gly Gln Ser Ser Thr Tyr Gln Lys Asn Gly
 1 5 10 15

Lys

<210> 659
 <211> 29
 <212> PRT
 <213> Oryza sativa

<400> 659
 Lys Gln Glu Ala Met Val Leu Lys Gln Glu Ile Asn Leu Leu Gln Lys
 1 5 10 15

Gly Leu Arg Tyr Ile Tyr Gly Asn Arg Ala Asn Glu His
 20 25

<210> 660
 <211> 22
 <212> PRT
 <213> Oryza sativa

<400> 660
 Lys Gln Glu Ile Asn Leu Leu Gln Lys Gly Leu Arg Tyr Ile Tyr Gly
 1 5 10 15

Asn Arg Ala Asn Glu His
 20

SEQ.List.txt

<210> 661
 <211> 38
 <212> PRT
 <213> Oryza sativa

<400> 661
 Lys Ser Lys Glu Gly Met Leu Lys Ala Ala Asn Glu Ile Leu Gln Glu
 1 5 10 15
 Lys Ile Val Glu Gln Asn Gly Leu Ile Asp Val Gly Met Met Val Ala
 20 25 30
 Asp Gln Gln Asn Gly His
 35

<210> 662
 <211> 31
 <212> PRT
 <213> Oryza sativa

<400> 662
 Lys Ala Ala Asn Glu Ile Leu Gln Glu Lys Ile Val Glu Gln Asn Gly
 1 5 10 15
 Leu Ile Asp Val Gly Met Met Val Ala Asp Gln Gln Asn Gly His
 20 25 30

<210> 663
 <211> 11
 <212> PRT
 <213> Zea mays

<400> 663
 Lys Val Leu Ala Ala His Arg Tyr Gly Ile Lys
 1 5 10

<210> 664
 <211> 17
 <212> PRT
 <213> Zea mays

<400> 664
 Lys Leu Lys Ile Ala Met Lys His Leu Ile Pro Arg Val Leu Glu Gln
 1 5 10 15

SEQ.List.txt

His

<210> 665
 <211> 8
 <212> PRT
 <213> Zea mays

<400> 665
 Lys Leu Lys Ile Ala Met Lys His
 1 5

<210> 666
 <211> 33
 <212> PRT
 <213> Zea mays

<400> 666
 Lys Thr Ser Leu Ala Ser Ser Ile Ala Lys Ala Leu Asn Arg Lys Phe
 1 5 10 15
 Ile Arg Ile Ser Leu Gly Gly Val Lys Asp Glu Ala Asp Ile Arg Gly
 20 25 30

His

<210> 667
 <211> 24
 <212> PRT
 <213> Zea mays

<400> 667
 Lys Ala Leu Asn Arg Lys Phe Ile Arg Ile Ser Leu Gly Gly Val Lys
 1 5 10 15
 Asp Glu Ala Asp Ile Arg Gly His
 20

<210> 668
 <211> 19
 <212> PRT
 <213> Zea mays

SEQ.List.txt

<400> 668

Lys Phe Ile Arg Ile Ser Leu Gly Gly Val Lys Asp Glu Ala Asp Ile
1 5 10 15

Arg Gly His

<210> 669

<211> 37

<212> PRT

<213> Zea mays

<400> 669

Lys Val Arg Leu Ser Lys Ala Thr Glu Leu Val Asp Arg His Leu Gln
1 5 10 15

Ser Ile Leu Val Ala Glu Lys Ile Thr Gln Lys Val Glu Gly Gln Leu
20 25 30

Ser Lys Ser Gln Lys
35

<210> 670

<211> 24

<212> PRT

<213> Zea mays

<400> 670

His Leu Gln Ser Ile Leu Val Ala Glu Lys Ile Thr Gln Lys Val Glu
1 5 10 15

Gly Gln Leu Ser Lys Ser Gln Lys
20

<210> 671

<211> 14

<212> PRT

<213> Zea mays

<400> 671

Lys Val Arg Leu Ser Lys Ala Thr Glu Leu Val Asp Arg His
1 5 10

<210> 672

SEQ.List.txt

<211> 34
 <212> PRT
 <213> Zea mays

<400> 672
 Lys Val Gly Gly Ser Ala Val Glu Ser Ser Lys Gln Asp Thr Lys Asn
 1 5 10 15

