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(54) Title: POLYPEPTIDE SEQUENCE INVOLVED IN THE MODULATION OF THE IMMUNOSUPPRESIVE EFFECT OF VIRAL PROTEINS

(57) Abstract: The present invention relates to a polypeptide having a sequence of 7 to 20 amino acid residues, which is capable of modulating the immunosuppressive properties of a viral protein or a fragment thereof, against the host in which it is expressed (immunosuppression-modulatory sequence) when it substitutes the homologous sequence of said viral protein or fragment, said polypeptide comprising the minimum following consensus amino acid sequence: $X_1Y_9Y_{10}Y_{11}CY_{12}X_2$ wherein, X_1 and X_2 are selected to impact on said immunosuppressive properties, and Y_9 to Y_{12} represent variable amino acid residues.

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POLYPEPTIDE SEQUENCE INVOLVED IN THE MODULATION OF THE IMMUNOSUPPRESSIVE EFFECT OF VIRAL PROTEINS

FIELD OF THE INVENTION

The present invention relates to an amino acid sequence capable of modulating the immunosuppressive properties of a protein, especially from antigenic proteins. The invention also provides polypeptides, derived from an antigenic and immunosuppressive protein, having acquired modulated immunosuppressive properties with respect to the protein from which it is derived, while substantially retaining its antigenic properties.

The invention especially concerns the field of viral or retroviral infections, including the field of endogenous retroviruses, and provides means for the design of agents for the prophylaxis and/or treatment of hosts susceptible to such viruses or retroviruses, including animal or human hosts.

Polypeptides of the invention can especially be used in the generation of immunogenic compositions and in the production of attenuated viruses, for use in methods for prophylaxis and/or treatment of viral infections or their detrimental consequences or for prophylaxis and/or treatment of the detrimental consequences of the induction of expression of endogenous retroviruses (ERV).

BACKGROUND OF THE INVENTION

Any discussion of the prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of common general knowledge in the field.

Infectious agents, such as viruses, have evolved mechanisms and strategies to invade their hosts and to escape their immune response. Various publications have demonstrated the immunosuppressive properties of proteins encoded by viruses: the Epstein Barr human herpes virus 4 (Suzuki et al. 1995. J. Exp. Med.182, 477-486; Qin et al. 1996 J. Immunol. 156, 2316-2323), the Mason-Pfizer monkey virus (Blaise et al. 2001 J. Gen.

Virol. 82, 1597-1600), the Moloney murine leukaemia virus (Mangeney and Heidmann. 1998. Proc. Natl. Sci. USA. 95, 14920-14925) and others (see review Alcami et al. 2002 EMBO reports. 3(10), 927-932). This may be confirmed by the fact that infection by retroviruses is frequently associated with dysfunctions of the immune system of the host.

These immunosuppressive effects include the inhibition of interleukin-2-dependent lymphocyte proliferation, of the cytolytic activity of human natural killer cells, and of monocyte-medicated tumor cell killing as well as modulation of cytokine synthesis.

In vivo tests demonstrated that inactivated viruses, as well as synthetic peptides similar to retrovirus envelope proteins have immunosuppressive properties (Oostendorp et al. 1993 Crit. Rev. Oncol. Hematol. 14, 189-206; Haraguchi et al. 1997 J. Leukocyte Biol. 61, 654-666). More recently, Mangeney et al. (1998. Proc. Natl. Sci. USA. 95, 14920-14925) showed that murine tumoral cells from C57BL/6 strain, expressing a retroviral envelope protein, form tumours when injected in Balb/c mice (allograft), whereas the same cells, which do not express the retroviral envelope protein, are rejected. By carrying out different deletions in the envelope protein, a domain responsible for the immunosuppressive function that was called ISU (for "immunosuppressive") domain, was identified.

The ISU domain was first identified in the transmembrane moiety of the envelope glycoprotein. The *env* (envelope) gene of retroviruses encodes a precursor polypeptide which is then cleaved into two proteins: the surface glycoprotein (SU) and the transmembrane subunit (TM). The SU protein is responsible for the recognition and the binding to the cellular receptor for the virus. The TM moiety is involved in anchoring the envelope complex (SU and TM) to the target cell membrane, and is directly responsible for cell membrane fusion and virus entry.

The structure of the TM subunit has been elucidated for many viruses, especially for the Moloney murine leukaemia virus (Mo-MuLV), the

human immunodeficiency virus 1 (HIV-1) and the human T-cell leukaemia virus type 1 (HTLV-1). A highly conserved organization in the envelope proteins has also been found in non-retroviral proteins, such as those of influenza virus and Ebola virus.

Immunosuppressive effects have also been discovered in another class of proteins, characterized in the ERVs, especially HERVs (Human Endogenous Retroviruses). HERVs comprise elements which are sequences of retroviral origin that have spread into the human genome, and represent proviral remnants of ancestral infections. Therefore, strong similarities can be inferred between HERVs and retroviruses. Some of these HERV elements are still functional and can encode active proteins, i.e., viral-like proteins although most of them have accumulated mutations, deletions and/or truncations.

A role for these functional HERVs has been proposed, including a protection against retrovirus infection (Best et al. 1997 Trends Microbiol. 5, 313-318) or a protection of the foetus against the maternal immune system via immunosuppressive effects (Cianciolo et al. 1985 Science 230, 453-455; Mangeney and Heidmann 1998 Proc. Natl. Sci. USA. 95, 14920-14925). An HERV encoding an envelope protein having immunosuppressive properties was identified by Mangeney et al. (2001 J. Gen. Virology 82, 2515-2518). This publication reports that the protein encoded by HERV-H allows the envelope-expressing cells to escape immune response and to proliferate, whereas the same cells transfected with empty vectors are normally rejected by engrafted mice.

Other ERVs, especially HERVs, encoding functional envelope proteins were identified, which have fusogenic properties, *i.e.* are able to form syncytia *in vitro* (multi-nucleate cells): they include HERV-FRD and HERV-W (Blond et al. 2000 J. Virol. 74, 3321-3329 ; Blaise et al. 2003 Proc. Natl. Acad. Sci. 22, 13013-13018). Moreover, *in vivo* experiments have shown that when co-expressed with MoMLV viral particles deficient for the production of their own envelope protein, the HERV-W envelope

protein can form functional viral particles, capable of infecting human cells (Patience et al. 1998 J. Virol. 72, 2671-2676). In conclusion, HERV-W has conserved its fusogenic and infectiosity properties. Analog fusogenic and infectious properties have been observed for HERV-FRD.

The observed immunosuppressive effects may be related, depending on the context, on the one hand to a virulent viral infection and on the other hand to an active proliferation of tumour cells, in mammals and particularly in human. Active proliferation of tumour cells is especially a consequence of expression of ERV viral-like proteins. However, whereas more insights are needed to completely understand the mechanisms of immunosuppression, the identification of these immunosuppressive proteins opens new perspectives for therapeutic, including vaccinal, strategies against viral infections, against induction of expression of endogenous retroviruses, or against their detrimental consequences in a host.

Vaccines currently used can especially be classified as follows:

- live attenuated vaccines (bacteria or virus vaccine) consisting in an attenuated or weakened, modified pathogen. After administration to the host, the modified pathogenic organism replicates in the host and stimulates an immune response. This type of vaccine generally produces a long-lasting immunity upon single dose administration, but may cause side effects, i.e. a mild case of the illness caused by said pathogen, and thus should not be given to people with a weakened immune system.

- inactivated or killed vaccines, consisting in killed or inactivated pathogen, especially as a result of heat and/or chemical treatments (whole organism). Such treated pathogens cannot replicate, and cannot cause the disease they normally raise. Therefore, they are safe and can be administered even to hosts whose immune system is

weakened. However, they are not usually as effective as live vaccines and therefore require multiple dose administration.

- vaccines consisting in antigenic fractions of a pathogen organism, including whole proteins or antigenic determinants thereof, especially obtained by recombinant technologies, as a result of the expression of genes encoding the antigen. The expressed protein can be administered to a patient, or the gene encoding the protein can be inserted into an expression vector which is administered to the host. Such vaccines however are usually not as effective as live vaccines and therefore require multiple doses.

Principles applied for the design of compounds suitable for vaccine preparations capable of eliciting an immune response in a host, in order to protect a host from infection due to pathogens, including viruses, bacteria or others, have been transposed to the design of compounds suitable for treatment of established infections, by immunotherapy. Efficiency of such compounds has however not proved to be sufficient enough, especially in the field of anti-viral or anti-viral-like prophylaxis or immunotherapy. Moreover, the use of compounds still raises many issues regarding safety.

One drawback observed in the use of some retroviral envelope proteins for immunisation, either as vaccine principles or for immunotherapy, lies in their immunosuppressive properties which can prevent or affect the efficiency of the host's immune response. Consequently these proteins cannot be administered to a patient in their native form because of their potential inhibition of the immune response. A great challenge would hence be to suppress or modulate the immunosuppression properties of these proteins, without altering their antigenic properties and/or their properties related to host cell infection. However, attempts to mutate the envelope protein complex, have led to a strong alteration of its fusion and infection functions and therefore of their interest as active principle to raise an immune response (Delamarre et al.

1997 J. Virol. 71(1), 259-266; Rosenberg et al. 1999 J. Cell Biol. 145, 57-68).

The present invention relates to the identification of determinants of the immunosuppressive properties of proteins, including polypeptide sequences and amino acid residues involved in the modulation of the immunosuppressive properties of proteins, particularly viral or viral-like proteins, which substantially retain their antigenic properties of said immunosuppressive proteins.

The invention also relates to identifying such determinants of the immunosuppressive properties of the protein, and to use the same for the design of polypeptides having modified, i.e., modulated immunosuppressive properties.

The present invention also relates to providing such polypeptides, which are derived from an antigenic and immunosuppressive protein, which polypeptides are characterized by modulated immunosuppressive properties while retaining antigenic properties of the starting protein.

The present invention further relates to providing means to promote an efficient immune response against pathogen organisms, especially against viruses, *i.e.*, a cell-mediated and/or humoral immune response which would be protective against infection by such pathogen organisms, especially viruses, or protective against their detrimental effects in the host, or protective against the detrimental consequences of expression of endogenous retroviruses in a host, with reduced risks of immune system alteration. The invention also provides means suitable for treatment by immunotherapy, of patients infected with pathogen organisms including viruses, or for treatment of their detrimental effects, including malignant effects or for the treatment of patients suffering from pathologies associated with induction of the expression of endogenous viruses which are normally silent in hosts.

It is an object of the present invention to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

SUMMARY OF THE INVENTION

According to a first aspect, the present invention provides an isolated polypeptide having a sequence of 7 to 20 amino acid residues encoded

by a nucleic acid, derived from a viral gene, which is capable of modulating the immunosuppressive properties of a viral protein or a fragment thereof, against the host in which it is expressed (immunosuppression-modulatory sequence) when it substitutes the homologous sequence of said viral protein or fragment,

said isolated polypeptide comprising the minimum following consensus amino acid sequence:

$$X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

wherein X_1 and X_2 are selected to impact on said immunosuppressive properties, such that

- X_1 is E, K or Q, and X_2 is such that it ensures that the structure of the viral protein is conserved, or
- X_1 is E, K or Q and X_2 is A or
- X_1 is W and X_2 is I or V, or
- X_1 is R,H or K, X_2 is such that it ensures that the structure of the viral protein is conserved or
- X_1 is R,H or K and X_2 is F, W Y or H, or
- X_1 is F, W Y or H and X_2 is R, H or K

and Y_9 to Y_{12} represent variable amino acid residues.

According to a second aspect, the present invention provides an isolated mutated ENV protein resulting from the mutation of a wild-type ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

in which X_1 is E, K or Q and X_2 is A, V, L, I, or K and Y_1 to Y_{12} represent any amino acid

wherein amino acid X_1 is substituted by R or H,

said mutated ENV protein having almost no immunosuppressive activity with respect to the wild-type ENV protein,

or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries the mutated amino acid X_1 and optionally X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, which is almost no immunosuppressive activity, and that optionally its antigenic structure

is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein with at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or a fragment thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

According to a third aspect, the present invention provides an isolated mutated ENV protein resulting from the mutation of a wild-type ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

in which X_1 is R and X_2 is F and Y_1 to Y_{12} represent any amino acid

wherein amino acid X_1 is substituted by E or Q ,

said mutated ENV protein having an immunosuppressive activity whereas the wild-type ENV protein is deprived of such an activity,

or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries the mutated amino acid X_1 and optionally X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and has an immunosuppressive activity, and that optionally its antigenic structure is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein presenting at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated

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ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

According to a fourth aspect, the present invention provides a eukaryotic or prokaryotic expression vector, comprising a nucleic acid according to the invention as well as the elements necessary for the expression of said nucleic acid.

According to a fifth aspect, the present invention provides a recombinant cell, comprising a nucleic acid according to the invention, or a eukaryotic or prokaryotic expression vector according to the fourth aspect.

According to a sixth aspect, the present invention provides a pharmaceutical or a vaccine composition comprising as active substance:

at least one isolated polypeptide according to the first aspect, or

at least one isolated mutated ENV protein, or a fragment thereof, according to the second or third aspects, or

at least one nucleic acid according to the invention, or

at least one prokaryotic or eukaryotic expression vector according to the fourth aspect, or

at least one recombinant cell according to the fifth aspect,

in association with a pharmaceutically acceptable carrier.

According to a seventh aspect, the present invention provides the use of at least one protein comprising or constituted of an isolated mutated ENV protein, or a fragment thereof, according to the invention, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of a viral disease, such as HTLV or FeLV infections.

According to an eighth aspect, the present invention provides the use of at least one protein comprising or constituted of an isolated mutated ENV protein, or a fragment thereof, according to the invention, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancer.

According to a ninth aspect, the present invention provides the use of at least one protein comprising or constituted of an isolated mutated ENV protein, or a fragment thereof, according to the invention, or of a nucleic acid

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coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of a pathology requiring an inhibition of the immune system, such as an autoimmune disease, allergy or graft rejection.

According to a tenth aspect, the present invention provides the use of at least one isolated polypeptide according to the invention, or of a nucleic acid coding for said isolated polypeptide, for the manufacture of a medicament intended for the prevention and/or the treatment of cancer, of a viral disease, or of a pathology requiring an inhibition of the immune system, such as an autoimmune disease, allergy or graft rejection.

According to an eleventh aspect, the present invention provides the use of at least one protein or of a nucleic acid coding for said protein, said protein comprising or being constituted of:

- an immunosuppressive ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

wherein amino acids Y_1 to Y_{12} represent any amino acid, amino acid X_1 represents E, K or Q, and amino acid X_2 is such that it ensures that the structure of the viral protein is conserved, preferably X_2 represents A,

- or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of said ENV protein, and has an immunosuppressive activity,
- or a protein derived from said ENV protein presenting at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of the mutated ENV protein,

for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancer, of a viral disease, or of a pathology requiring an inhibition of the immune system, such as an autoimmune disease, allergy or graft rejection.

According to a twelfth aspect, the present invention provides an antibody or a fragment thereof, scFv polypeptide, aptamer, or binding peptide, directed against mutated ENV proteins according to the second or third aspects provided that said antibody or a fragment thereof, scFv polypeptide, aptamer, or binding peptide does not bind to the corresponding wild-type ENV proteins.

According to a thirteenth aspect, the present invention provides a method of preventing and/or treating a viral disease such as HTLV or FeLV infections said method comprising the step of administering to a subject in need thereof at least one protein comprising or constituted of an isolated mutated EMF protein or a fragment thereof according to the invention or a nucleic acid coding for said protein.

According to a fourteenth aspect, the present invention provides a method of preventing and/or treating cancer said method comprising a step of administering to a subject in need thereof at least one protein comprising or constituted of an isolated mutated EMF protein or a fragment thereof according to the invention or a nucleic acid coding for said protein.

According to a fifteenth aspect, the present invention provides a method of preventing and/or treating a pathology requiring an inhibition of the immune system including an autoimmune disease, allergy or graft rejection said method comprising the step of administering to a subject in need thereof at least one protein comprising or constituted of an isolated mutated EMF protein or a fragment thereof according to the third aspect or a nucleic acid coding for said protein.

According to a sixteenth aspect, the present invention provides a method of preventing and/or treating cancer, a viral disease or a pathology requiring an inhibition of the immune system such as an autoimmune disease, allergy or graft rejection said method comprising the step of administering to a subject in need thereof at least one isolated polypeptide according to the first aspect or a nucleic acid coding for said polypeptide.

According to a seventeenth aspect, the present invention provides a method of preventing and/or treating cancer, a viral disease or a pathology requiring an inhibition of the immune system such as

an autoimmune disease, allergy or graft rejection, said method comprising the step of administering to a subject in need thereof at least one protein or nucleic acid coding for said protein comprising or constituted of

- an immunosuppressive ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

wherein amino acids Y_1 to Y_{12} represent any amino acid, amino acid X_1 represents E, K or Q, and amino acid X_2 is such that it ensures that the structure of the viral protein is conserved, preferably X_2 represents A,

- or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of said ENV protein, and has an immunosuppressive activity,
- or a protein derived from said ENV protein presenting at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of the mutated ENV protein.

Unless the context clearly requires otherwise, throughout the description and the claims, the words "comprise", "comprising", and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of "including, but not limited to".

In another aspect, the invention provides a polypeptide which is capable of modulating the immunosuppressive properties of a viral protein or a fragment thereof against the host in which it is expressed when it substitutes the homologous sequence of said protein or fragment, said polypeptide having the minimum following consensus amino acid sequence:

$$X1\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}X2$$

wherein, X1 and X2 are selected to impact on said immunosuppressive properties, Y represents variable amino acid residues, and 3 and 1 represent the

number of variable amino acid residues respectively between X1 and C and between C and X2.

Said minimum consensus sequence is designated "immunosuppression-modulatory sequence".

In an embodiment, peptides replying to the above definition, comprising an immunosuppression-modulatory sequence, are derived from a viral including from a viral-like protein, especially a retroviral protein, in particular, a viral or retroviral envelope protein or an envelope protein from an endogenous retrovirus, especially from a human endogenous retrovirus (HERV).

The amino acid sequences of several envelope proteins of viruses (including ERV) have been disclosed in Figure 3 of Benit et al (J Virol. December 2001, p. 11707-11719).

Particular pairs of amino acid residues impacting on the immunosuppressive properties in the context of a determined protein have been characterized, and accordingly sequences having the desired "immunosuppression-modulatory" properties have been identified and can be selected from the group consisting of: ———————————————

a) sequences involved in the occurrence of immunosuppressive properties of a protein in which they are present comprise:

$$E\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}A$$

$$Q\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}A$$

and b) sequences altering, e.g. decreasing or suppressing immunosuppressive properties of an immunosuppressive protein when they are present therein, comprise

$$R\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}F$$

In another aspect, the invention provides a polypeptide derived from a determined antigenic and immunosuppressive protein, said polypeptide comprising an amino acid sequence (so-called immunosuppression-modulatory sequence) represented by $X1\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}X2$ wherein in said polypeptide Y represents variable amino acid residues, 3 and 1 represent the number of variable amino acid residues Y respectively between X1 and C and between C and X2, and X1 and X2 are chosen to confer to said polypeptide altered immunosuppressive properties with respect to the immunosuppressive properties of said determined protein.