Gly Lys Glu Pro Ile His Trp His Ser Lys Gly Val Ala Ala Arg Ala
 20 25 30

Leu His

<210> 673
 <211> 24
 <212> PRT
 <213> Zea mays

<400> 673
 Lys Val Gly Gly Ser Ala Val Glu Ser Ser Lys Gln Asp Thr Lys Asn
 1 5 10 15

Gly Lys Glu Pro Ile His Trp His
 20

<210> 674
 <211> 22
 <212> PRT
 <213> Zea mays

<400> 674
 Lys Val Gly Gly Ser Ala Val Glu Ser Ser Lys Gln Asp Thr Lys Asn
 1 5 10 15

Gly Lys Glu Pro Ile His
 20

<210> 675
 <211> 24
 <212> PRT
 <213> Zea mays

<400> 675
 Lys Gln Asp Thr Lys Asn Gly Lys Glu Pro Ile His Trp His Ser Lys

SEQ.List.txt

1 5 10 15
 Gly Val Ala Ala Arg Ala Leu His
 20

<210> 676
 <211> 12
 <212> PRT
 <213> Zea mays

<400> 676
 Lys Gln Asp Thr Lys Asn Gly Lys Glu Pro Ile His
 1 5 10

<210> 677
 <211> 33
 <212> PRT
 <213> Zea mays

<400> 677
 His Arg Asp Leu Arg Arg Ala Arg Ala Ala Ala Leu Asn Ile Val Pro
 1 5 10 15
 Thr Ser Thr Gly Ala Ala Lys Ala Val Ser Leu Val Leu Pro Asn Leu
 20 25 30

Lys

<210> 678
 <211> 18
 <212> PRT
 <213> Zea mays

<400> 678
 Lys Val Leu Asp Gln Lys Phe Gly Ile Ile Lys Gly Thr Met Thr Thr
 1 5 10 15

Thr His

<210> 679
 <211> 16
 <212> PRT

SEQ.List.txt

<213> Zea mays

<400> 679

His Ile Gln Ala Gly Ala Lys Lys Val Leu Ile Thr Ala Pro Gly Lys
1 5 10 15

<210> 680

<211> 28

<212> PRT

<213> Zea mays

<400> 680

His Gly Arg Gly Asp Ala Ser Pro Leu Asp Val Ile Ala Ile Asn Asp
1 5 10 15

Thr Gly Gly Val Lys Gln Ala Ser His Leu Leu Lys
20 25

<210> 681

<211> 51

<212> PRT

<213> Zea mays

<400> 681

Lys Val Arg Arg Val Leu Ser Lys Asp Tyr Ser Ser Leu Lys Gln Leu
1 5 10 15

Met Thr Leu Met Met Asp Asp Asp Ile Ser Lys His Leu Gln Ile Ile
20 25 30

Glu Ser Gly Leu Glu Glu Arg Glu Asp Lys Val Trp Met Lys Glu Asn
35 40 45

Ile Ile Lys
50

<210> 682

<211> 28

<212> PRT

<213> Zea mays

<400> 682

Lys Val Arg Arg Val Leu Ser Lys Asp Tyr Ser Ser Leu Lys Gln Leu
1 5 10 15

SEQ.List.txt

Met Thr Leu Met Met Asp Asp Asp Ile Ser Lys His
20 25

<210> 683
<211> 24
<212> PRT
<213> Zea mays

<400> 683
His Leu Gln Ile Ile Glu Ser Gly Leu Glu Glu Arg Glu Asp Lys Val
1 5 10 15

Trp Met Lys Glu Asn Ile Ile Lys
20

<210> 684
<211> 17
<212> PRT
<213> Zea mays

<400> 684
His Asp Leu Arg Glu Asn Ile Ile Met Lys Ala Asp Asp Leu Ala Ser
1 5 10 15

Lys

<210> 685
<211> 18
<212> PRT
<213> Zea mays

<400> 685
His Val Gln Asn Leu Glu Asn Val Ile Gly Lys Asp Glu Ala Leu Ala
1 5 10 15