In a particular embodiment, the protein having antigenic and immunosuppressive properties is encoded by a gene derived from a virus, and especially by an env gene from a retrovirus.

Such protein comprises an immunosuppressive sequence determinant having the following consensus sequence: E/Q-G-G-L/T/I-C-A/K/L/M/V/I-A. The same protein wherein X1 (E/Q) and optionally X2 (A) residues are substituted can be devoid of immunosuppressive properties but retains its antigenic properties. An example of modified immunosuppression-modulatory sequence is R-G-G-L/T/I-C-A/K/L/M/V/I-F, which alters immunosuppressive properties and especially can give rise to a non-immunosuppressive polypeptide which contains said sequence. A

particular modified immunosuppression-modulatory sequence is selected from the group of:

RGGLCAF (SEQ ID NO: 1)
RGGLCKF (SEQ ID NO: 2)
RGGLCLF (SEQ ID NO: 3)
RGGLCMF (SEQ ID NO: 4)
RGGLCVF (SEQ ID NO: 5)
RGGLCIF (SEQ ID NO: 6)
RGGTCAF (SEQ ID NO: 7)
RGGTCKF (SEQ ID NO: 8)
RGGTCMF (SEQ ID NO: 9)
RGGTCIF (SEQ ID NO: 10)
RGGICAF (SEQ ID NO: 11)
RGGICKF (SEQ ID NO: 12)
RGGICLF (SEQ ID NO: 13)
RGGICMF (SEQ ID NO: 14)
RGGICVF (SEQ ID NO: 15)
RGGICIF (SEQ ID NO: 16)

In a particular embodiment, the protein further has infectious and/or fusion properties. The modification of the immunosuppression-modulatory sequence, e.g. by substitution of X1 and optionally X2 amino acid residues can advantageously be carried out in a way that does not affect one of these or both supplementary properties.

In another aspect, the invention relates to compositions comprising such polypeptides or recombinant viral particles expressing these polypeptides. Such compositions or particles can be used in the prevention or treatment of a viral infection including for the prevention or treatment of its detrimental effects, or for prevention or treatment or the consequences in a host, of the expression of an endogenous virus, especially an HERV, by the elicitation of an immune response in the host in which they are injected. They can also be used in the preparation of attenuated viruses.

In another aspect, the invention relates to methods to modulate the immunosuppressive properties of a protein by modifying the amino acid composition of the immunosuppression-modulatory sequence.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: schematic representation of vectors containing the env nucleic acid of MoMLV or its derived polypeptides.

Nucleic acids contained in these vectors encode the wild-type envelope protein of MoMLV (envMoMLV) or its derived polypeptides of the invention by substitutions of codons encoding X1 and/or X2.

Figure 1A represents the phCMV-envMOMLV vector.

Figure 1B represents the pDFG-envMoMLV-iresHygro vector.

Figure 2: schematic representation of vectors containing the env nucleic acid of MPMV or its derived polypeptides.

Nucleic acids contained in these vectors encode the wild-type envelope protein of MPMV (envMPMV) or its derived polypeptides of the invention by substitutions of codons encoding X1 and/or X2.

Figure 2A represents the phCMV-envMPMV vector

Figure 2B represents the pDFG-envMPMV-iresHygro vector

Figure 3: schematic representation of vectors containing the HERV-W nucleic acid of HERV-W or its derived polypeptides.

Nucleic acids contained in these vectors encode the wild-type envelope protein W (envW) or its derived polypeptides of the invention by substitutions of codons encoding X1 and/or X2.

Figure 3A represents the phCMV-envW vector

Figure 3B represents the pDFG-envW-iresHygro vector

Figure 4: Schematic representation of the cell-cell fusion assay.

The vector used comprises the nucleic acid encoding an envelope protein of interest (SU and TM subunits), a CMV promoter and a poly A nucleotide element (pA).

Figure 5: Schematic representation of the establishment of Envelope Expressing tumours cells and *in vivo* assay.

The vector used comprises the nucleic acid encoding an envelope protein of interest (env), the hygromycin gene (hygro) and an IRES (Internal Ribosome Entry Site). White boxes represent LTRs and the arrow indicates the start of transcription.

Figure 6: Results of infectious property assay.

The numbers 1 to 12 refer to lines used in the present specification. This diagram presents the results of infection for wild-type (wt) or mutant envelope proteins according to the invention.

Figure 7: Results of immunosuppressive property assay.

The diagram presents the results of immunosuppressive property assay of MCA205 cells expressing envelope when injected in allogenic balb/c mice. In insets, results of MCA205 cells expressing envelope protein injected in syngenic C57Bl/6 mice. Filled bars represent HERV-W envelope protein, white bars represent MPMV envelope protein and shaded bars represent double-mutant (R44Q+F50A) HERV-W envelope protein.

Figure 8: Structural design of the TM subunit of the HERV-W ENV protein.

This structural design shows the position of the Arginine (X1) and Phenylalanine (X2) amino acid residues of the immunosuppression-modulatory sequence, as well as the two amino acid residues (Alanine and Threonine) not involved in such properties.

Figure 9: Examples of immunosuppression-modulatory sequence of different viruses and HERVs.

The first column indicates the common names of viruses or HERVs, the second column indicates the origin of the viruses or HERVs, the third column indicates the nucleotide sequences of identified immunosuppression-modulatory sequences (one letter amino acid used) and the last column indicates the Accession Number of the envelope protein. The X1 and X2 amino acid residues are in bold.

Figure 10: Nucleotide and amino acid sequences of wild-type envelope proteins.

In the amino acid sequences, the X1 and X2 positions have been underlined.

A and B represent the nucleotide and protein sequences of the envelope protein of MoMLV, C and D represent the nucleotide and protein sequences of the envelope protein of MPMV and E and F represent the nucleotide and protein sequences of the envelope protein of HERV-W (envW).

The nucleotide sequences (A, C and E) are the coding sequences of the envelope proteins, with the first codon (ATG) being the first codon of transcription and the last codon (TAG) being the termination codon.

For the protein sequences (B, D and F), the first letter amino acid code is used. The first M represents the first methionine of the protein, and the symbol "*" represent the termination codon.

Figure 11A, Figure 11B and Figure 11C: *In vitro* properties of the immunosuppression-defective FV envelope protein. Figure 11A, Infectivity of FV wild type (wt) envelope protein, E14R mutant envelope protein, A20F mutant envelope protein, and E14R+A20F double mutant (DM) envelope protein as expressed on the surface of a MLV viral

pseudotypes, using NIH 3T3 cells as a target. The vertical axis represents the infectivity (ffu/ml) Figure 11B, *In vivo* immunosuppressive activity (horizontal axis, immunosuppression index) of the wild-type (wt) and the double-mutant (DM) FV envelope protein. Figure 11C, Comparison of *in vitro* propagation rates of the wild-type (black circles) and immunosuppression-defective (gray circles) FV virions, using NIH 3T3 cells as a target. Viral load of cell supernatants (vertical axis, RNA copy number/mL) is assayed by quantitative RT-PCR. Horizontal axis represents the number of days after infection. The white circles represent a control.

Figure 12A and Figure 12B: *In vivo* effects of the loss of envelope-driven immunosuppression on FV infection. Serum viral loads (Vertical axis, RNA copy numbers/mL) of irradiated (Figure 12A) and non-irradiated (Figure 12B) Swiss mice after injection of the wild-type FV (black circles) or the non-immunosuppressive mutant FV (gray circles). The signal for PBS-injected mice was below detection treshold (white circles). Horizontal axis represents the days after injection.

Figure 13: Immunological detection of FV in infected mice. IgGs directed against the SU subunit of the FV envelope protein were quantitated (vertical axis, arbitrary units) in the sera of mice injected with the wild-type FV (black circles and line), the non-immunosuppressive mutant FV (gray circles and line) or PBS (white circles and dotted lines). The lines represent the geometric means of the IgG levels. Horizontal axis represents the days after injection.

Figure 14A and Figure 14B: Antigenicity of the wild-type and non-immunosuppressive mutant FV envelope proteins. Figure 14A, IgMs and IgGs directed against the TM subunit of the FV envelope protein were quantitated in the sera of mice injected with recombinant TM subunits of the FV envelope protein (left) or UV-inactivated FV viral particles (right). Black:

wild-type FV; gray: non-immunosuppressive mutant FV; white: adjuvant only. Mean ± standard deviation on 5 (left) or 14 (right) Swiss mice. The vertical axis represents the anti-TM ELISA signal in arbitrary units (a.u.). Figure 14B, same as in Figure 14A with mice injected with the wild type (wt) or double mutant (dm) recombinant TM subunits of MoMLV (left) and HERV-W ENV (right) as described in Example 1. The vertical axis represents the IgG level in ng/mL.

Figure 15: Vaccination assays. Figure 15 represents the viral load (Vertical axis, RNA copies/mL serum) of mice immunized with UV-inactivated wild-type or non-immunosuppressive double mutant Friend Virus (FV), with intact non-immunosuppressive double mutant Friend Virus (FV), or with CpG adjuvant only, and challenged with the wild-type FV. Immunization was performed on day 1, day 7 and day 14 before challenge on day 21, and the corresponding viral loads are represented as grey dots. 5 days post-challenge viral loads are represented as black dots. The detection threshold is represented as a horizontal line at 2.10^3 RNA copies/mL. On top of the graph is indicated the number and the percentage of mice having a viral load below the detection level at 5 days post-challenge. Horizontal bars represent the geometric means of the viral loads.

Figure 16A, Figure 16B and Figure 16C: Knockdown procedure and rationale of the assay. Figure 16A represents the procedure to knock down ERV expression, a pIncx-derived vector was constructed making use of the pSUPER vector to generate, under control of the H1-RNA promoter, short double-stranded transcripts for RNA interference. B16 cells were transduced with these expression vectors, submitted to G418 selection, and the resulting ERV^{KD} and control B16 cells were injected subcutaneously into the flank of the mice, whose tumor growth was monitored. Figure 16B, predicted structure of the dsRNA generated by the ERV and control (gfp) vectors; numbers refer to nt positions within the respective targeted

sequences (see Methods). Figure 16C, Western blot analysis of Gag (anti-Gag) and Env (anti-Env) expression in the supernatant of ERV-knocked down (ERV^{KD}) and control cells. Molecular weights are represented on both side of the Figure.

Figure 17A and Figure 17B: Knocked down cells have conserved a transformed phenotype. Figure 17A, *in vitro* analysis of the transformed phenotype using soft agar assay. Left panel, ERV^{KD} (right plates) and control B16 (left plates) cells ($2x10^3$ or $2x10^4$) were plated onto a semi-solid layer for 4 weeks, and then colonies were numbered (right panel). Figure 17B, assay for the transformed phenotype *in vivo* using immuno-incompetent mice. ERV^{KD} and control B16 cells ($2x10^5$) were injected subcutaneously into the flank of either X-irradiated (5 Gy) C57Bl/6 (left panel) or SCID mice (right panel) (2-5 independent experiments with 5 mice per group) and tumor growth was determined by measuring tumor area (vertical axis, mm^2) as a function of time (horizontal axis, days post injection).

Figure 18A, Figure 18B and Figure 18C: Inhibition of tumor cell growth and increased mouse survival upon ERV knockdown. Figure 18A, tumor cell growth of control (black dots) and ERV^{KD} B16 cells (white dots) engrafted into immunocompetent C57Bl/6 mice (22 mice per group; same experimental conditions as in Figure 17B). Tumor area (vertical axis, mm^2) is measured as a function of time (horizontal axis, days post injection). Figure 18B, percentage of survivors (vertical axis) among the control (black dots) and ERV^{KD} B16 cells (white dots) engrafted mice (10 mice per group) as a function of time (horizontal axis, days post injection). Figure 18C, percentage of survivors (vertical axis) (10 mice per group) among MelARV *env* - transduced ERV^{KD} B16 cells (grey dots) and ERV^{KD} B16 cells (white dots) engrafted mice as a function of time (horizontal axis, days post injection).

Figure 19: Immunostaining for ERV envelope protein detection. Control, ERV ^{KD}, and ERV ^{KD}+env B16 cells were labelled with the 9B6 antibody (directed against the MelARV envelope protein; gift from E. Gorelik, Cancer Res 1988;48:4954-4958) revealed by a goat anti-mouse FITC antibody (Caltag, Burlingame, USA). Flow cytometry analysis was performed using a Facscalibur cytometer. The number of counts (vertical axis) is represented as a function of ERV envelope expression (horizontal axis).

Figure 20A and Figure 20B: *In vivo* systemic administration of siRNA reduces tumor cell progression. Synthetic siRNA targeted to the 19 nt ERV (white dots) and control (gfp) (black dots) sequences referred to in Figure 16B were purchased from MWG Biotech. They were injected intraperitoneously (3 µg of siRNA in 50 µl of PBS), at day 12 after prior engraftement of $2x10^5$ B16 cells in the right flank of the mice. Figure 20A, the tumor area (vertical axis, mm^2) is measured as a function of time (horizontal axis, days post tumour injection), siRNA injection is represented as an arrow. Figure 20B, the percentage of survivors (vertical axis) were monitored (5 mice per group in two independent experiments) as a function of time (horizontal axis, days post tumour injection).

DETAILED DESCRIPTION

The present invention provides a polypeptide having a sequence of 7 to 20 amino acid residues, which is capable of modulating the immunosuppressive properties of a viral protein or a fragment thereof against the host in which it is expressed when it substitutes the homologous sequence of said viral protein or fragment, said polypeptide comprising the minimum following consensus amino acid sequence:

$$X1\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}X2$$

wherein, X1 and X2 are selected to impact on said immunosuppressive properties, Y represents variable amino acid residues, and 3 and 1 represent the number of variable amino acid residues Y, respectively between X1 and C and between C and X2.

In all the sequences of the present invention, the amino acid one-letter code is used. X and Y are used to designate variable amino acid residues, X being determined to influence the immunosuppressive properties of a determined protein.

Y represents amino acid residues that can vary for different polypeptides and within one determined polypeptide. "$(Y)_3$" indicates that 3 amino acid residues are present between the X1 residues and the cysteine residue (C). The 3 amino acid residues can be different or identical and can be selected independently of each other. The indication of a particular amino acid residue in a sequence, like the cysteine in the sequence above, means that this amino acid residue is invariant, *i.e.* it has a constant position in said sequence.

Optionally the consensus sequence can also be noted as follows:

$$X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

wherein X_1 represents X1, X_2 represents X2, and Y_9 to Y_{12} represent any amino acid. As intended herein amino acids Y_9 to Y_{12} are identical or different.

In the present invention, the expressions "virus" or "viral" apply both exogenous or endogenous viruses or their compounds, unless otherwise stated. Therefore, "viral protein" encompasses "viral-like proteins" which may also be referred to when describing the expression products of endogenous viruses, especially ERV, in particular HERV.

The above consensus sequence of the polypeptide according to the invention is called "immunosuppression-modulatory sequence" meaning that, when it is present in the polypeptide having 7 to 20 amino acid residues, the polypeptides can be used to modulate

immunosuppressive properties of a protein which has been identified as harbouring such immunosuppressive properties or, as lacking such properties despite the fact that is comprises a peptidic motif having a sequence X1-$(Y)_3$-C-$(Y)_1$-X2.

More especially, X represents both amino acid residues (X1 and X2) directly involved, individually or together, in the modulation of the immunosuppressive properties of a protein comprising the above consensus sequence. They are respectively located at the N-terminal and C-terminal ends of the minimum polypeptide having 7 amino acid residues.

A protein is said to have immunosuppressive properties, when this protein, expressed in tumour cells engrafted in a host which would normally be rejected by said host, to the contrary allows these tumour cells to proliferate and to escape immune rejection by the host.

An *in vivo* procedure to assay the immunosuppressive activity of a protein is that used by Mangeney M. and Heidmann T., 1998 PNAS or by Blaise et al. 2001 represented in Figure 5. A wild-type or modified nucleic acid expressing the protein to be tested is transfected in tumour cell lines such as MCA 205 or CI8.1 cell lines by known transfection methods. The tumour cells expressing the protein to be tested are then injected especially s.c. injection to a host, generally mice. Following said injection, the establishment of tumour or, to the contrary, its rejection, is determined and the tumour area is measured. *In vitro* assay could be carried out, using high doses of synthetic peptides but they are indirect and less convincing, since the expression "immunosuppressive" is relevant when applied to animals possessing a complete immune system and not to cell lines.

The expression "modified nucleic acid" as used herein refers to any genetic alteration such as nucleotide substitution, deletion or insertion that change the amino acid composition of the encoded polypeptide or protein. Thus, an amino acid sequence can substitute, *i.e.* replace a homologous sequence present in the original protein.

The terms "homologous sequence" in the protein which is tested for modulation of its immunosuppressive properties refer to a sequence having the same amino acid sequence as that replacing (i.e. substituting) it for the assay, i.e., $X1-(Y)_3-C-(Y)_1-X_2$ except for the X1 and X2 residues; at least one of which and possibly both, are selected to be different from their corresponding amino acid residues in the original sequence. Thus, the Y amino acid residues are conserved between the homologous sequence of the protein to be modified and the sequence of the polypeptide having 7-20 amino acid residues as defined above.

Such homologous sequences are disclosed in Figure 9 for various viruses and are illustrated in the context of the TM subunit of various envelopes for several viruses in Benit L. et al. (J. Virol. Vol. 75, No. 23, December 2001, p. 11709-11719) in Figure 3.

The X1 and X2 amino acid residues are chosen to modulate the immunosuppressive properties of the original viral protein. The term "modulate" as used herein refers to an increase or decrease of the immunosuppressive activity of the modified protein with respect to the immunosuppressive activity of the original (i.e., non modified) protein, when tested in the same conditions.

The invention especially relates to an "immunosuppression-modulatory sequence" which allows a decrease in the immunosuppressive properties of the modified protein with respect to the originally immunosuppressive protein. The modulation is preferably significant meaning that the immune response of the host becomes detectable, and advantageously becomes sufficient to eliminate the pathogen agent or becomes sufficient to stop, stabilize or reverse the detrimental consequences of infection by said pathogen in a host or of the expression of endogenous viruses, especially of normally silent ERV, especially HERV, in a host.

In a particular embodiment, modulation results in decreasing the immunosuppressive properties of the original protein.

In a particular embodiment it corresponds to at least a two-fold decrease of the immunosuppressive properties of the original protein, in the modified, i.e., derived protein.

The above defined polypeptide of the invention having 7 to 20 amino acid residues and comprising sequence X1-$(Y)_3$-C-$(Y)_1$-X2 is such that X1 and/or X2 are selected to modulate the immunosuppressive properties of a protein and accordingly:

in a particular embodiment of the invention, X1 is an alkaline amino acid residue and X2 is an aromatic residue or *vice versa*.

As intended herein "alkaline" relates to basic amino acids.