Ser Lys

<210> 686
<211> 21
<212> PRT
<213> Zea mays

SEQ.List.txt

<400> 686

Lys Lys Gln Gly Tyr Glu Leu Arg Gln Leu Lys Asp Leu Asn Glu Leu
1 5 10 15

Gly Gly Ser Leu His
20

<210> 687

<211> 20

<212> PRT

<213> Zea mays

<400> 687

Lys Gln Gly Tyr Glu Leu Arg Gln Leu Lys Asp Leu Asn Glu Leu Gly
1 5 10 15

Gly Ser Leu His
20

<210> 688

<211> 28

<212> PRT

<213> Zea mays

<400> 688

Lys Leu Tyr Leu Lys Ser Arg Leu Lys Glu Leu Ile Leu Glu Trp Ser
1 5 10 15

Ser Glu Asn Gly Met Asp Ala Met Asn Ile Leu His
20 25

<210> 689

<211> 39

<212> PRT

<213> Zea mays

<400> 689

His Leu Gln Leu Leu Gln Leu Asn Gly Met Val Glu Arg Leu Pro Asn
1 5 10 15

Lys Val Cys Asn Leu Ser Lys Leu Arg Tyr Leu Arg Gly Tyr Lys Asp
20 25 30

Gln Ile Pro Asn Ile Gly Lys
35

SEQ.List.txt

<210> 690
 <211> 31
 <212> PRT
 <213> Zea mays

<400> 690
 His Leu Gln Leu Leu Gln Leu Asn Gly Met Val Glu Arg Leu Pro Asn
 1 5 10 15
 Lys Val Cys Asn Leu Ser Lys Leu Arg Tyr Leu Arg Gly Tyr Lys
 20 25 30

<210> 691
 <211> 23
 <212> PRT
 <213> Zea mays

<400> 691
 His Leu Gln Leu Leu Gln Leu Asn Gly Met Val Glu Arg Leu Pro Asn
 1 5 10 15
 Lys Val Cys Asn Leu Ser Lys
 20

<210> 692
 <211> 14
 <212> PRT
 <213> Zea mays

<400> 692
 His Asn Ser Asn Lys Leu Pro Lys Ser Val Gly Glu Leu Lys
 1 5 10

<210> 693
 <211> 11
 <212> PRT
 <213> Zea mays

<400> 693
 Lys Leu Pro Lys Ser Val Gly Glu Leu Lys His
 1 5 10

SEQ.List.txt

<210> 694
 <211> 18
 <212> PRT
 <213> Zea mays

<400> 694
 His Leu Ser Val Arg Val Glu Ser Met Gln Lys His Lys Glu Ile Ile
 1 5 10 15

Tyr Lys

<210> 695
 <211> 8
 <212> PRT
 <213> Zea mays

<400> 695
 Lys His Lys Glu Ile Ile Tyr Lys
 1 5

<210> 696
 <211> 23
 <212> PRT
 <213> Zea mays

<400> 696
 Lys Leu Arg Asp Ile Leu Gln Glu Ser Gln Lys Phe Leu Leu Val Leu
 1 5 10 15

Asp Leu Ala Leu Phe Lys His
 20

<210> 697
 <211> 46
 <212> PRT
 <213> Zea mays

<400> 697
 His Ala Phe Ser Gly Ala Glu Ile Lys Asp Gln Leu Leu Arg Met Lys
 1 5 10 15

Leu Gln Asp Thr Ala Glu Cys Ile Ala Lys Arg Leu Gly Gln Cys Pro
 20 25 30

SEQ.List.txt

Leu Ala Ala Lys Val Leu Gly Ser Arg Met Cys Arg Arg Lys
 35 40 45

<210> 698
 <211> 16
 <212> PRT
 <213> Zea mays

<400> 698
 His Ala Phe Ser Gly Ala Glu Ile Lys Asp Gln Leu Leu Arg Met Lys
 1 5 10 15

<210> 699
 <211> 47
 <212> PRT
 <213> Zea mays

<400> 699
 Lys Leu Gln Asp Thr Ala Glu Glu Ile Ala Lys Arg Leu Gly Gln Cys
 1 5 10 15

Pro Leu Ala Ala Lys Val Leu Gly Ser Arg Met Cys Arg Arg Lys Asp
 20 25 30

Ile Ala Glu Trp Lys Ala Ala Asp Val Trp Phe Glu Lys Ser His
 35 40 45

<210> 700
 <211> 27
 <212> PRT
 <213> Zea mays

<400> 700
 Lys Val Leu Gly Ser Arg Met Cys Arg Arg Lys Asp Ile Ala Glu Trp
 1 5 10 15