In another particular embodiment of the invention, X1 is an alkaline residue or X2 is an aromatic residue or *vice versa*.

The inventors have observed that the modulation effect of X1 and X2 on immunosuppressive proteins is lower when only one of X1 or X2 residues is modified in an original immunosuppressive protein.

Therefore, modification of both X1 and X2 in an immunosuppression-modulatory sequence may be regarded as advantageous.

In another particular embodiment of the invention, residues X1 or X2 located in amino acid sequence represented as X1-$(Y)_3$-C-$(Y)_1$-X2 are selected as follows:

where X1 is chosen among R, H and K, X2 is chosen among F, W, Y and H or where X1 is chosen among F, W, Y and H, X2 is chosen among R, H and K.

In a further embodiment of the invention, X1 is R, H or K and X2 is F, or *vice versa*.

In a further embodiment of the invention, X1 is R and X2 is F, W, Y or H.

In another further embodiment of the invention X1 and X2 are selected from the group consisting of:

a. X1 is E, K or Q and X2 is A

b. X1 is W and X2 is I or V

c. X1 is R and X2 is F

d. X1 is K and X2 is F.

The inventors have identified the effects of particular X1 and X2 residues, in a immunosuppression-modulatory sequence on modulation of the immunosuppressive properties of a viral envelope protein.

Their observations enable to consider that, when X1 is either glutamic acid (E) or glutamine (Q) and X2 can be alanine (A), the resulting viral envelope protein comprising the consensus sequence of the invention harbours immunosuppressive properties. To the contrary, when X1 is arginine (R) and X2 is phenylalanine (F), the resulting viral envelope protein having the consensus sequence of the invention has low or has no immunosuppressive properties. Interestingly, whereas van der Waals interactions are suspected in the pair E/A, an electrostatic interaction may occur in the pair R/F, between the positively charged side chain of Arginine and the pi-electrons (negative pole) of Phenylalanine.

Accordingly, in a particular embodiment of the invention, the polypeptide having 7 to 20 amino acid residues has an immunosuppression-modulatory sequence X1-$(Y)_3$-C-$(Y)_1$-X2 suitable to confer low or no immunosuppressive properties to a protein, wherein X1 is R and/or X2 is F.

In another embodiment, X1 is K and X2 is F to confer low or no immunosuppressive properties to a protein. In particular, such a protein has low immunosuppressive properties.

It is recalled that the immunosuppressive properties are assayed in a test as defined above and illustrated in the Examples.

The consensus sequence, X1-$(Y)_3$-C-$(Y)_1$-X2, can be identified in viral proteins and especially in viral envelope proteins. Particular envelope proteins are those of retroviruses that comprise two subunits: the SU and TM subunits. Such consensus sequences have been found in MoMLV, Friend retrovirus, FeLV, HTLV-1, HTLV-2, STLV-1, GLV-

X, Pox viruses, MPMV or SSAV, or in Ebola or Marburg viruses or in endogenous retroviruses such as FRD, PyERV, PERV or HERV-T.

The Y amino acid residues thus identified in various proteins allow determining particular sequences of the invention such as E/Q-G-G-L/T/I-C-A/K/L/M/V/I-A or R-G-G-L/T/I-C-A/K/L/M/V/I-F. The "/" indicates that this sequence position accepts several types of amino acid residues according to the indications which are provided.

Therefore, the above-defined polypeptide of the invention comprises, in a particular embodiment, a minimum sequence which can be selected from the group consisting of:

QGGLCK**A** (SEQ ID NO: 17)
QGGLCA**A** (SEQ ID NO: 18)
QGGLCL**A** (SEQ ID NO: 19)
QGGICL**A** (SEQ ID NO: 20)
EGGLCA**A** (SEQ ID NO: 21)
EGGLCV**A** (SEQ ID NO: 22), wherein these immunosuppression-modulatory sequences provide immunosuppressive properties to a protein comprising them, or
RGGTCL**F** (SEQ ID NO: 23)
KGGTCM**F** (SEQ ID NO: 24)
KGRTCL**F** (SEQ ID NO: 25)
KGGLCI**F** (SEQ ID NO: 26)
RGGLCK**F** (SEQ ID NO: 27)
RGGLCA**F** (SEQ ID NO: 28)
RGGLCL**F** (SEQ ID NO: 29)
RGGICL**F** (SEQ ID NO: 30)
RGGLCV**F** (SEQ ID NO: 31)
RGGTCV**F** (SEQ ID NO: 32), these immunosuppression-modulatory sequences providing low or no immunosuppressive properties to a protein comprising them.

More particularly, the above-defined polypeptide of the invention comprises, in another embodiment, a minimum sequence which can be selected from the group consisting of:

QGGLCK**A** (SEQ ID NO: 17)
QGGLCA**A** (SEQ ID NO: 18)

QGGLCL**A** (SEQ ID NO: 19)
QGGICL**A** (SEQ ID NO: 20)
EGGLCA**A** (SEQ ID NO: 21)
EGGLCV**A** (SEQ ID NO: 22), wherein these immunosuppression-modulatory sequences provide immunosuppressive properties to a protein comprising them, or
KGGTCM**F** (SEQ ID NO: 24)
KGRTCL**F** (SEQ ID NO: 25)
KGGLCI**F** (SEQ ID NO: 26), wherein these immunosuppression-modulatory sequences provide low immunosuppressive properties to a protein comprising them, or
RGGTCL**F** (SEQ ID NO: 23)
RGGLCK**F** (SEQ ID NO: 27)
RGGLCA**F** (SEQ ID NO: 28)
RGGLCL**F** (SEQ ID NO: 29)
RGGICL**F** (SEQ ID NO: 30)
RGGLCV**F** (SEQ ID NO: 31)
RGGTCV**F** (SEQ ID NO: 32), these immunosuppression-modulatory sequences providing essentially no immunosuppressive properties to a protein comprising them.

As intended herein, "low immunosuppressive properties" relates to a polypeptide which provides lower immunosuppressive properties to a protein comprising it than polypeptides represented by SEQ ID NO: 17 to 22, but provides higher immunosuppressive properties to a protein comprising it than polypeptides represented by SEQ ID NO: 23 to and 27 to 32. In particular, a protein comprising a polypeptide which provides low immunosuppressive properties is less immunosuppressive than a HERV-W ENV R393Q F399A double mutant, such as represented by SEQ ID NO: 118. More particularly, the immunosuppressive index of a protein comprising a polypeptide which provides low immunosuppressive properties is positive but lower than the immunosuppressive index of said HERV-W ENV R393Q F399A double mutant, and preferably lower than 50% the immunosuppressive index of said HERV-W ENV R393Q F399A double mutant.

All the polypeptides of the invention are encoded by nucleic acids that can be obtained by all known methods to enable expression of the polypeptides in host cells, especially in prokaryotic or eukaryotic cells. As example, nucleic acids can be isolated from samples expressing viruses, using suitable probes and amplification technique. They can also be chemically synthesized or obtained by enzymatic digestion from existing plasmids or plasmids from the invention.

Furthermore, the polypeptides of the invention can also be chemically synthesized or semi-synthesized according to well-established procedures.

A particular 20-amino acid polypeptide has the following consensus sequence:

$$(Y)_{13}\text{-X1-}(Y)_3\text{-C-}(Y)_1\text{-X2}$$

As above explained, X1 and X2 are selected to impact on the immunosuppressive properties of a tested i.e., original viral immunosuppressive protein in which the polypeptide is inserted, including by replacement of X1 and X2 residues in an homologous sequence as defined above, wherein Y represents variable amino acid residues, 3 and 1 represent the number of variable amino acid Y residues respectively between X1 and C and between C and X2, and 13 represents the number of amino acid residues in the N-terminal part of the polypeptide. The Y residues can independently be identical or different in the sequence.

The identification of invariant amino acid residues in various protein sequences allows defining a particular sequence: $(Y)_2$-N-$(Y)_3$-L-$(Y)_2$-L-$(Y)_3$-X1-$(Y)_3$-C-$(Y)_1$-X2, *i.e.* from the N-terminal-end to C-terminal end: two variable amino acid residues, an asparagine (N), three variable amino acid residues, a leucine (L), two variable amino acid residues, a leucine (L), three variable amino acid residues, the X1 residue, three variable amino acid residues, a cysteine (C), one variable amino acid residue and the X2 residue.

Optionally the above consensus sequence can be noted as follows:

$Y_{13}Y_{14}NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2$

wherein X_1 and X_2 are respectively identical to X1 and X2, and Y_1 to Y_{14} represent any aminoacid. As intended herein amino acids Y_1 to Y_{14} can be identical or different.

Particular amino acid sequences presenting the capacity to modulate the immunosuppressive properties of a viral immunosuppressive protein in the above disclosed test, can be selected from the group consisting of:

AQNRRGLDLLFWE**Q**GGLCK**A** (SEQ ID NO: 33)
LQNCRCLDLLFLS**Q**GGLCA**A** (SEQ ID NO: 34)
LQNRRGLDMLTAA**Q**GGLCL**A** (SEQ ID NO: 35)
LQNRRGLDLLTAE**Q**GGICL**A** (SEQ ID NO: 36)
LQNRRGLDILFLQ**E**GGLCA**A** (SEQ ID NO: 37)
LQNRRGLDLLFLK**E**GGLCA**A** (SEQ ID NO: 38)
LQNRRGLDLLFLK**E**GGLCV**A** (SEQ ID NO: 39), wherein these immunosuppression-modulatory sequences provide immunosuppressive properties to a protein comprising them, or
LQNRRALDLLTAE**R**GGTCL**F** (SEQ ID NO: 40)
LQNWRALDLLTAK**R**GGTCL**F** (SEQ ID NO: 41)
LQNWRALDLLIAK**R**GGTCV**F** (SEQ ID NO: 42)
LQNRRGLDLLTAE**R**GGTCL**F** (SEQ ID NO: 43)
LQNRRALDLLTAE**R**GGICL**F** (SEQ ID NO: 44)
LQNRRGLDLLTAE**K**GGLCI**F** (SEQ ID NO: 45)
MQNRRALDLLTAD**K**GGTCM**F** (SEQ ID NO: 46)
AQNRQALDLLMAE**K**GRTCL**F** (SEQ ID NO: 47)
AQNRRGLDLLFWE**R**GGLCK**F** (SEQ ID NO: 48)
LQNCRCLDLLFLS**R**GGLCA**F** (SEQ ID NO: 49)
LQNRRGLDMLTAA**R**GGLCL**F** (SEQ ID NO: 50)
LQNRRGLDLLTAE**R**GGICL**F** (SEQ ID NO: 51)
LQNRRGLDILFLQ**R**GGLCA**F** (SEQ ID NO: 52)
LQNRRGLDLLFLK**R**GGLCA**F** (SEQ ID NO: 53)
LQNRRGLDLLFLK**R**GGLCV**F** (SEQ ID NO: 54), these immunosuppression-modulatory sequences providing low or no immunosuppressive properties to a protein comprising them.

According to a preferred embodiment, particular amino acid sequences presenting the capacity to modulate the immunosuppressive properties of a viral immunosuppressive protein in the above disclosed test, can be selected from the group consisting of:

AQNRRGLDLLFWE**Q**GGLCK**A** (SEQ ID NO: 33)
LQNCRCLDLLFLS**Q**GGLCA**A** (SEQ ID NO: 34)
LQNRRGLDMLTAA**Q**GGLCL**A** (SEQ ID NO: 35)
LQNRRGLDLLTAE**Q**GGICL**A** (SEQ ID NO: 36)
LQNRRGLDILFLQ**E**GGLCA**A** (SEQ ID NO: 37)
LQNRRGLDLLFLK**E**GGLCA**A** (SEQ ID NO: 38)
LQNRRGLDLLFLK**E**GGLCV**A** (SEQ ID NO: 39), wherein these immunosuppression-modulatory sequences provide immunosuppressive properties to a protein comprising them, or
LQNRRGLDLLTAE**K**GGLCI**F** (SEQ ID NO: 45)
MQNRRALDLLTAD**K**GGTCM**F** (SEQ ID NO: 46)
AQNRQALDLLMAE**K**GRTCL**F** (SEQ ID NO: 47), wherein these immunosuppression-modulatory sequences provide low immunosuppressive properties to a protein comprising them, or
LQNRRALDLLTAE**R**GGTCL**F** (SEQ ID NO: 40)
LQNWRALDLLTAK**R**GGTCL**F** (SEQ ID NO: 41)
LQNWRALDLLIAK**R**GGTCV**F** (SEQ ID NO: 42)
LQNRRGLDLLTAE**R**GGTCL**F** (SEQ ID NO: 43)
LQNRRALDLLTAE**R**GGICL**F** (SEQ ID NO: 44)
AQNRRGLDLLFWE**R**GGLCK**F** (SEQ ID NO: 48)
LQNCRCLDLLFLS**R**GGLCA**F** (SEQ ID NO: 49)
LQNRRGLDMLTAA**R**GGLCL**F** (SEQ ID NO: 50)
LQNRRGLDLLTAE**R**GGICL**F** (SEQ ID NO: 51)
LQNRRGLDILFLQ**R**GGLCA**F** (SEQ ID NO: 52)
LQNRRGLDLLFLK**R**GGLCA**F** (SEQ ID NO: 53)
LQNRRGLDLLFLK**R**GGLCV**F** (SEQ ID NO: 54), these immunosuppression-modulatory sequences providing essentially no immunosuppressive properties to a protein comprising them.

The present invention also relates to the use of a first mutation of a first amino acid and optionally of a second mutation of a second amino acid in a wild type viral envelope (ENV) protein essentially comprising the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X_2$$

wherein the first amino acid to be mutated is X_1 and the second amino acid to be mutated is X_2, and Y_1 to Y_{12} represent any amino acid,

for manufacturing a mutated ENV protein having a modified immunosuppressive activity with respect to said wild type ENV protein.

The expression "wild type viral envelope protein" relates to an envelope protein in which amino acid X_1 has not been mutated. In particular, it is not excluded that other mutations or modifications have been brought to the envelope protein.

The expression "essentially comprising" means that at least two of the four constant amino acids of the above sequence (represented in bold) are present in said wild type viral envelope. Two amino acids are sufficient to unambiguously determine the position of X_1 and X_2 in the envelope sequence. Advantageously, the above sequence is usually localized in the transmembrane (TM) subunit, more particularly in the ectodomain of the TM subunit.

As intended herein, amino acids Y_1 to Y_{12}, independently of each other are different or identical.

As intended herein the mutated ENV protein essentially carries the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X'_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X'_2$$

wherein X'_1 corresponds to the mutated X_1 and X'_2 corresponds to the mutated X_2.

The expression "modified immunosuppressive activity" means that the mutated ENV protein has either increased or decreased immunosuppressive activity with respect to the corresponding wild-type ENV protein. In particular, the mutated ENV protein can be essentially deprived of any residual immunosuppressive activity. In another instance, the mutated ENV protein can have immunosuppressive activity whereas the corresponding wild-type ENV protein is essentially deprived of immunosuppressive activity. The immunosuppressive activity can be

measured as described above and in the Examples, for instance by using the immunosuppressive index method.

Advantageously, mutated ENV proteins having a modified immunosuppressive activity have many applications, in particular therapeutic applications, which will be discussed hereafter.

In a preferred embodiment of the above-defined use, structures responsible for the antigenicity of the mutated ENV protein are essentially preserved.

As intended herein, the expression "structures responsible for antigenicity" relates to structures of the protein which are liable to interact with components of the immune system such as antibodies or membrane receptors of immune cells, in particular T cells.

According to the invention, at least one or more of these structures presents the same conformation in the mutated ENV protein with respect to the corresponding wild type ENV protein. Advantageously, this means that an immune reaction elicited against a mutated ENV protein will also be directed against the corresponding wild type ENV protein.

According to a preferred embodiment, the invention also relate to the above -defined use of a first mutation of a first amino acid and optionally of a second mutation of a second amino acid in a wild type viral envelope (ENV) protein essentially comprising the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X_2$$

wherein the first amino acid to be mutated is X_1 and the second amino acid to be mutated is X_2, and Y_1 to Y_{12} represent any amino acid,

for manufacturing a mutated ENV protein having a decreased immunosuppressive activity with respect to said wild type ENV protein.

In a most preferred embodiment, the decrease in immunosuppressive activity is such that almost no residual activity is seen in the mutated ENV protein.

According to a preferred embodiment, the invention also relates to the above-defined use of a first mutation of a first amino acid and a second

mutation of a second amino acid in a wild type viral envelope (ENV) protein essentially comprising the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X_2$$

wherein the first amino acid to be mutated is X_1 and the second amino acid to be mutated is X_2, and Y_1 to Y_{12} represent any amino acid,

for manufacturing a mutated ENV protein having a decreased immunosuppressive activity with respect to said wild type ENV protein.

The mutation of X_1 alone is sufficient to modify the immunosuppressive activity of the mutated ENV protein with respect to the corresponding wild type ENV. However, it is advantageous that X_2 be also mutated because it ensures that the structure of the mutated ENV protein is essentially conserved with respect to the corresponding wild type ENV protein.

In a preferred embodiment of the above-defined use, the mutation is a substitution.

In another preferred embodiment of the above-defined use, X_1 is substituted by R or H.

In another preferred embodiment of the above-defined use, X_2 is substituted by F, M, Y or W.

In a further preferred embodiment of the above-defined use, X_1 is E, K, or Q and is substituted by R or H.

In a preferred embodiment of the above defined use, the ENV protein is HERV-H ENV and X_1 is K.

In a further preferred embodiment of the above-defined use, X_2 is A, V, L, I, or K and is substituted by F, M, Y, or W.

In a particularly preferred embodiment of the above defined use, the ENV protein is a HERV ENV, in particular selected from:

HERV-FRD ENV (SEQ ID NO: 82), wherein X_1 is Q427 and X_2 is A433, or

HERV-T ENV (SEQ ID NO: 84), wherein X_1 is Q516 and X_2 is A522, or

HERV-R ENV (SEQ ID NO: 86), wherein X_1 is E561 and X_2 is K567, or

HERV-V ENV (SEQ ID NO: 88), wherein X_1 is Q381 and X_2 is V387, or

HERV-R(b) ENV (SEQ ID NO: 90), wherein X_1 is E391 and X_2 is L397.

HERV relates to Human Endogenous RetroVirus, which have been described previously. HERV ENV proteins have been found to be expressed in cancer cells. The HERV ENV listed above present an immunosuppressive activity and can help cancer cells carrying them escape immune response. These HERV are well known to the man skilled in the art and are in particular discussed in Benit et al. J. Virol. 2001, 75:11709-11719. As will be apparent later HERV ENV proteins having decreased immunosuppressive activity are advantageous to prepare vaccines inhibiting the activity of wild type ENV proteins expressed by cancer cells.

In an advantageous embodiment of the above-defined use, the ENV protein is HERV-FRD ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 120,

SEQ ID NO: 122.

SEQ ID NO: 120 carries the mutation Q427R.

SEQ ID NO: 122 carries the mutation Q427R + A433F.

The mutated HERV-FRD ENV represented by SEQ ID NO: 120 or 122 presents a decreased immunosuppressive activity with respect to the corresponding wild-type HERV-FRD ENV.

In another advantageous embodiment of the above-defined use, the ENV protein is HERV-V ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 124,

SEQ ID NO: 126.

SEQ ID NO: 124 carries the mutation Q381R.

SEQ ID NO: 126 carries the mutation Q381R + V387F.

The mutated HERV-V ENV represented by SEQ ID NO: 124 or 126 presents a decreased immunosuppressive activity with respect to the corresponding wild-type HERV-V ENV.

In another advantageous embodiment of the above-defined use, the ENV protein is HERV-T ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 128,

SEQ ID NO: 130.

SEQ ID NO: 128 carries the mutation Q516R.

SEQ ID NO: 130 carries the mutation Q516R + A522F.

The mutated HERV-T ENV represented by SEQ ID NO: 128 or 130 presents a decreased immunosuppressive activity with respect to the corresponding wild-type HERV-T ENV.

In another advantageous embodiment of the above-defined use, the ENV protein is HERV-R ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 146,

SEQ ID NO: 148.

SEQ ID NO: 146 carries the mutation E561R.

SEQ ID NO: 148 carries the mutation E561R + K567F.

The mutated HERV-R ENV represented by SEQ ID NO: 128 or 130 presents a decreased immunosuppressive activity with respect to the corresponding wild-type HERV-R ENV.

In another particularly preferred embodiment of the above defined use, the ENV protein is selected from:

HTLV-1 ENV (SEQ ID NO: 92), wherein X_1 is Q389 and X_2 is A395, or

HTLV-2 ENV (SEQ ID NO: 94) wherein X_1 is Q385 and X_2 is A391, or

FeLV ENV (SEQ ID NO: 96), wherein X_1 is E527 and X_2 is A533, or

PERV ENV (SEQ ID NO: 98), wherein X_1 is E545 and X_2 is A551, or

STLV-1 ENV (SEQ ID NO: 100), wherein X_1 is Q389 and X_2 is A395, or

MoMLV ENV (SEQ ID NO: 70), wherein X_1 is E551 and X_2 is A557, or

MPMV ENV (SEQ ID NO: 72), wherein X_1 is Q471 and X_2 is A477, or

FV ENV (SEQ ID NO: 102), wherein X_1 is E561 and X_2 is A567.

HTLV-1 and 2 relate to Human T-cell Leukemia Virus type 1 and 2.

FeLV relates to Feline Leukemia Virus.

PERV relates to Porcine Endogenous RetroVirus.

STLV-1 relates to Simina T-cell Leukemia Virus type 1.

MoMLV relates to Moloney Murine Leukemia Virus.

MPMV relates to Mason-Pfizer Monkey Virus.

FV relates to the mouse Friend Virus.

These virus are well known to the man skilled in the art and are notably described in Benit et al. J. Virol. 2001, 75:11709-11719. The propagation of these viruses is notably favoured by the presence of an immunosuppressive ENV protein, which helps viruses escape the immune response. As will be apparent later viral ENV proteins having decreased immunosuppressive activity are advantageous to inhibit the activity of wild type ENV proteins expressed by viruses.

In an advantageous embodiment of the above-defined use, the ENV protein is FeLV ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 104,

SEQ ID NO: 106.

SEQ ID NO: 104 carries the mutation E527R.

SEQ ID NO: 106 carries the mutation E527R + A533F.

The mutated FeLV ENV represented by SEQ ID NO: 104 or 106 presents a decreased immunosuppressive activity with respect to the corresponding wild-type FeLV ENV.

In another advantageous embodiment of the above-defined use, the ENV protein is HTLV-1 ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 108,

SEQ ID NO: 110.

SEQ ID NO: 108 carries the mutation Q389R.

SEQ ID NO: 110 carries the mutation Q389R + A395F.

The mutated HTLV-1 ENV represented by SEQ ID NO: 108 or 110 presents a decreased immunosuppressive activity with respect to the corresponding wild-type HTLV-1 ENV.

In another advantageous embodiment of the above-defined use, the ENV protein is HTLV-2 ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 112,

SEQ ID NO: 114.

SEQ ID NO: 112 carries the mutation Q385R.

SEQ ID NO: 114 carries the mutation Q385R + A391F.

The mutated HTLV-2 ENV represented by SEQ ID NO: 112 or 114 presents a decreased immunosuppressive activity with respect to the corresponding wild-type HTLV-2 ENV.

In another advantageous embodiment of the above-defined use, the ENV protein is PERV ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 150,

SEQ ID NO: 152.

SEQ ID NO: 150 carries the mutation E545R.

SEQ ID NO: 152 carries the mutation E545R + A551F.

The mutated PERV ENV represented by SEQ ID NO: 150 or 152 presents a decreased immunosuppressive activity with respect to the corresponding wild-type PERV.

The present invention also relates to the above use of a first mutation of a first amino acid and optionally of a second mutation of a second amino acid in a wild type viral envelope (ENV) protein essentially comprising the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X_2$$

wherein the first amino acid to be mutated is X_1 and the second amino acid to be mutated is X_2, and Y_1 to Y_{12} represent any amino acid,

for manufacturing a mutated ENV protein having an increased immunosuppressive activity with respect to said wild type ENV protein.

The mutation of X_1 alone is sufficient to increase the immunosuppressive activity of the mutated ENV protein with respect to the corresponding wild type ENV. However, it is advantageous that X_2 be also mutated because it ensures that the structure of the mutated ENV protein is essentially conserved with respect to the corresponding wild type ENV protein.

Advantageously, it is possible according to the invention to obtain a mutated ENV protein with immunosuppressive activity whereas the corresponding wild-type ENV protein is essentially deprived of such an activity. Such mutated ENV proteins with increased immunosuppressive activity are useful to inhibit the immune system, for instance in graft rejections or autoimmune diseases.

In a preferred embodiment of the above mentioned use for manufacturing a mutated ENV protein having an increased immunosuppressive activity, the mutation is a substitution.

In another preferred embodiment of the above mentioned use for manufacturing a mutated ENV protein having an increased immunosuppressive activity, X_1 is substituted by E, ***K*** or Q and X_2 is substituted by A.

In another preferred embodiment of the above mentioned use for manufacturing a mutated ENV protein having an increased immunosuppressive activity, the ENV protein is HERV-W ENV, such as represented by SEQ ID NO: 74, and the sequence of the mutated HERV-W ENV is preferably selected from

SEQ ID NO: 116,

SEQ ID NO: 118.

SEQ ID NO: 116 carries the mutation R393E/Q.

SEQ ID NO: 118 carries the mutation R393E/Q + F399A.

The mutated HERV-W ENV represented by SEQ ID NO: 116 or 118 presents an increased immunosuppressive activity with respect to the corresponding wild-type HERV-W which is essentially deprived of such an activity.

The present invention also provides a polypeptide derived from a determined antigenic and immunosuppressive protein, said polypeptide comprising an amino acid sequence (so-called "immunosuppression-modulatory sequence") represented by X1-$(Y)_3$-C-$(Y)_1$-X2 wherein in said polypeptide Y represents variable amino acid residues, 3 and 1 represent the number of variable amino acid Y residues, respectively between X1 and C and between C and X2, and X1 and X2 are chosen to confer to said polypeptide, altered immunosuppressive properties with respect to the immunosuppressive properties of said determined protein.

The term "derived" as used herein indicates that the amino acid sequence, and especially the immunosuppression-modulatory sequence, in the polypeptide, is modified with respect to the sequence of the determined protein. Said "determined" protein is hence the original protein whose modification is required to modulate its immunosuppressive properties. A polypeptide according to the invention can be derived, biologically or chemically, from a determined protein by substitution, deletion, addition, recombination or insertion of one or several amino acid residues or sequences, provided the consensus sequence of the invention is such that X1 and X2 are selected to modulate the immunosuppressive properties of the starting determined protein, and therefore provided X1 and/or X2 are mutated by substitution with respect to their original corresponding residues in said determined immunosuppressive protein. In case of sequence insertion, the immunosuppression-modulatory sequence can replace a homologous sequence present in the determined protein, or can replace a sequence known or likely to be involved in the same function of modulation of the immunosuppressive properties as the inserted

sequence, or can be inserted within the starting amino acid sequence. In all cases, the open reading frame of the amino acid sequence following the site of insertion (at the C-terminal part of the polypeptide) is conserved.

Obviously, the invention can be carried out with or without actually starting from said determined protein to derive the polypeptide of the invention. Hence, said determined protein is a reference for the design ofthe derived polypeptide rather than a necessary starting material from a biological or chemical point of view.

In a particular embodiment of the invention, the derived polypeptide has lower immunosuppressive properties than said determined starting polypeptide and advantageously has substantially lost said immunosuppressive properties, e.g. has no immunosuppressive properties.

The expressions "polypeptide" and "protein" throughout the present invention define molecules, whatever their length (except otherwise stated in the present description) comprising an amino acid sequence.

In a particular embodiment, the polypeptide or protein is multimeric, especially trimeric.

"Determined" as used herein refers to a starting protein from which the polypeptide of the invention is designed, i.e., derived to have modulated immunosuppressive properties. This protein can be a wild-type protein (for example isolated from a viral, especially retroviral, strain) or a protein previously modified (for example expressed from a vector in a host). Such protein is chosen among those having antigenic and immunosuppressive properties.

The determined protein has immunosuppressive properties has defined above: when this determined protein is expressed in tumour cells normally rejected by an engrafted host, it allows these tumour cells to proliferate and to escape immune rejection.

Second, it is an antigenic protein, *i.e.* it is capable of being recognized by antibodies formed in a host to whom it is administered. Advantageously it is capable of inducing an immune response, in the host

to whom it is administered in appropriate known conditions, and accordingly said antigenic protein is advantageously an immunogenic protein. This involves that said host produces antibodies against epitopes of the protein.

In view of these desired property of the protein to be antigenic, especially immunogenic, and in view of the required property for the derived polypeptide to substantially retain these antigenic, especially immunogenic properties, the determined protein used to derive the polypeptide of the invention encompasses native or naturally occurring proteins or antigenic, especially immunogenic, fragments thereof, provided said fragments further have immunosuppressive properties. It also encompasses modified proteins with respect to the native or naturally occurring protein, provided the modified proteins have antigenic and immunosuppressive properties.

The determined protein used as reference to derive the polypeptide of the invention can be a viral protein, *i.e.* coded by nucleic acids of infectious agents like viruses, or a protein coded by nucleic acid of viral origin, such as endogenous retroviruses, especially HERV. A particular protein is a protein originating from a subclass of viruses: retroviruses. In a particular embodiment, the determined protein is an envelope protein, *i.e.,* the expression product of the env gene.

"Nucleic acid" as used herein refers to viral nucleic acids in DNA or RNA forms, including cellular nucleic acids such as genomic DNA, complementary DNA, coding sequences. All the nucleic acid quoted in the present application can be single or double-stranded.

The X1 and X2 amino acid residues of the X1-$(Y)_3$-C-$(Y)_1$-X2 motif are chosen as described above.

The above defined polypeptide of the invention derived from an antigenic and immunosuppressive protein and comprising sequence X1-$(Y)_3$-C-$(Y)_1$-X2 can be defined as follows:

in a particular embodiment of the invention, X1 is an alkaline amino acid residue and X2 is an aromatic residue or *vice versa*.

In another particular embodiment of the invention, X1 is an alkaline residue or X2 is an aromatic residue or *vice versa*.

The inventors have observed that the modulation effect of X1 and X2 on immunosuppressive properties of proteins is usually lower when only one of X1 or X2 residues is modified in an original immunosuppressive protein.

Therefore, modification of both X1 and X2 is an immunosuppression-modulatory sequence may be regarded as advantageous.

In another particular embodiment of the invention, residues X1 or X2 located in amino acid sequence represented as X1-$(Y)_3$-C-$(Y)_1$-X2 are selected as follows:

where X1 is chosen among R, H and K, X2 is chosen among F, W, Y and H or where X1 is chosen among F, W, Y and H, X2 is chosen among R, H and K.

In a further embodiment of the invention, X1 is R, H or K and X2 is F, or *vice versa*.

In a further embodiment of the invention, X1 is R and X2 is F, W, Y or H.

The inventors have especially identified that a polypeptide, derived from an antigenic and immunosuppressive protein, has altered immunosuppressive properties compared to the immunosuppressive properties of the protein from which is derived when particular interesting X1 and X2 residues are respectively R and F or K and F.

The determined protein can advantageously be a viral protein and particularly a retroviral protein or a protein of viral origin like one of an HERV, having antigenic and immunosuppressive properties.

Known naturally occurring low or non-immunosuppressive envelope proteins of HERV-W, H1, F(c)1 or F(c)2 are not, as such, the object of the present invention.

In a particular embodiment of the present invention, the polypeptide derived from an antigenic protein has altered immunosuppressive properties and especially reduced immunosuppressive properties, while retaining its antigenic properties.

In another particular embodiment, these proteins have, further to antigenic and immunosuppressive properties, infectious and/or fusion properties.

When the determined starting protein further has fusion and infectious properties, such as those identified for viral envelope proteins, one of these or both properties can be retained, but not necessary, in the derived polypeptide.

The evaluation or measurement of fusion and/or infectious properties to determine whether these properties of the original determined protein are maintained in the derived polypeptide of the invention can provide useful indications as to whether the derived polypeptide has substantially retained the structure, especially the antigenic structure, e.g., immunogenic determinants, of the original determined protein.

A protein is said to have fusion properties when cells transfected with nucleic acids encoding said protein are able to form syncytia (multi-nucleated cells) with other cells probably not expressing the same protein. Indeed, it is suspected that a strong expression of a protein with fusion properties blocks the expression of the receptors of said protein involved in the fusion event. Therefore, the capacity of fusion can be defined by the formation of syncytia between cells expressing said protein with fusion properties and cells expressing its receptor. Cells can be transfected having recourse to various known methods such as calcium phosphate precipitation or with liposomes, such as Lipofectamine™.

A protein is said to have infectious properties when pseudotypes coated with this protein are able to infect cells. "Pseudotypes" as used herein refers to viral particles in which an ENV protein from a different strain is incorporated. MLV core particles are currently used.

Pseudotypes are produced in cell lines (such as 293T cells) in which a vector encoding the infectious protein is co-transfected with one or several vector(s) encoding the GAG and POL proteins of another viral strain.

Particular polypeptides having the properties described are derived from viral envelope protein (ENV) and especially retroviral envelope proteins. Such retroviral ENV can be selected from the group of retroviruses consisting of: MoMLV, Friend retrovirus, FeLV, HTLV-1, STLV-1 and MPMV. Other interesting polypeptides are those encoded by nucleic acids of viral origin such as HERV. As far as viruses are concerned, Ebola and Marburg viruses have ENV proteins from which the polypeptides of the invention can be derived.

Said envelope protein can be all or part of the native or naturally occurring protein or from an antigenic, especially immunogenic variant thereof, including a fragment thereof, i.e., an analogue of a naturally occurring viral envelope protein as far as antigenic, especially immunogenic properties, and immunosuppressive properties are concerned.

Within the amino acid sequence of determined proteins described above, inventors have identified particular residues that are involved in the regulation of immunosuppression. Such a sequence, called immunosuppression-modulatory sequence which confers immunosuppressive properties to a protein is the following: E/Q-G-G-L/T/I-C-A/K/L/M/V/I-A, wherein "/" indicates that this sequence position accepts several types of amino acid residues. Thus, proteins comprising an immunosuppression-modulatory sequence selected from the group consisting of

QGGLCK**A** (SEQ ID NO: 17)
QGGLCA**A** (SEQ ID NO: 18)
QGGLCL**A** (SEQ ID NO: 19)
QGGICL**A** (SEQ ID NO: 20)
EGGLCA**A** (SEQ ID NO: 21)
EGGLCV**A** (SEQ ID NO: 22)

are particular determined proteins having immunosuppressive properties, from which the polypeptides of the invention can be derived by modifying the terminal E/Q and or A residues figuring X1 and X2 positions of the consensus sequence of the invention.

As described above, the term "derived" as used herein indicates that the amino acid sequence, and especially the immunosuppression-modulatory sequence, of the polypeptide is modified with respect to the sequence of the determined protein in order to impact on immunosuppressive properties, especially to decrease said properties. These altered immunosuppressive properties can be the consequence of substitution of the X1 and X2 residues according to the amino acid characteristics described above.

These altered immunosuppressive properties can also be the consequence of the insertion of the polypeptide comprising X1-$(Y)_3$-C-$(Y)_1$-X2 sequence wherein X1 and X2 are selected to alter the immunosuppressive properties, in a permissive site of the chosen protein.

"Permissive site" as used herein refers to a site which does not substantially alter the antigenic properties of a protein.

The insertion can replace a homologous sequence or a sequence involved in immunosuppression. The polypeptide of 7 to 20 amino acid residues according to the invention can also be inserted without deletion of amino acid residues from the determined protein.

A polypeptide derived from a determined protein as described above, and having altered immunosuppressive properties comprises a sequence having the following sequence R-G-G-L/T/I-C-A/K/L/M/V/I-F, and particularly a sequence selected from the group consisting of:

RGGLC**K**F (SEQ ID NO: 27)
RGGLCA**F** (SEQ ID NO: 28)
RGGLCL**F** (SEQ ID NO: 29)
RGGICL**F** (SEQ ID NO: 30)
RGGLCV**F** (SEQ ID NO: 31)

The sequences given above have been derived by mutation of said X1 and X2 residues in identified naturally occurring retroviral ENV proteins.

The same strategy can be applied with viruses which express proteins presenting a sequence similar to $X1\text{-}(Y)_3\text{-}C\text{-}(Y)_1\text{-}X2$. In particular, the Y residues can be different amino acid residues from those described above (Benit et al. 2001).

Moreover, the structure, e.g. their 3-dimensional structure of the determined ENV proteins of the present application have been shown to share similar structural features with that of other viruses and especially with other retroviruses, despite amino acid sequence diversity. Thus, a highly conserved organization of the TM structure has been found in proteins of Ebola or Marburg viruses, most probably relevant to a common mechanism for triggering the fusion process and viral entry. Consequently, a same approach can be applied to identify particular sequences, involved in the modulation of the immunosuppression in such viruses.

The present invention also relates to a mutated ENV protein resulting from the mutation of a wild type ENV protein essentially carrying the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X_2$$

wherein amino acid X_1 and optionally amino acid X_2 are mutated, and Y_1 to Y_{12} represent any amino acid, said mutated ENV protein having a modified immunosuppressive activity with respect to the wild type ENV protein,

or a fragment thereof, provided that said fragment carries the mutated amino acid X_1 and optionally X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that optionally its antigenic structure is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an

immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

As intended herein the mutated ENV protein essentially carries the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X'_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X'_2$$

Wherein X'_1 corresponds to the mutated X_1 and X'_2 corresponds to the mutated X_2.

As intended herein fragments of the mutated ENV protein according to the invention are in particular at least 7 amino acids long and comprise the mutated amino acid X_1. Optionally, fragments are at least 7 amino acids long and comprise both X_1 and X_2. Preferred fragments of the mutated ENV protein according to the invention are notably constituted of the TM subunit or of the ectodomain of the TM subunit.