Lys Ala Ala Asp Val Trp Phe Glu Lys Ser His
 20 25

<210> 701
 <211> 17
 <212> PRT
 <213> Zea mays

SEQ.List.txt

<400> 701

Lys Asp Ile Ala Glu Trp Lys Ala Ala Asp Val Trp Phe Glu Lys Ser
1 5 10 15

His

<210> 702

<211> 11

<212> PRT

<213> Zea mays

<400> 702

Lys Ala Ala Asp Val Trp Phe Glu Lys Ser His
1 5 10

<210> 703

<211> 40

<212> PRT

<213> Zea mays

<400> 703

His Val Pro Thr Thr Thr Ser Leu Pro Thr Ser Lys Val Phe Gly Arg
1 5 10 15

Asn Ser Asp Arg Asp Arg Ile Val Lys Phe Leu Leu Gly Lys Thr Thr
20 25 30

Thr Ala Glu Ala Ser Ser Thr Lys
35 40

<210> 704

<211> 18

<212> PRT

<213> Zea mays

<400> 704

Lys Ala Ile Leu Thr Glu Ala Lys Gln Leu Arg Asp Leu Leu Gly Leu
1 5 10 15

Pro His

<210> 705

SEQ.List.txt

<211> 29
 <212> PRT
 <213> Zea mays

<400> 705

Lys Ala Lys Ala Lys Ser Gly Lys Gly Pro Leu Leu Arg Glu Asp Glu
 1 5 10 15

Ser Ser Ser Thr Ala Thr Thr Val Met Lys Pro Phe His
 20 25

<210> 706

<211> 29
 <212> PRT
 <213> Zea mays

<400> 706

Lys Ser Pro His Arg Gly Lys Leu Glu Ser Trp Leu Arg Arg Leu Lys
 1 5 10 15

Glu Ala Phe Tyr Asp Ala Glu Asp Leu Leu Asp Glu His
 20 25

<210> 707

<211> 16
 <212> PRT
 <213> Zea mays

<400> 707

Lys Ser Pro His Arg Gly Lys Leu Glu Ser Trp Leu Arg Arg Leu Lys
 1 5 10 15

<210> 708

<211> 13
 <212> PRT
 <213> Zea mays

<400> 708

His Arg Gly Lys Leu Glu Ser Trp Leu Arg Arg Leu Lys
 1 5 10

<210> 709

<211> 7
 <212> PRT

SEQ.List.txt

<213> Zea mays

<400> 709

Lys Ser Pro His Arg Gly Lys
1 5

<210> 710

<211> 8

<212> PRT

<213> Zea mays

<400> 710

Lys Gln Ala Ser His Leu Leu Lys
1 5

<210> 711

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Replikin formula
sequence

<220>

<221> MOD_RES

<222> (1)

<223> Lys, His, Arg, Tyr, Ile, Ser, Val, Ala, Phe, Pro or Gln

<220>

<221> MOD_RES

<222> (3)

<223> Ser, Cys or Trp

<220>

<221> MOD_RES

<222> (4)

<223> Tyr, Phe or Pro

<220>

<221> MOD_RES

<222> (7)

<223> Leu, Gln, Ser, Ala or Arg

<220>

<221> MOD_RES

SEQ.List.txt

<222> (8)
<223> Val, Ile or Leu

<220>
<221> MOD_RES
<222> (10)
<223> Phe or Leu

<220>
<221> MOD_RES
<222> (11)
<223> Gln, His, Ile, Leu, Met or Asn

<220>
<221> MOD_RES
<222> (12)
<223> Lys, Thr, Asn, Met or Ser

<220>
<221> MOD_RES
<222> (14)
<223> Gly, Ala, Gln or Arg

<220>
<221> MOD_RES
<222> (16)
<223> Gly, Ala, Val or Ser

<220>
<221> MOD_RES
<222> (17)
<223> Ile or Leu

<220>
<221> MOD_RES
<222> (18)
<223> Ser or Tyr

<220>
<221> MOD_RES
<222> (19)
<223> Tyr or His

<220>
<221> MOD_RES
<222> (20)
<223> Gly or Gln

.SEQ.List.txt

<400> 711

Xaa Cys Xaa Xaa His Cys Xaa Xaa Cys Xaa Xaa Xaa Lys Xaa Leu Xaa /
1 5 10 15

Xaa Xaa Xaa Xaa Arg Lys Lys
20