In a preferred embodiment of the invention the above mentioned protein derived from the mutated ENV protein presents at least 80% sequence identity with said mutated ENV protein, in particular at least 90% sequence identity.

In a preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, the structures responsible for the antigenicity of said mutated ENV protein, or fragment thereof, are essentially preserved with respect to the wild type ENV protein.

According to a preferred embodiment, the present invention relates to an above-defined mutated ENV protein resulting from the mutation of a wild type ENV protein essentially comprising the following sequence:

$$\mathbf{N}Y_1Y_2Y_3\mathbf{L}Y_4Y_5\mathbf{L}Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}\mathbf{C}Y_{12}X_2,$$

wherein amino acid X_1 and optionally amino acid X_2 are mutated, and Y_1 to Y_{12} represent any amino acid, said mutated ENV protein having a decreased immunosuppressive activity with respect to the wild type ENV protein,

or a fragment thereof, provided that said fragment carries the mutated amino acid X_1 and optionally X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that optionally its antigenic structure is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

According to a preferred embodiment, the present invention relates to an above-defined mutated ENV protein resulting from the mutation of a wild type ENV protein essentially comprising the following sequence:

N$Y_1Y_2Y_3$**L**Y_4Y_5**L**$Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}$**C**$Y_{12}X_2$,

wherein amino acid X_1 and amino acid X_2 are mutated, and Y_1 to Y_{12} represent any amino acid, said mutated ENV protein having a decreased immunosuppressive activity with respect to the wild type ENV protein,

or a fragment thereof, provided that said fragment carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that optionally its antigenic structure is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

In a preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, the mutation is a substitution.

In another preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, X_1 is substituted by R or H.

In another preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, X_2 is substituted by F, M, Y or W.

In another preferred embodiment of the above-defined mutated ENV protein, or fragment thereof X_1 is E, K, or Q and is substituted by R or H.

In a preferred embodiment, the above defined mutated ENV protein, or fragment thereof, is HERV-H ENV wherein X_1 is K.

In another preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, X_2 is A, V, L, I, or K and is substituted by F, M, Y, or W.

In a particularly preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is a HERV ENV, in particular selected from:

HERV-FRD ENV (SEQ ID NO: 82), wherein X_1 is Q427 and X_2 is A433, or
HERV-T ENV (SEQ ID NO: 84), wherein X_1 is Q516 and X_2 is A522, or
HERV-R ENV (SEQ ID NO: 86), wherein X_1 is E561 and X_2 is K567, or
HERV-V ENV (SEQ ID NO: 88), wherein X_1 is Q381 and X_2 is V387, or
HERV-R(b) ENV (SEQ ID NO: 90), wherein X_1 is E391 and X_2 is L397.

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is HERV-FRD ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 120

SEQ ID NO: 122

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is HERV-V ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 124

SEQ ID NO: 126

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is HERV-T ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 128

SEQ ID NO: 130

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is HERV-R ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 146,

SEQ ID NO: 148.

In a particularly preferred embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is selected from:

HTLV-1 ENV (SEQ ID NO: 92), wherein X_1 is Q389 and X_2 is A395, or

HTLV-2 ENV (SEQ ID NO: 94) wherein X_1 is Q385 and X_2 is A391, or

FeLV ENV (SEQ ID NO: 96), wherein X_1 is E527 and X_2 is A533, or

PERV ENV (SEQ ID NO: 98), wherein X_1 is E545 and X_2 is A551, or

STLV-1 ENV (SEQ ID NO: 100), wherein X_1 is Q389 and X_2 is A395, or

MoMLV ENV (SEQ ID NO: 70), wherein X_1 is E551 and X_2 is A557, or

MPMV ENV (SEQ ID NO: 72), wherein X_1 is Q471 and X_2 is A477, or

FV ENV (SEQ ID NO: 102), wherein X_1 is E561 and X_2 is A567.

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is FeLV ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 104

SEQ ID NO: 106

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is HTLV-1 ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 108

SEQ ID NO: 110

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is HTLV-2 ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 112

SEQ ID NO: 114

In an advantageous embodiment of the above-defined mutated ENV protein, or fragment thereof, the ENV protein is PERV ENV and the sequence of the mutated ENV protein is selected from:

SEQ ID NO: 150,

SEQ ID NO: 152.

According to a preferred embodiment, the present invention relates a mutated ENV protein as defined above resulting from the mutation of a wild type ENV protein essentially comprising the following sequence:

N$Y_1Y_2Y_3$**L**Y_4Y_5**L**$Y_6Y_7Y_8X_1Y_9Y_{10}Y_{11}$**C**$Y_{12}X_2$ according to claim 27 or 28,

wherein amino acid X_1 and optionally amino acid X_2 are mutated, and Y_1 to Y_{12} represent any amino acid, said mutated ENV protein having an increased immunosuppressive activity with respect to the wild type ENV protein,

or a fragment thereof, provided that said fragment carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that optionally its antigenic structure is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

In a preferred embodiment of the above-defined mutated ENV protein having increased immunosuppressive activity, or fragment thereof, the mutation is a substitution.

In a preferred embodiment of the above-defined mutated ENV protein having increased immunosuppressive activity, or fragment thereof, X_1 is substituted by E, K, or Q and X_2 is substituted by A.

In a preferred embodiment of the above-defined mutated ENV protein having increased immunosuppressive activity, or fragment thereof, the ENV protein is HERV-W ENV, such as represented by SEQ ID NO: 74, and the sequence of the mutated HERV-W ENV is selected from:

SEQ ID NO: 116

SEQ ID NO: 118

The present invention also relates to a protein, characterized in that it comprises at least one polypeptide as defined above, or at least one mutated ENV protein, or a fragment thereof, as defined above, provided that when said polypeptide originates from a wild type ENV protein then said protein comprising said polypeptide is different from said wild type ENV protein.

The present invention also relates to nucleic acids, and especially polynucleotides, encoding polypeptides of the invention. In a particular embodiment, these nucleic acids are inserted in a vector. The recombinant vector can be a plasmid, a phage for bacterium introduction or a YAC able to transform yeast, or any expression vector.

In addition, the recombinant vector comprises transcription regulation regions (including promoter) allowing either inducible expression or conditional expression of the nucleic acid under control or if appropriate, constitutive expression. A tissue specific transcription region can also be used. Moreover, the recombinant vector comprises an origin of replication and/or marker genes.

In a particular embodiment of the invention, the vector comprises also nucleic acid encoding viral GAG and/or POL proteins or

sufficient fragments thereof to express functional viral proteins. Optionally, the vector can comprises nucleic acids encoding viral accessory proteins, like NEF, TAT or fragments thereof.

Alternatively, GAG and POL coding sequences can be inserted in separate vectors, including in vector(s) different from the ENV expressing vector.

In a particular embodiment of the invention, a provirus genome is modified with a nucleic acid encoding a polypeptide of the invention having antigenic properties but altered immunosuppressive properties with respect to a determined protein or a nucleic acid encoding a polypeptide of the invention having infectious, fusion and antigenic properties, but altered immunosuppressive properties with respect to a determined protein.

The present invention also relates to cells comprising nucleic acids encoding polypeptides of the invention.

In a particular embodiment, a cell is transformed with a polynucleotide of the invention, in a way that the polynucleotide is integrated in the cell genome either by a recombination with the homologous cellular sequence or by insertion in the cellular genome. The cell can also be transfected with a vector of the invention, by methods well known to the man skilled in the art. The transfection or infection can occurred *ex vivo*, *i.e.* in an artificial environment outside the living organism.

In another embodiment, a vector containing a nucleic acid encoding a polypeptide according to the invention cells is complemented with the introduction of other nucleic acids, contained in additional vectors, especially encoding viral GAG protein and/or POL protein.

These cell lines are useful to the production of recombinant viral particles. In a particular embodiment, the GAG and POL polypeptides originate from the same virus strain as the ENV protein. In another embodiment, the GAG and POL polypeptides originate from a different strain from the ENV protein.

The recombinant viral particles produced comprise a nucleic acid encoding a functional POL protein, a nucleic acid encoding a functional GAG protein and a nucleic acid encoding the polypeptide of the invention.

Moreover, the ENV protein can be chosen among viral amphotropic ENV protein according to the host, *i.e.* able to infect cells of a species from which the virus is not originated, or viral ecotropic ENV proteins according to the host, *i.e.* able to replicate only in the cells of the species from which the virus is originated.

To ensure that the recombinant viral particles be infectious and replicative, the vector comprises various nucleic sequences chosen among transcription, expression and encapsidation signals, such as LTRs, cPPT, PPT3', CTS, SA, SD, psi sequence and RRE. However, such elements can be deleted to produce non-replicative viral particles. Moreover, the proviral genome comprises nucleic acids encoding accessory proteins.

Optionally the particles can be prepared to express additional compounds useful for medical application in a host.

The present invention also relates to a nucleic acid coding for a polypeptide as defined above, for a mutated ENV protein according as defined above or for a protein as defined above.

In a preferred embodiment the above-defined nucleic acid is characterized in that it is represented by a sequence selected from the list comprising:

SEQ ID NO: 103,
SEQ ID NO: 105,
SEQ ID NO: 107,
SEQ ID NO: 109,
SEQ ID NO: 111,
SEQ ID NO: 113,
SEQ ID NO: 115,
SEQ ID NO: 117.

SEQ ID NO: 119,
SEQ ID NO: 121,
SEQ ID NO: 123,
SEQ ID NO: 125,
SEQ ID NO: 127,
SEQ ID NO: 129,
SEQ ID NO: 145,
SEQ ID NO: 147,
SEQ ID NO: 149, and
SEQ ID NO: 151.

The above mentioned SEQ ID NO: 103 to 129 and SEQ ID NO: 147 to 151 (odd numbers) respectively encode SEQ ID NO: 104 to 130 and SEQ ID NO: 146 to 152 (even numbers).

The present invention also relates to an eukaryotic or prokaryotic expression vector, characterized in that it comprises a nucleic acid as defined above as well as the elements necessary for the expression of said nucleic acid.

In a preferred embodiment, the above-defined eukaryotic or prokaryotic expression vector is a viral vector, in particular a pox vector, such as a fowlpox , a canarypox, or a MVA (modified vaccinia virus Ankara) vector, an adenoviral vector, a measles vector, or a CMV (cytomegalovirus) vector.

In a further preferred embodiment, the above-defined eukaryotic or prokaryotic expression vector is a viral vector, in particular a canarypox vector, comprising a nucleic acid sequence coding for an as above defined mutated ENV protein, or a fragment thereof, in particular a mutated FeLV ENV, such as represented by SEQ ID NO: 103 or SEQ ID NO: 105, as well as optionally a nucleic acid coding for a GAG protein originating from the same virus as said mutated ENV.

The present invention also relates to a recombinant cell, characterized in that it comprises a nucleic acid as defined above, or an eukaryotic or prokaryotic expression vector as defined above.

The present invention also relates to a composition comprising a polypeptide of the invention having altered immunosuppressive properties with respect to a determined protein and particularly a polypeptide substantially retaining antigenic properties, especially immunogenic properties of the protein from which they derive.

A particular composition of the invention has lower immunosuppressive properties with respect to the starting determined protein, or even has substantially no immunosuppressive properties.

Other compositions comprise polynucleotides or vectors comprising nucleic acid encoding polypeptides of the invention. In this case, tissue specific promoters can be chosen depending upon the organ in which the composition is administered, for example injected and depending upon the expression intensity required.

Other compositions of the invention comprise recombinant viral particles or viruses harbouring the polypeptides of the invention and optionally expressing further compounds having a medical interest in a host.

The polypeptides and compositions of the invention are useful for the design of active principle for drugs and have accordingly interesting properties for the prophylaxis and or treatment of infections especially viral infections or for the treatment of detrimental consequences, especially malignant states, including tumors, resulting from the viral infection or also for the prophylaxis and/or for the treatment of detrimental consequences, in particular malignant states, including tumors associated with the expression of endogenous viruses, especially HERV, which are normally silent in a host. The expression "treatment" encompasses the curative effect achieved with the polypeptides and compositions of the invention and also the

alleviation of the symptoms observed in a patient or the improvement of the patient's condition.

In a particular embodiment, the composition of the invention further comprises additional active compounds useful for the prophylaxis or the treatment of infections, especially viral infections, in particular retroviral infections, including cytokines or useful for the treatment of consequences resulting from the expression of normally silent ERV.

When used for administration either for systemic or local administration, especially by injection, the composition further comprises a pharmaceutically suitable excipient or carrier and/or vehicle.

Several types of compositions can be used to elicit an immune response against an antigenic polypeptide of the invention.

First, a composition comprising a nucleic acid is administered to a host, for instance injected (known as DNA vaccination) and said nucleic acid expresses *in vivo* a polypeptide according to the invention. DNA vaccines usually consist of plasmid vectors comprising eukaryotic promoter, cloning site, a polyadenylation sequence, a selectable marker and a bacterial origin of replication. All these elements are well known to the man skilled in the art. The delivery of naked DNA has shown to be poorly efficient, and some carriers are needed to improve the delivery of DNA into cells. Two types of carriers have been developed: viral carriers (adenoviruses, lentiviruses) or non-viral carriers such as polymers (and especially cationic polymers), encapsulated-DNA (liposomes) or DNA linked to gold microparticles.

Another type of composition comprises a polypeptide of the invention having altered immunosuppressive properties with respect to a determined protein and having antigenic properties. Such a composition may be immunogenic, *i.e.* it is capable of elicit an immune response in a host in which it is administered. However, since proteins are sometimes non-immunogenic or poorly immunogenic, an adjuvant can be administered with the polypeptide, to elicit or improve the immune response. An adjuvant

is defined as any substance that enhances the immunogenicity of an antigen mixed with said adjuvant. Some adjuvants convert soluble antigens into small particles, such as aluminium hydroxide gel, oil in water emulsion or immune stimulatory complexes (ISCOMs). Another class of adjuvants comprises sterile constituents of bacteria such as cell wall or polysaccharides, Freund adjuvant.

Therefore, a composition comprising a polypeptide having antigenic properties but altered immunosuppressive properties with respect to a determined protein is interesting in the elicitation of an immune response in a host in which it is administered and in the production of a humoral and/or cell-mediated immune response.

Indeed, the administration, e.g., the injection, of a polypeptide having non-immunosuppressive properties provides a more efficient immune reaction than the administration of the determined protein (having immunosuppressive properties), because the immune system of the host is fully functional.

In a particular embodiment, a polypeptide according to the invention has antigenic, fusion and infectious properties but has altered immunosuppressive properties with respect to a determined immunosuppressive protein.

Altered immunosuppressive properties according to the invention advantageously correspond to decreased immunosuppressive properties with respect to the original starting protein.

Viral particles coated with a polypeptide having said properties described above can be constructed in recombinant cell lines transfected with gag-pol vectors and vector comprising a nucleic acid encoding said polypeptide.

Optionally, these viral particles also express other compounds of therapeutic or prophylactic interest.

Interestingly, such viral particles are able to infect and to fuse with the cells of a host, and incorporate a non-immunosuppressive

envelope protein. A composition comprising such viral particles elicits an efficient immune reaction, better than viral particle incorporating the determined protein having immunosuppressive properties. Indeed, the envelope protein is not able to immunosuppress its host, resulting in an optimal immune reaction. Another consequence is that viral particles that would have the capacity to replicate, due to recombination events which do not involve the ENV gene, would have their propagation in the host limited, since recombinant viral particle cannot evade the immune response.

A composition comprising viral particles coated with an antigenic envelope protein with fusion and infectious properties appears to be an efficient and safe vaccine.

Interestingly, such viral particles can be either replicative (functional) or non-replicative. This can have consequences on the time of residence of the particles once administered in the host and on the quality of the immune response.

All compositions quoted above can be injected in a host via different routes: subcutaneous (s.c.), intradermal (i.d.), intramuscular (i.m.) or intravenous (i.v.) injection, oral administration and intranasal administration or inhalation.

The present invention also relates to a pharmaceutical or a vaccine composition comprising as active substance:

at least one polypeptide as defined above, or

at least one mutated ENV protein, or fragments thereof, as defined above, or

at least one nucleic acid as defined above, or

at least one prokaryotic or eukaryotic expression vector as defined above, or

at least one recombinant cell as defined above,

in association with a pharmaceutically acceptable carrier.

As will be described hereafter these pharmaceutical compositions are particularly useful for treating cancers, immune disorders or viral diseases.

The present invention also relates to the use of at least one protein comprising or constituted of a mutated ENV protein, or fragments thereof, having decreased immunosuppressive activity as defined above, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of viral diseases, such as HTLV or FeLV infections.

The administration to an individual of mutated ENV protein having decreased immunosuppressive activity is liable to protect said individual from infection by the corresponding virus. Indeed, the immune response elicited against the mutated ENV protein is also directed against the corresponding wild type ENV protein. As demonstrated herein, this immune response effectively blocks the immunosuppressive activity of the wild type ENV protein and prevents the immune escape of the virus.

Furthermore, the mutated ENV protein is also liable to act as a molecular decoy which competes with the viral wild-type ENV for binding to its natural receptor, thus inhibiting the activity of said wild-type ENV.

The present invention also relates to the use of at least one protein comprising or constituted of a mutated HERV ENV protein, or fragments thereof, as defined above, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancer.

As demonstrated herein, blocking the activity of HERV ENV proteins expressed by cancer cells prevents immune escape of these cells. As such, the immune response effectively elicited against mutated HERV ENV proteins having decreased immunosuppressive activity would also be directed against wild-type HERV ENV expressed by cancer cells and thus prevent them from enabling immune escape of these cancer cells.

Furthermore, the mutated ENV protein is also liable to act as a molecular decoy which competes with the wild-type ENV expressed by cancer cells for binding to its natural receptor, thus inhibiting the activity of said wild-type ENV.

The present invention also relates to the use of at least one protein comprising or constituted of a mutated ENV protein having increased immunosuppressive activity, or fragments thereof, as defined above, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of pathologies requiring an inhibition of the immune system, such as autoimmune diseases, allergies or graft rejections.

As intended herein graft rejections also encompass Graft Versus Host Disease (GVHD).

The present invention also relates to the use of at least one polypeptide as defined above, or of a protein comprising said polypeptide as defined above, or of a nucleic acid coding for said polypeptide or said protein, for the manufacture of a medicament intended for the prevention and/or the treatment of cancer, of viral diseases, or of pathologies requiring an inhibition of the immune system, such as autoimmune diseases, allergies or graft rejections.

Polypeptides as defined above, and proteins comprising them, can have several applications. When originating from wild type immunosuppressive ENV protein they can be used directly to inhibit the immune system. Otherwise, whether originating from an immunosuppressive or non-immunosuppressive ENV protein they can be used as decoys intended to bind to the natural receptors of the corresponding wild type ENV proteins expressed by cancer cells or viruses, which prevents the activity of said wild type ENV proteins.

The present invention also relates to the use of at least one protein or of a nucleic acid coding for said protein, said protein comprising or being constituted of:

- an immunosuppressive ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

wherein amino acids Y_1 to Y_{12} represent any amino acid, amino acid X_1 represents E, K or Q, and optionally amino acid X_2 represents A,

- or a fragment thereof, provided that said fragment carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of said ENV protein,

- or a protein derived from said ENV protein, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of the mutated ENV protein,

for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancers, of viral diseases, or of pathologies requiring an inhibition of the immune system, such as autoimmune diseases, allergies or graft rejections.

In a preferred embodiment of the above-defined use at least one protein comprising or constituted of an immunosuppressive ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancers, of viral diseases, or of pathologies requiring an inhibition of the immune system, such as autoimmune diseases, allergies or graft rejections, the ENV protein is selected from:

HERV-T ENV, such as represented by SEQ ID NO: 84, or

HERV-R ENV, such as represented by SEQ ID NO: 86, or

HERV-V ENV, such as represented by SEQ ID NO: 88, or

HERV-R(b) ENV, such as represented by SEQ ID NO: 90, or

HTLV-1 ENV, such as represented by SEQ ID NO: 92, or

HTLV-2 ENV, such as represented by SEQ ID NO: 94, or

FeLV ENV, such as represented by SEQ ID NO: 96, or
PERV ENV, such as represented by SEQ ID NO: 98, or
STLV-1 ENV, such as represented by SEQ ID NO: 100, or
FV ENV, such as represented by SEQ ID NO: 102.

As for the above-mentioned polypeptides, these proteins, and fragments thereof, can have several application. They can be used either directly to inhibit the immune system or as decoys intended to bind to the natural receptors of the corresponding wild type ENV proteins expressed by cancer cells or viruses.

The invention also relates to a method for producing antibodies comprising:

a. modifying the nucleotide immunosuppression-modulatory sequence in a way to modulate the immunosuppression effect, but to retain the fusion, infectious and immunosuppressive properties,
b. expressing the modified gene,
c. purifying the modified polypeptide,
d. injecting the modified polypeptide in an animal to induce a immune response,
e. purifying the produced antibodies reacting against the modified polypeptide.

The invention also provides a method to modulate the immunosuppressive properties of a antigenic and immunosuppressive protein while retaining its antigenic properties comprising:

a. identifying the nucleic acid sequence encoding an immunosuppression-modulatory sequence encoding a consensus amino acid sequence as defined above in a nucleic acid sequence encoding said antigenic and immunosuppressive properties,

b. identifying the codons encoding amino acids X1 and X2 impacting on the immunosuppressive properties in sequence X1-$(Y)_3$-$C(Y)_1$-X2 as defined above,

c. modifying the codons encoding said both amino acids in such a way that the resulting protein retains its antigenic properties but has modified immunosuppressive properties,

d. expressing the obtained modified nucleic acid sequence encoding said antigenic protein having modified immunosuppressive properties.

A particular method to modulate the immunosuppressive properties of an antigenic and immunosuppressive protein having further infectious and fusion properties while retaining its fusion, infectious and antigenic properties comprises:

a. identifying the immunosuppression-modulatory sequence of an env gene encoding an amino acid sequence similar to that defined above,

b. modifying the codons coding amino acids impacting on the immunosuppressive properties in such a way that the resulting protein retains its fusion, infectious and antigenic properties but has modified its immunosuppressive properties.

The invention also provides a method to prepare attenuated virus comprising:

a. modifying the gene coding for an antigenic and immunosuppressive protein of a virus in a way to modulate its immunosuppressive properties, but to retain its antigenic properties,

b. expressing the modified gene in a recombinant cell lines, to produce attenuated recombinant viral particles integrating a modified proviral genome.

The invention also concerns a method to prepare attenuated virus comprising:

a. modifying the gene coding for an antigenic and immunosuppressive ENV protein of a virus having further fusion and infectious properties in a way to modulate its immunosuppressive properties but to retain its fusion, infectious and antigenic properties,
b. expressing the modified gene in a recombinant cell lines, to produce attenuated recombinant viral particles integrating a modified proviral genome.

The invention also more generally relates to the use non-immunosuppressive or low-immunosuppressive polypeptides for the preparation of an immunogenic composition suitable for prophylaxis, or treatment of a viral disease or of a malignant state, or a tumor disease.

Naturally occurring proteins which have no immunosuppressive or low-immunosuppressive properties can be used accordingly; they encompass HERV-W or HERV-H.

The present invention relates to the use of a polypeptide as defined above, or of a mutated protein or a protein as defined above, for the preparation of ligands of ENV proteins selected from:

- polyclonal or monoclonal antibodies, or fragments thereof, such as Fab or F(ab)'$_2$ fragments,
- scFv polypeptides,
- aptamers,
- binding peptides.

Such ligands and methods for preparing them are well known to man skilled in the art.

The present invention also relates to antibodies or fragments thereof, scFv polypeptides, aptamers, or binding peptides, directed against mutated ENV proteins as defined above, or proteins or polypeptides comprising

them as defined above, provided that said antibodies or fragments thereof, scFv polypeptides, aptamers, or binding peptides do not bind to the corresponding wild type ENV proteins.

The present invention also relates to the use of polypeptides as defined above, or of proteins as defined above, for screening compounds liable to modulate the immunosuppressive activity of viruses or tumor cells.

The present invention also relates to the use of antibodies or fragments thereof, scFv polypeptides, aptamers, or binding peptides as defined above, for screening compounds liable to modulate the immunosuppressive activity of viruses or tumor cells.

In a preferred embodiment of the above defined uses of polypeptides as defined above, of proteins as defined above, or of antibodies or fragments thereof, scFv polypeptides, aptamers, or binding peptides as defined above, the compounds to screen are peptides, in particular peptides comprising from 5 to 30 amino acids, such as peptides originating from combinatorial peptide libraries.

EXAMPLES

EXAMPLE 1

METHODS:

Mice and Cell Lines.

The cell lines used in these tests were:

- 293T, embryonal kidney cells (ATCC CRL11268),
- HeLa, human epithelioid carcinoma cells (ATCC CCL2)
- MCA205, methylcholanthrene-induced murine fibrosarcoma cells (Shu and Rosenberg, 1985)
- NIH 3T3, mouse fibroblasts

Cells were cultured in DMEM supplemented with 10% fetal calf serum, streptomycin (100 µg/ml) and penicillin (100 units/ml).

In order to test the immunosuppressive effect of the modified protein, C57BL/6 and BALB/c mice, 8- to 12-wk-old, obtained from Janvier (Laval, France), were used.

Constructions.

The vectors expressing the envelope of HERV-W and HERV-T (phCMV-envW and phCMV–envT) have been previously described (Blaise et al., 2003). In brief, they comprise a promoter (human cytomegalovirus early promoter), the rabbit β-globin intron and polyadenylation sequences. The cDNA of HERV-W env was inserted between the EcoRI sites of the vector (Figure 3A).

The envelope gene of MPMV was retrieved from the pTMO vector (Brody et al., 1994) by PCR using the following primers:

Atacatctcgagaccggtccaactagaaccatgaacttcaattatcatttcatctgga (SEQ ID NO: 55) and

Atacatacgcgtctatgttaaggtcaaatatgagccacc (SEQ ID NO: 56) digested with XhoI and MluI (underlined), and cloned into phCMV-envT digested with the same enzymes. The phCMV-envMPMV expression vector containing and expressing the envelope gene of MPMV was obtained (Figure 2A). These vectors are used in the cell-cell fusion assay and for the production of pseudotypes.

Amino-acid positions * in the following description of the constructions were numbered according to the model structure of the TM subunit of HERV-W generated with the Swiss-Model software (Figure 8) (http://swissmodel.expasy.org/) and the structure of Moloney murine leukaemia virus TM subunit as a template (Protein Data Bank ID: 1MOF(1), http://www.resb.org/pdf/). The positions 44 and 50 according to this numbering scheme represent therefore the following positions when identified in the SU-TM precursors of the corresponding envelopes disclosed as NCBI sequence accession number:

Envelope	Position*36	Position*44	Position*47	Position*50	NCBI sequence accession number
HERV-W	A385	R393	T396	F399	AF072503[(2)]
MPMV	G463	Q471	I474	A477	AF033815[(3)]
MoMLV	G543	E551	L554	A557	AF033811[(3)]

NCBI URL: http://www.ncbi.nlm.nih.gov:80/entrez/

(1) Fass D, Harrison SC, Kim PS. Nat Struct Biol. 1996 May; 3(5): 465-9.

(2) Blond, J.L., Beseme, F., Duret, L., Bouton, O., Bedin, F., Perron, H., Mandrand, B. and Mallet, F.J. Virol. 73(2), 1175-1185 (1999)

(3) Petropoulos, C.J. Appendix 2: Retroviral taxonomy, protein structure, sequences and genetic maps, in RETROVIRUSES: 757, Coffin, J.M. (Ed.); Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, NY, USA (1997)

Site-directed mutagenesis of phCMV-envW was performed as described previously (Kunkel et al., 1987), using single-stranded uracilated DNA as template and mutagenic oligonucleotides (mutation in bold face), which also introduced silently a restriction site (underlined) for easier screening:
A36G: tagtccttcaaatcgccgc**gg**tttagacttgctaa (SEQ ID NO: 57),
R44Q: a**caa**gggggtacctgtttatttttaggggaaga (SEQ ID NO: 58),
T47I: ccgctgaaagaggggg**ata**tgtttatttttagggga (SEQ ID NO: 59),
F50A: aaccgctgaaagaggggtacctgttta**gct**ttaggggaaga (SEQ ID NO: 60),
R44Q/F50A: aaccgctgaa**caa**gggggtacctgttta**gct**ttaggggaaga (SEQ ID NO: 61).

Site-directed mutagenesis of phCMV-envMPMV was performed by the same method except that PCR fragments linking a silently XhoI-introducing antisense primer (cttcggcgtctctcgagagacgccgaag) (SEQ ID NO: 62) to the mutagenic primers Silent: caaaacagaagaggattagatctacttacagc (SEQ ID NO: 63),
Q44R: tacttacagcagag**aga**ggaggtatctgcttag (SEQ ID NO: 64),
A50F: gggaggtatctgctta**ttt**ttacaggaaaaatgtt (SEQ ID NO: 65),
Q44R/A50F: acttacagcagag**aga**ggaggtatctgctta**ttt**ttacaggaaaaatg) (SEQ ID NO: 66) were used instead of synthetic oligonucleotides.

Mutant derivatives of pDFG-envW were constructed by triple ligation of the BstBI-BsrGI and BsrGI-BstEII fragments of pDFG-envW with the BstEII-BstBI fragment of phCMV-envW.

pDFG-envMPMV and its mutant derivatives (Figure 2B) were constructed by ligation of the AgeI-MluI fragments of phCMV-envMPMV into the pDFG-MoTMTag vector digested with the same enzyme. The pDFG plasmid is an envelope expressing vector containing LTRs, splice sites (SD and SA) a psi sequence and an IRES (internal ribosome entry site) element, as well as a selection gene (antibiotic resistant gene). These vectors (Figures 1B, 2B and 3B) are used in the Envelope-Expressing Tumor Cells and *in Vivo* Assay.

Fusion property: the Cell–Cell Fusion Assay.

HeLa cells were transfected using Lipofectamine (Invitrogen, 2 µg of DNA for 5 x 10^5 cells). Fusion activity of envelope glycoproteins was measured 24 h after transfection with the corresponding expression vectors (Figures 1A, 2A and 3A). To visualize syncytia, cells were fixed in methanol and stained by adding May–Grünwald and Giemsa solutions (Sigma) according to the manufacturer's instructions. The fusion index, which represents the percentage of fusion events in a cell population is defined as $[(N - S)/T] \times 100$, where N is the number of nuclei in the syncytia, S is the number of syncytia, and T is the total number of nuclei counted (Figure 4). A phCMV vector not expressing envelope protein was used as a negative control.

Infectious property: the Infectivity Assay.

7.5 x 10^5 293T cells were cotransfected with 1.75 µg of CMV-gag-pol-MoMLV, 1.75 µg MFG-nls-lacZ and 0.55 µg phCMV vector (Figures 1A, 2A and 3A) expressing the envelope glycoproteins (wild-type or mutated) using the phosphate calcium method. MFG-nls-lacZ vector comprises the MoMLV LTRs, the psi sequence, a NLS (nuclear localisation signal) and the LacZ gene. Supernatants containing the pseudotypes (viral body of MoMLV with envelope protein from another virus strain) were recovered 2 days later, filtered, serially diluted in culture medium and used for infection of 4 x 10^3 HeLa cells in 96-well culture plates in the presence of 4 µg/mL polybrene.

Plates were fixed 2 days later, X-gal coloured for 1 hour, and foci of β-galactosidase-expressing infected cells were counted to determine pseudotype titers (number of infectious particles by ml of supernatant). A phCMV vector not expressing envelope protein was used as a negative control.

Immunosuppressive properties: the Establishment of Envelope-Expressing Tumor Cells and *in Vivo* Assay.

pDFG retroviral expression vectors (1.75 µg) were packaged by transient cotransfection into 7.5 x 10^5 293T cells with 1.75 µg of CMV-gag-pol-MoMLV and 0.55 µg CMV-envAmpho, using the calcium phosphate method. Supernatants were recovered 2 days later, filtered and used for infection of 5 x 10^5 MCA205 tumor cells in the presence of 4 µg/mL polybrene, as described in Mangeney & Heidmann, 1998. Cells were maintained in selective medium (400 units/mL hygromycin) for 2 weeks. For *in vivo* assays, tumor cells were trypsinized, centrifuged and resuspended in PBS at a concentration of 1 x 10^7 cells/mL. 100 µL of each suspension were injected s.c. in the shaved right flank of 3 C57/BL6 and 8 to 10 BALB/c mice. Tumor establishment was determined by palpation and tumor area (mm^2) was determined by measuring perpendicular tumor diameters (Figure 5). Immunosuppression index is defined as $i= (S_{env}-S_{none})/S_{none}$, wherein S_{env} is the maximum area reached by a tumour expressing an envelop protein and S_{none} is the maximum area reached by a tumour not expressing envelop protein (negative control).

RESULTS

1- Determination of the infectious properties of various wild-type envelope proteins

The infectiosity of envelope proteins was tested in NIH 3T3 cells (MoMLV) or HeLa cells (HERV-W and MPMV). Figure 6 shows that the three wild-type envelope proteins (lines 1, 5 and 9) were able to sustain an infection.

2- Determination of the immunosuppressive effects of various wild-type envelope proteins

The immunosuppressive effect of MPMV retrovirus and HERV-W was tested in MCA205 cells, injected in allogenic balb/c or syngenic C57Bl/6 mice. Figure 7 shows that tumour expressing MPMV (black bars) were large comparing to tumours expressing HERV-W (white bars). Whereas inventors confirmed the immunosuppressive effect of MPMV envelope, they showed that HERV-W was not able to immunosuppress an allogenic host.

In conclusion, the envelope proteins of MPMV and HERV-W have the same properties in term of fusogenicity and infectiosity, but differ for their immunosuppressive properties.

3- Strategy for the identification of envelope protein with altered immunosuppressive properties

Based on the different properties of HERV-W and MPMV, inventors attempted to identify domains in the amino acid sequence, which could be involved in the modulation of immunosuppression.

A putative 17 amino acid immunosuppressive domain (ISU) was previously characterized in several publications between amino acid 30 and amino acid 47 of the cristallized subdomain, the TM domain, respectively two leucines (L) in the MoMLV (Blaise et al. 2001 J Virol. 82, 1597-1600).

A two-step strategy was applied; the first step was to modify an envelope protein that in such a way that the derived protein (i.e., the modified protein) retains the fusion and infectious properties of the corresponding none modified protein. Once such a modified envelope protein has been identified, its immunosuppressive effect was tested and compared to that of the none modified protein.

4- Study of modified HERV-W

One difficulty lays in the fact that previous attempts to modify the amino acid composition of the TM subunit have lead to the loss of association of SU-TM and have altered the infectivity. A deletion from Leucine 30 to Threonine 40 of the MPMV immunosuppressive domain for instance completely abrogates the infectivity of the envelope proteins (Brody et al. 1992 J Virol 66, 3466-3475; Brody et al. 1994 Virology 202, 673-683).

Despite these unsuccessful attempts, the inventors studied the amino acid composition of the ISU domain, and their possible impact on the structure of the domain and achieve a novel definition of said ISU domain involved in immunosuppressive properties observed *in vivo*. They further determined that some positions in the amino acid sequence of proteins together with the nature of the amino acid residues at these positions were critical for the immuno suppressive effect.

The inventors especially designed some modifications in the amino acid sequence of a non-immunosuppressive envelope protein, i.e., HERV-WEnv protein, to render it immunosuppressive, using for instance substitution of determined residues by the corresponding residues of MPMV.

a. Infectious properties

The A36G and T47I substitutions of the HERV-W envelope do not modify the infectiosity, the fusogenicity and the immunosuppressive effect of the envelope protein (Table 1). These two amino acids appear not to be determinant for these functions. To the contrary, the R44Q or F50A substitutions strongly altered both the infectious and fusion properties of the envelope protein (Table 1, and Figure 6, lines 2 and 3).

A double mutant comprising both the R44Q and F50A substitutions was constructed. Surprisingly, the double mutant retained fusion and infectious properties similar to those of the wild type polypeptide (Table 1 and Figure 6, line 4).

This result and the design of this modified envelope protein using some homologous positions found in the envelope of MoMLV (Figure 8) suggest that these two amino acids could interact together because of both their respective location in the structure of the TM unit of the envelope protein, and their nature. This possible interaction may explain the compensatory behaviour of this pair of mutations. This was unexpected, because of the previous attempts that fail to identify such amino acids.

b. Immunosuppressive properties

Another result, as surprising as the above-mentioned, arises from the study of the immunosuppressive effect. Indeed, whereas the wild-type HERV-W envelope protein was not immunosuppressive in view of the size of the tumours, the HERV-W double mutant was more immunosuppressive than the wild-type MPMV envelope proteins (Table 1 and Figure 7, white bars).

Moreover, inventors identified two amino acids positions in the sequence, one of which was previously not reported as forming part of the ISU domain (position 50), which, taken together, revealed to be involved in the

modulation of the immunosuppressive effect of the HERV-W envelope proteins.

Mutant	Fusion	Infection	Immunosuppression
Wild Type	55.0 ± 3.7 %	800 ± 200	-0.30 ± 0.06
R44Q	32.5 ± 1.3 %	< 10	-0.12 ± 0.30
F50A	5.6 ± 3.0 %	< 10	-0.16 ± 0.14
R44Q+F50A	53.0 ± 2.8 %	947 ± 542	0.61 ± 0.10
A36G	54.5 ± 4.5 %	3950 ± 2250	*-0.02 ± 0.01*
T47I	50.5 ± 1.2 %	300 ± 80	*-0.25 ± 0.04*
Negative control	3.2 ± 1.2 %	< 10	0.00 ± 0.00

Table 1: Results obtained for fusion, infectious and immunosuppression properties of HERV-W modified envelope proteins.

5- Study of modified retrovirus envelope proteins

To confirm the fact that these amino acids residues belong to a determinant of immunosuppression, other retroviruses comprising similar amino acid at positions 44 (E or Q) and 50 (F) were screened. Several of these retroviruses have been identified and are disclosed in Figure 9: Moloney Murine Leukaemia virus (MoMLV), Friend virus, Feline Leukaemia virus (FeLV), Human T-cell lymphotropic virus type-1 (HTLV-1) and simian T-cell lymphotropic virus type-1 (STLV-1).

In two of them, MPMV and MoMLV viruses, amino acid residues 44 and 50 were substituted by the corresponding amino acids found in HERV-W. The following constructs were made: E44R, A50F and E44R/A50F (MoMLV) and, Q44R, A50F and Q44R/A50F (MPMV).

a. Infectious property

Interestingly, in MoMLV, the simple mutant loses its infectivity properties (Table 2 and Figure 6, lines 6 and 7), whereas the double mutant has the same properties as the wild-type protein (Table 2 and Figure 6, line 8).

In MPMV, slight differences were observed between mutants and wild-type, but only the double mutant presents properties strictly identical to the wild-type proteins (Table 3 and Figure 6, lines 10 to 12).

b. Immunosuppressive properties

In MoMLV, both a protein with the E44R substitution or a double mutant (E44R+A50F) have their immunosuppressive properties reduced *in vivo* (Table 2).

In MPMV, both a protein with the Q44R substitution or a double mutant (Q44R+A50F) have their immunosuppressive properties reduced *in vivo* (Table 3).

Mutant	Infection	Immunosuppression
wt	$4.59 \pm 1.97.10^5$	0.60 ± 0.20
E44R	$6.97 \pm 3.98.10^4$	*0.03 ± 0.01*
A50F	$< 10^1$	n/d
E44R+A50F	$4.34 \pm 2.11.10^5$	0.00 ± 0.01
Negative control	$<10^1$	-0.00 ± 0.00

Table 2: Results obtained for infectious and immunosuppression properties of MoMLV modified envelope proteins (MoMLV is not fusiogenic).
n/d: not determined

Mutant	Fusion	Infection	Immunosuppression
wt	47.8 ± 3.0 %	$3.3 \pm 0.4\ 10^4$	0.45 ± 0.09
Q44R	29.8 ± 6.4 %	$3.6 \pm 0.5\ 10^3$	*-0.32 ± 0.12*
A50F	37.2 ± 5.9 %	$8.9 \pm 2.7\ 10^3$	*0.01 ± 0.01*
Q44R+A50F	52.6 ± 3.4 %	$2.8 \pm 1.0\ 10^4$	-0.27 ± 0.06
Negative control	5.1 ± 2.2 %	$< 10^1$	0.00 ± 0.00

Table 3: Results obtained for fusion, infectious and immunosuppression properties of MPMV modified envelope proteins.

Taken together, all these results allow to draw the following conclusions:

Firstly, a single mutation seems sufficient to modify the immunosuppressive properties of a retroviral immunosuppressive envelope protein. Indeed, the substitution of the glutamine or glutamic acid in position 44 with an arginine reduced the immunosuppressive behaviour of the mutants. However, the fusion and infectious properties, even if not abolished, are strongly reduced (MPMV).

Secondly, double mutants (at positions 44 and 50) have reduced immunosuppressive properties when compared to the corresponding wild-type envelope protein. Interestingly, MPMV double mutants have fusion properties as efficient as those of wild-type protein, and high infectious properties. The interest of such a protein in the production of viral particles and live vaccine is promising.

EXAMPLE 2

METHODS

Mice and cell lines: Swiss mice (FV permissive), 10 weeks old, were obtained from Janvier (Laval, France). The cell lines 293T (ATCC CRL11268), HeLa (ATCC CCL2), NIH/3T3 (ATCC CRL-1658) and MCA205 (REF) were cultured in DMEM supplemented with 10% fetal calf serum, streptomycin (100 µg/ml) and penicillin (100 units/ml).

Constructions: Plasmids p57 (Oliff et al. *J Virol* 33, 475-86 (1980)) and pET28(+)b (Novagen) were used.

phCMV-envFV was constructed as phCMV-envMPMV (Example 1), using p57 as PCR template and primers 16 and 17. Mutant derivatives were constructed by inserting into the ClaI/AvrII opened vector two PCR products, the first digested with ClaI, the second with AvrII. These fragments were generated with phosphorylated primer pairs 1-2 and 3-4

for E14R mutation (which corresponds to the E561R mutation of the full length ENV), 1-5 and 3-6 for A20F mutation (which corresponds to the A567F mutation of the full length ENV), and 1-2 and 4-6 for E14R+A20F mutation. pDFG-envFV and its mutant derivative were constructed by inserting the AgeI/MluI fragments of phCMV-envFV into pDFG-MoTMTag digested with the same enzymes. The double mutant p57 was constructed by inserting the BstZ11I/BsmI fragment of the double mutant phCMV-envFV into p57 digested with the same enzymes.

The bacterial expression vector for the SU subunit of the FV envelope protein was constructed by inserting a PCR fragment generated with phCMV-envFV as a template and primer pair 7-8, and digested with NcoI and XhoI, into pET28(+)b digested with the same enzymes.

The bacterial expression vectors for the SU and the TM subunits of the FV envelope protein were constructed by inserting a PCR fragment generated with wild-type or double-mutant phCMV-envFV as a template and primer pair 7-8 or 9-10, and digested with NcoI and XhoI, into pET28(+)b digested with the same enzymes.

	SEQUENCE	SEQ ID
1	CAACCTTACCAACCCTGATAAAACTCAAGA	SEQ ID NO: 131
2	CAGTCCTCCTCTTTTTAGGAACAACAGGTCTAGGC	SEQ ID NO: 132
3	TGTGCTGCCCTAAAAGAAGAATGTTGTT	SEQ ID NO: 133
4	GGACTAAAGCCTGGACTACTGAGATCCTG	SEQ ID NO: 134
5	CAGTCCTCCTTCTTTTAGGAACAACAGGT	SEQ ID NO: 135
6	TGTGCTTTCCTAAAAGAAGAATGTTGTTTCTAT	SEQ ID NO: 136
7	ATACATCCATGGCGTGTTCAACGCTCCCAAAATCCCCTA	SEQ ID NO: 137
8	ATACATCTCGAGTTCTCTTTTATGTCTATAGGATTTTTCAAAC	SEQ ID NO: 138
9	ATACATCCATGGCTGCCGTACAAGATGATCTCA	SEQ ID NO: 140
10	ATACATCTCGAGATCTCTTACTAGGCCTGTATGGTCAGC	SEQ ID NO: 141

Virus production, quantitation and inactivation: $7.5x10^5$ 293T cells were transfected with 4 µg of p57 DNA using a calcium phosphate transfection kit (Invitrogen). 48h later, cell supernatants were used to infect $5x10^5$ NIH/3T3 cells in the presence of 4 µg/mL polybrene and infected cells were cultured for 4 additional days. Viral particles were collected from cell supernatants, concentrated by ultracentrifugation, resuspended in PBS, and frozen. Inactivation was performed by exposing a viral suspension in PBS to UV light at 0.5 mW/cm^2 during 30 minutes.

Immunosuppression assay: MCA205 cells were transduced with either an envelope gene expression vector or an empty vector, and engrafted into allogenic mice where they established transient tumors, as described in example 1. The immunosuppression index was calculated as $(A_{env}-A_{none})/A_{none}$, where A_{env} and A_{none} are the mean tumor areas obtained with cells expressing the envelope gene and the empty cassette, respectively.

Cell-cell fusion and infectivity assays were performed as described in Example 1, with phCMV-envFV and their mutant derivatives as envelope expression vectors.

Viral load assay: RNA from 2 µl of concentrated virus or 20 µl of cell supernatant or serum was extracted using the RNAeasy microkit (QIAgen), reverse-transcribed using the MoMuLV reverse transcription kit (Applied) and random hexamers as primers, and cDNA was quantitated by real-time PCR using the Platinum SYBR Green qPCR kit (Invitrogen) and primers CTCAGGGAGCAGCGGGA (SEQ ID NO: 142) and TAGCTTAAGTCTGTTCCAGGCAGTG (SEQ ID NO: 143).

Recombinant proteins: Recombinant proteins were produced in BL21(DE3) *E.coli* cells (Stratagene) using pET28(+)b (Novagen) as an expression vector. The SU subunit was produced as inclusion bodies, and

the wild-type and mutant TM subunits as soluble material. They were purified on HiTrap Chelating HP columns (Amersham) according to the manufacturer's instructions. The TM subunits were further purified on a Superdex 75 HR10/30 column (Amersham) to isolate the major trimeric form, their LPS contents were quantitated using the LAL QCL-1000 kit (Cambrex) and adjusted to 5 µg/mg of protein by addition of *E.coli* LPS (strain 0111:B4, Sigma).

Mice immunization: Mice were injected thrice at one week interval with either 100 µg of recombinant TM subunits or 1.5 10^{10} RNA copies of an intact or UV-inactivated FV viral particles. 100 µg of CpG (phosphorothioate oligonucleotide TCCATGACGTTCCTGACGTT (SEQ ID NO: 144)) was systematically added as an adjuvant. Sera were collected 4 days after the last immunization. Inactivated viral particles-immunized mice were challenged with 10^6 RNA copies of the wild-type FV, and post-challenge sera were collected 5 days later.

Immunological FV detection: Recombinant SU subunit was produced as inclusion bodies in BL21(DE3) *E.coli* cells (Stratagene) using pET28(+)b (Novagen) as an expression vector, purified on a HiTrap Chelating HP column (Amersham) according to the manufacturer's instructions, and used to coat MaxiSorp microplates (Nunc) at a concentration of 2 µg/ml. IgG levels in serially diluted sera were quantitated using an anti-mouse IgG antibody conjugated to HRP (Amersham) and OPD as a chromogenic reagent (Sigma).

RESULTS

1. Loss of envelope protein-induced immunosuppression leads to complete immune rejection of an infectious retrovirus: The genetic, double-mutation-generated disjunction between immunosuppression and

infectivity evidenced in Example 1 opens the possibility to generate an entire retrovirus devoid of the immunosuppressive activity of its envelope protein, but still replicative and infectious.

The Friend Murine Leukemia Virus (FV) was chosen as a model, because the mouse genome does not contain a related endogenous retrovirus that could impair its *in vivo* detection.

The key residues of the FV envelope were replaced by those of Syncytin-1 (HERV-W ENV), and it was checked, as for the MPMV envelope, that the double mutation E14R + A20F (which corresponds to the E561R + A567F mutation of the full length ENV) reversed immunosuppression without altering infectivity (Figures 11A and 11B). The wild-type envelope gene was replaced by its non-immunosuppressive mutant in the FV molecular clone 57, and each type of retroviral particles was produced *in vitro*. The virus yields were similar as measured by a quantitative RT-PCR assay of the viral RNA in the cell supernatants.

As expected, both virus types display the same propagation kinetics in an *in vitro* infection assay in NIH/3T3 cells (Figure 11C), and similarly when injected *in vivo* in 5-Gray irradiated, immunocompromised mice (Figure 12A).

In normal mice, the wild-type FV first established high viremia in all mice during the primo-infection phase (at day 7 after virus injection, Figures 12A-12B). This phase was followed by the establishment of persistent infections, the mice being able to control viral replication to various extents, as expected with non-congenic, outbred mice. After 4 months, 80% of the infected mice disclosed an erythroleukemia syndrome, with a hematocrit level below 35%.

In contrast the mutated non-immunosuppressive FV was undetectable as early as 14 days after injection of even very high doses of viral copies (10^6 RNA copies, 10^2 ID_{50}) with no evidence for any pathology. Noteworthily, IgG directed against the FV envelope protein were detected persistently in mice infected with wild-type FV, but only transiently in mice infected with

the double-mutant FV (Figure 13), indicating complete clearance of the mutated virus.

In conclusion, the present experiments demonstrate that envelope-driven immunosuppression is essential for FV infection, as its absence leads to thorough immune rejection of the incoming virus.

2. Increased immunogenicity of immunosuppression-negative recombinant envelope proteins and inactivated viral particles: As the key element for viral entry into the target cell, retroviral envelope proteins are systematically included in every vaccinal formulation, either as recombinant proteins, as fragments thereof, or as genes carried by a defective viral vector. One could suspect that envelope protein-mediated immunosuppression could inhibit the response mounted against an immunogen containing the ISU, thus lowering its vaccinal efficiency.

To test this hypothesis, two kinds of ISU-containing immunogens were generated: 1) recombinant proteins corresponding to the ectodomains of the TM subunit of the wild-type or mutant FV envelope protein, produced in *E.coli* as soluble - thus correctly folded - and trimeric forms displaying identical behavior upon purification; 2) wild-type and mutant FV particles that were intact or inactivated by exposure to UV light, in order to preserve the native structure of their envelope proteins. These immunogens were injected thrice in Swiss mice to generate a strong secondary humoral response.

As illustrated in Figure 14A, only the mutant non-immunosuppressive envelope protein raises such a response, with high IgG levels. In every cases, the signals obtained with plates coated with the wild-type or the mutant TM subunits were quantitatively the same, indicating that the anti-TM antibodies in the mice sera are not preferentially directed against the ISU itself but rather against other epitopes within the TM subunits.

Thus, the double mutation introduced in FV envelope protein does not convert its ISU into a highly efficient epitope. In addition, IgM levels raised

by the wild-type envelope protein are much higher than those raised by its non-immunosuppressive mutant counterpart. These results suggest that the immunosuppressive domain of FV envelope protein directly inhibits the immune system, and that this effect does not require viral entry and replication in the target cell nor even any other viral component than the TM subunit alone.

Figure 14B confirms these results with MoMLV ENV and HERV-W ENV. Almost no IgG response is elicited against the wild type recombinant TM subunit of MoMLV ENV, whereas the non immunosuppressive double mutant (see Example 1) shows a strong IgG response. Furthermore, as expected, an IgG response is seen against the TM subunit HERV-W ENV, which is naturally deprived of immunosuppressive activity, whereas the immunosuppressive double mutant (see Example 1) elicits only a slight IgG response.

3. Loss of envelope protein-induced immunosuppression improves the vaccinal efficiency of inactivated viral particles: One could suspect that this antigenicity-inhibiting effect of the ISU might lower the efficiency of any vaccine formulation containing an immunosuppressive envelope protein, and thus, that the specific, double mutation-induced disruption of this effect might improve vaccinal efficiency.

To test this hypothesis, mice immunized with either wild type and double mutant inactivated viral particles or with intact double mutant viral particles were challenged with the intact wild-type FV. Serum viral loads were then assayed at peak viremia, five days after challenge (Figure 15).

The virus was detectable in all mice immunized with the wild-type inactivated FV, yet with a geometric mean viral load 50-fold lower than that of control mice immunized with the adjuvant only, indicating a significant but incomplete protection conferred by immunization with wild-type particles. In contrast, the viral loads of 6 of the 14 mice immunized with the non-

immunosuppressive inactivated double mutant FV were below the detection threshold of the assay, and the geometric mean viral load was reduced 7500-fold as compared to mice immunized with adjuvant only. Furthermore, the viral loads of 12 out of 14 mice immunized with the intact non-immunosuppressive double mutant FV were below the detection threshold and the geometrical mean viral load was also below the detection threshold.

These results show that disrupting immunosuppression by mutations that preserve the canonical function – thus the structure – of an envelope protein improves the efficiency of vaccinal formulation based on such proteins.

EXAMPLE 3

METHODS

Mice and cell lines: C57BL/6 and SCID mice, 8-12 weeks old, were obtained from Janvier (France). B16 (murine melanoma cell line of C57BL/6 origin, EACC 94042254) and 293T (human embryonic kidney cells, ATCC CRL11268) were maintained in DMEM supplemented with 10% heat-inactivated foetal calf serum and antibiotics.

Constructions: a pIncxH1 expression vectors derived from the pIncx (Miller and Rosman Biotechniques 1989;7: 989-90) and the pSUPER (Brummelkamp et al. Science 2002;296: 550-3) vectors was constructed to generate short transcripts directed against MelARV (targeted to the genomic transcript within the gag sequence; nt positions 1220-1238 from the start codon), or against the green fluorescent protein transcript (nt position 215-233 from the start codon) as a control. They were obtained by

first inserting annealed 64-mer oligonucleotides (sequences in Figure 1B) into pSUPER opened at the *Bgl*II and *Hind*III sites, followed by introduction of the *BamH*I-*Hind*III fragment from these constructs into pIncx opened at the corresponding sites. The expression vector for the MelARV envelope (pDFG MelARVenv) and the control (pDFG none) were constructed by introducing (or not) a RT-PCR product, generated from the MelARV viral RNA using an *Age*I-containing primer at the envelope 5'-end and a *Xho*I-containing primer at the envelope 3'-end, into a hygromycin-containing pDFG vector (Mangeney and Heidmann Proc Natl Acad Sci USA 1998;95: 14920-14925) opened at the same sites.

Establishment of ERV^{KD} B16 tumor cells: $7.5x10^5$ 293T cells were cotransfected with the pIncxH1 vector (1.75 µg) and expression vectors for the MLV proteins (0.55 µg for the amphotropic MLV envelope vector and 1.75 µg for the MLV gag and pol vector, see Blaise et al. J Virol 2004;78: 1050-1054). Thirty six hours post-transfection, viral supernatants were collected for infection of the B16 tumor cells (2.5 ml of supernatant for $5x10^5$ cells, with 8 µg/ml polybrene). Cells were maintained in selective medium (1 mg/ml neomycin) for three weeks. In some experiments, the pDFG MelARVenv expression vector (or control pDFG none) was additionally introduced into the cells using the same protocol and infected cells were selected with 300 units/ml hygromycin.

Expression of MelARV proteins: Analysis of MelARV expression was performed by Western blot analyses. The supernatants of 10^7 cells were collected, centrifuged for 10 min at 100xg, filtered and concentrated by ultra-centrifugation in a SW41 Beckman rotor (150,000xg, 1 hour, 4°C). Pellets were resuspended in lysis buffer, submitted to SDS-PAGE, blotted and revealed with an anti-Env mAb (Ciancolo et al. J Exp Med 1984; 159:964-969) and an anti-Gag goat serum (Viromed Biosafety Labs).

***In vitro* transformation assay:** Both control- and ERV^{KD}- B16 cells were plated in soft agar to determine the efficiency of anchorage-independent growth. Cells ($2x10^3$ or $2x10^4$) were plated in 5 ml of 0.33% agar in DMEM with 10% foetal bovine serum overlaid onto a solid layer of 0.5% agar in DMEM supplemented with 10% foetal bovine serum. The culture was maintained for 4 weeks, the colonies were stained with INT solution (Sigma-Aldrich) and then counted.

Tumor progression *in vivo*: For *in vivo* assays, tumor cells were washed three times with PBS, scrapped without trypsination, and subcutaneously inoculated in the shaved area of the right flank of the mice. Tumor establishment was determined by palpation and tumor area was determined by measuring perpendicular tumor diameters.

$CD4^+CD25^+$ T cell purification and adoptive transfer in syngenic C57BL/6 mice: $CD4^+CD25^+$ cells were freshly isolated from spleens of C57BL/6 mice engrafted with $2x10^5$ B16 cells 17 days before. Cells were purified by a two step procedure of negative and positive selections, using MACS magnetic beads (mouse regulatory T cell isolation kit, Miltenyi Biotech), according to the manufacturer's instructions. Fifty thousands purified lymphocytes were transferred intravenously into naive C57BL/6 mice. Recipient mice were challenged the same day with $2x10^5$ control- or ERV^{KD}- B16 cells in the right flank.

RESULTS

1. Knocking down ERV does not modify the transformed phenotype of B16 melanoma cells.

An RNA interference approach was used based on stable vectors producing short double-stranded RNA (dsRNA) directed against the viral genome of the MelARV element and the irrelevant *gfp* gene as a control. The rationale of the

procedure and the structure of the plasmids used are illustrated in Figures 16A-16B. Figure 16C clearly shows that the ERV-specific dsRNA vector almost completely abolished ERV expression in the transduced B16 cells (ERV^{KD} B16 cells), with a >10-fold reduction in the amount of both the Env and Gag viral proteins as compared to the control transduced cells (control B16 cells). As a next step, the transformed phenotype of the ERV^{KD} and control B16 cells was assayed both *in vitro* and *in vivo*. *In vitro*, the anchorage-independent growth rate was measured after plating in semi-solid media (soft agar assay). As illustrated in Figure 17A, the ERV^{KD} B16 cell line gave rise to a similar number of colonies as the control B16 cells. *In vivo*, the growth rate of the two cell populations was analyzed after engrafting into X-irradiated or SCID mice. As illustrated in Figure 17B, both cell populations have a transformed phenotype, with similar growth rates. Altogether, these results show that knocking down the MelARV endogenous retrovirus has no effect on the transformed state of the melanoma cells.

2. Knocking down ERV inhibits B16 tumor cell growth *in vivo* and increases survival of immunocompetent hosts.

To investigate whether tumor cells may overwhelm the antitumor response *in vivo* through an ERV-dependent mechanism, the Inventors explored the impact of the knocking down of MelARV on tumor progression by injecting C57BL/6 immunocompetent mice with the control and the ERV^{KD} B16 cells. As illustrated in Figure 18A, growth of control B16 cells, as expected, led to large tumors in most of the animals, whereas the ERV^{KD} B16 cells yielded tumors of a limited size and in only a small number of engrafted mice. The difference in tumor cell growth is also clearly substantiated by the extent of animal survival (Figure 18B): as soon as day 70, 90% of the mice engrafted with the control B16 cells had been killed by their tumor, whereas 80% of mice engrafted with ERV^{KD} B16 cells were alive and tumor-free (and still so at day 130). In an attempt to identify the MelARV genes involved in the observed effects, an expression vector (lacking the dsRNA-targeted sequence) for the sole MelARV

env gene was introduced back into the ERV^{KD} B16 cells. The resulting double-transduced ERV^{KD}+env (or control) B16 cells were then engrafted into C57BL/6 mice. As illustrated in Figure 18C, this resulted in partial reversion of the knockdown effect, with already 50% of the mice engrafted with the Env-expressing cells dead by day 70. This reversion indicates that the *env* gene is - at least in part - responsible for tumor immune escape. The partial effect of the reversion is most likely explained by the lower expression (Figure 19) of the Env protein when expressed by the exogenous vector.

Along this line, it is of interest that a first series of experiments using synthetic siRNA targeted to MelARV, and injected intraperitoneously 12 days after engraftment of B16 cells into immunocompetent mice, actually resulted in a 1/3 inhibition of tumor growth as compared to mice injected with control siRNA (Figure 20A) and, as illustrated in the supplementary Figure 20B, in a reproducible increase in survival delay.

The present data demonstrate that tumors are able to overwhelm the immune system by expressing the envelope of an ERV and that blocking ERV expression resulted in enhanced tumor rejection.

It is noteworthy that in humans the expression of ERV *env* genes, mainly restricted to placenta and testis in normal tissues, can be observed in several tumor types such as seminomas and melanomas. Such HERV ENV proteins have been shown to be immunosuppressive. Therefore, inhibiting the expression or the activity of these ENV proteins is a promising approach to enhance immune response against ENV-expressing tumors. Such an inhibition of the activity of the tumoral ENV proteins could be performed, for instance, by an immune response elicited by a prophylactic or a therapeutic vaccination with mutated ENV proteins depleted of their immunosuppressive activity according to the invention or by compounds directly binding to tumoral ENV proteins.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. An isolated polypeptide having a sequence of 7 to 20 amino acid residues encoded by a nucleic acid, derived from a viral gene, which is capable of modulating the immunosuppressive properties of a viral protein or a fragment thereof, against the host in which it is expressed (immunosuppression-modulatory sequence) when it substitutes the homologous sequence of said viral protein or fragment,

said isolated polypeptide comprising the minimum following consensus amino acid sequence:

$$X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

wherein X_1 and X_2 are selected to impact on said immunosuppressive properties, such that

- X_1 is E, K or Q, and X_2 is such that it ensures that the structure of the viral protein is conserved, or
- X_1 is E, K or Q and X_2 is A or
- X_1 is W and X_2 is I or V, or
- X_1 is R,H or K, X_2 is such that it ensures that the structure of the viral protein is conserved or
- X_1 is R,H or K and X_2 is F, W Y or H, or
- X_1 is F, W Y or H and X_2 is R, H or K

and Y_9 to Y_{12} represent variable amino acid residues.

2. The isolated polypeptide according to claim 1, wherein X_1 is E, K or Q and X_2 is A.

3. The isolated polypeptide according to claim 1, wherein X_1 is K, and X_2 is F.

4. The isolated polypeptide according to claim 1, wherein X_1 is R, and X_2 is F.

5. The isolated polypeptide according to any one of claims 1 to 4, encoded by a nucleic acid, derived from a viral ENV gene.

6. The isolated polypeptide according to any one of claims 1 to 5, encoded by a nucleic acid, derived from a retroviral ENV gene.

7. The isolated polypeptide according to claim 6, wherein said retrovirus is selected from the group consisting of MoMLV, Friend retrovirus, FeLV, HTLV-1, HTLV-2, STLV-1 and MPMV.

8. The isolated polypeptide according to any one of claims 1, 2 or 5 to 7 comprising the following sequence:
E/Q-G-G-L/T/I-C-A/K/L/M/V/I-A.

9. The isolated polypeptide according to any one of claims 1 or 4 to 7 comprising the following sequence
R-G-G-L/T/I-C-A/K/L/M/V/I-F.

10. The isolated polypeptide according to any one of claims 1 or 2 or 5 to 7 comprising a sequence selected from the group consisting of:
QGGLCKA (SEQ ID NO: 17)
QGGLCAA (SEQ ID NO: 18)
QGGLCLA (SEQ ID NO: 19)
QGGICLA (SEQ ID NO: 20)
EGGLCAA (SEQ ID NO: 21)
EGGLCVA (SEQ ID NO: 22),
wherein these immunosuppression-modulatory sequences provide immunosuppressive properties to a protein comprising them.

11. The isolated polypeptide according to any one of claims 1 or 3 to 7 comprising a sequence selected from the group consisting of:
KGGTCMF (SEQ ID NO: 24)
KGRTCLF (SEQ ID NO: 25)
KGGLCIF (SEQ ID NO: 26),

wherein these immunosuppression-modulatory sequences provide low immunosuppressive properties to a protein comprising them, or

RGGTCLF (SEQ ID NO: 23)

RGGLCKF (SEQ ID NO: 27)

RGGLCAF (SEQ ID NO: 28)

RGGLCLF (SEQ ID NO: 29)

RGGICLF (SEQ ID NO: 30)

RGGLCVF (SEQ ID NO: 31)

RGGTCVF (SEQ ID NO: 32),

wherein these immunosuppression-modulatory sequences provide essentially no immunosuppressive properties to a protein comprising them.

12. The isolated polypeptide according to any one of claims 1 to 11, having the following consensus sequence:

$$Y_{13}Y_{14}NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

wherein X_1 and X_2 are as defined in claim 1 and Y_1 to Y_{14} represent any amino acid.

13. The isolated polypeptide according to claim 12, having a sequence selected from the group consisting of:

AQNRRGLDLLFWEQGGLCKA (SEQ ID NO: 33)

LQNCRCLDLLFLSQGGLCAA (SEQ ID NO: 34)

LQNRRGLDMLTAAQGGLCLA (SEQ ID NO: 35)

LQNRRGLDLLTAEQGGICLA (SEQ ID NO: 36)

LQNRRGLDILFLQEGGLCAA (SEQ ID NO: 37)

LQNRRGLDLLFLKEGGLCAA (SEQ ID NO: 38)

LQNRRGLDLLFLKEGGLCVA (SEQ ID NO: 39),

wherein these immunosuppression-modulatory sequences provide immunosuppressive properties to a protein comprising them.

14. The isolated polypeptide according to 12, having a sequence selected from the group consisting of:

LQNRRGLDLLTAEKGGLCIF (SEQ ID NO: 45)
MQNRRALDLLTADKGGTCMF (SEQ ID NO: 46)
AQNRQALDLLMAEKGRTCLF (SEQ ID NO: 47),
wherein these immunosuppression-modulatory sequences provide low immunosuppressive properties to a protein comprising them, or

LQNRRALDLLTAERGGTCLF (SEQ ID NO: 40)
LQNWRALDLLTAKRGGTCLF (SEQ ID NO: 41)
LQNWRALDLLIAKRGGTCVF (SEQ ID NO: 42)
LQNRRGLDLLTAERGGTCLF (SEQ ID NO: 43)
LQNRRALDLLTAERGGICLF (SEQ ID NO: 44)
AQNRRGLDLLFWERGGLCKF (SEQ ID NO: 48)
LQNCRCLDLLFLSRGGLCAF (SEQ ID NO: 49)
LQNRRGLDMLTAARGGLCLF (SEQ ID NO: 50)
LQNRRGLDLLTAERGGICLF (SEQ ID NO: 51)
LQNRRGLDILFLQRGGLCAF (SEQ ID NO: 52)
LQNRRGLDLLFLKRGGLCAF (SEQ ID NO: 53)
LQNRRGLDLLFLKRGGLCVF (SEQ ID NO: 54),
wherein these immunosuppression-modulatory sequences provide essentially no immunosuppressive properties to a protein comprising them.

15. An isolated mutated ENV protein resulting from the mutation of a wild-type ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

in which X_1 is E, K or Q and X_2 is A, V, L, I, or K and Y_1 to Y_{12} represent any amino acid

wherein amino acid X_1 is substituted by R or H,

said mutated ENV protein having almost no immunosuppressive activity with respect to the wild-type ENV protein,

or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries the mutated amino acid X_1 and optionally X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, which is

almost no immunosuppressive activity, and that optionally its antigenic structure is essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein with at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or a fragment thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

16. An isolated mutated ENV protein, according to claim 15, resulting from the mutation of a wild-type ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2\ ,$$

wherein amino acid X_1 is substituted by R or H and amino acid X_2 is substituted by F, M, Y or W.

17. A mutated ENV protein, or a fragment thereof, according to claim 18 or claim 19, wherein the structures responsible for the antigenicity of said mutated ENV protein, or fragment thereof, are essentially preserved with respect to the wild-type ENV protein.

18. An isolated mutated ENV protein, or a fragment thereof, according to any one of claims 15 to 17, wherein the ENV protein is a HERV ENV, in particular selected from:
HERV-FRD ENV (SEQ ID NO: 82), wherein X_1 is Q427 and X_2 is A433, or
HERV-T ENV (SEQ ID NO: 84), wherein X_1 is Q516 and X_2 is A522, or
HERV-R ENV (SEQ ID NO: 86), wherein X_1 is E561 and X_2 is K567, or
HERV-V ENV (SEQ ID NO: 88), wherein X_1 is Q381 and X_2 is V387, or
HERV-R(b) ENV (SEQ ID NO: 90), wherein X_1 is E391 and X_2 is L397.

19. An isolated mutated ENV protein, or a fragment thereof, according to claim 18, wherein the ENV protein is HERV-FRD ENV and the sequence of the mutated ENV protein is selected from SEQ ID NO: 120 and SEQ ID NO: 122.

20. An isolated mutated ENV protein, or a fragment thereof, according to claim 18, wherein the ENV protein is HERV-V ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 124 and SEQ ID NO: 126.

21. An isolated mutated ENV protein, or a fragment thereof, according to claim 18, wherein the ENV protein is HERV-T ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 128 and SEQ ID NO: 130.

22. An isolated mutated ENV protein, or a fragment thereof, according to claim 18, wherein the ENV protein is HERV-R ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 146 and SEQ ID NO: 148.

23. An isolated mutated ENV protein, or a fragment thereof, according to any one of claims 15 to 17, wherein the ENV protein is selected from:
HTLV-1 ENV (SEQ ID NO: 92), wherein X_1 is Q389 and X_2 is A395, or
HTLV-2 ENV (SEQ ID NO: 94) wherein X_1 is Q385 and X_2 is A391, or
FeLV ENV (SEQ ID NO: 96), wherein X_1 is E527 and X_2 is A533, or
PERV ENV (SEQ ID NO: 98), wherein X_1 is E545 and X_2 is A551, or
STLV-1 ENV (SEQ ID NO: 100), wherein X_1 is Q389 and X_2 is A395, or
MoMLV ENV (SEQ ID NO: 70), wherein X_1 is E551 and X_2 is A557, or
MPMV ENV (SEQ ID NO: 72), wherein X_1 is Q471 and X_2 is A477, or
FV ENV (SEQ ID NO: 102), wherein X_1 is E561 and X_2 is A567.

24. An isolated mutated ENV protein, or a fragment thereof, according to claim 23, wherein the ENV protein is FeLV ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 104 and SEQ ID NO: 106.

25. An isolated mutated ENV protein, or a fragment thereof, according to claim 23, wherein the ENV protein is HTLV-1 ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 108 and SEQ ID NO: 110.

26. An isolated mutated ENV protein, or a fragment thereof, according to claim 23, wherein the ENV protein is HTLV-2 ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 112 and SEQ ID NO: 114.

27. An isolated mutated ENV protein, or a fragment thereof, according to claim 23, wherein the ENV protein is PERV ENV and the sequence of the mutated ENV protein is selected from:
SEQ ID NO: 150 and SEQ ID NO: 152.

28. An isolated mutated ENV protein resulting from the mutation of a wild-type ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

in which X_1 is R and X_2 is F and Y_1 to Y_{12} represent any amino acid
wherein amino acid X_1 is substituted by E or Q ,
said mutated ENV protein having an immunosuppressive activity whereas the wild-type ENV protein is deprived of such an activity,
or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries the mutated amino acid X_1 and optionally X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and has an immunosuppressive activity, and that optionally its antigenic structure is

essentially similar to the structure it adopts in the context of the mutated ENV protein,

or a protein derived from the mutated ENV protein presenting at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries the mutated amino acid X_1 and X_2, that it has an immunosuppressive activity similar to that of the mutated ENV protein, and that, optionally, its antigenic structure is essentially similar to that of the mutated ENV protein, or fragment thereof.

29. A mutated ENV protein according to claim 28, resulting from the mutation of a wild-type ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2$$

wherein amino acid X_1 is substituted by E or Q and amino acid X_2 is substituted by A.

30. A mutated ENV protein, or a fragment thereof, according to claim 28 or claim 29, wherein the structures responsible for the antigenicity of said mutated ENV protein, or fragment thereof, are essentially preserved with respect to the wild-type ENV protein.

31. An isolated mutated ENV protein, or a fragment thereof, according to any one of claims 28 to 30, wherein the ENV protein is HERV-W ENV, such as represented by SEQ ID NO: 74, and the sequence of the mutated HERV-W ENV is selected from:
SEQ ID NO: 116 and SEQ ID NO: 118.

32. An isolated nucleic acid coding for an isolated polypeptide according to any one of claims 1 to 14, for an isolated mutated ENV protein according to any of claims 15 to 31.

33. An isolated nucleic acid according to claim 32, wherein said nucleic acid is represented by a sequence selected from the list comprising:
SEQ ID NO: 103, SEQ ID NO: 105, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 121, SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 145, SEQ ID NO: 147, SEQ ID NO: 149 and SEQ ID NO: 151.

34. A eukaryotic or prokaryotic expression vector, comprising a nucleic acid according to claim 32 or claim 33 as well as the elements necessary for the expression of said nucleic acid.

35. A eukaryotic or prokaryotic expression vector according to claim 34, wherein said vector is a viral vector, in particular a pox vector, including a fowlpox , a canarypox, or a MVA (modified vaccinia virus Ankara) vector, an adenoviral vector, a measles vector, or a CMV (cytomegalovirus) vector.

36. A eukaryotic or prokaryotic expression vector according to claim 34 or claim 35, wherein the vector is a viral vector, in particular a canarypox vector, comprising a nucleic acid sequence coding for an isolated mutated ENV protein, or a fragment thereof, according to claim 32 or claim 33, in particular a mutated FeLV ENV, such as represented by SEQ ID NO: 103 or SEQ ID NO: 105, as well as optionally a nucleic acid coding for a GAG protein originating from the same virus as said mutated ENV.

37. A recombinant cell, comprising a nucleic acid according to claim 32 or claim 33, or a eukaryotic or prokaryotic expression vector according to any one of claims 34 to 36.

38. A pharmaceutical or a vaccine composition comprising as active substance:

at least one isolated polypeptide according to any one of claims 1 to 14, or

at least one isolated mutated ENV protein, or a fragment thereof, according to any one of claims 15 to 31, or

at least one nucleic acid according to claim 32 or claim 33, or

at least one prokaryotic or eukaryotic expression vector according to any one of claims 34 to 36, or

at least one recombinant cell according to claim 37,

in association with a pharmaceutically acceptable carrier.

39. The use of at least one protein comprising or constituted of an isolated mutated ENV protein, or a fragment thereof, according to any one of claims 18 to 22, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of a viral disease, such as HTLV or FeLV infections.

40. The use of at least one protein comprising or constituted of an isolated mutated ENV protein, or a fragment thereof, according to any one of claims 21 to 25, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancer.

41. The use of at least one protein comprising or constituted of an isolated mutated ENV protein, or a fragment thereof, according to any one of claims 28 to 31, or of a nucleic acid coding for said protein, for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of a pathology requiring an inhibition of the immune system, such as an autoimmune disease, allergy or graft rejection.

42. The use of at least one isolated polypeptide according to any one of claims 1 to 14, or of a nucleic acid coding for said isolated polypeptide, for the manufacture of a medicament intended for the prevention and/or the

treatment of cancer, of a viral disease, or of a pathology requiring an inhibition of the immune system, such as an autoimmune disease, allergy or graft rejection.

43. The use of at least one protein or of a nucleic acid coding for said protein, said protein comprising or being constituted of:

- an immunosuppressive ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

wherein amino acids Y_1 to Y_{12} represent any amino acid, amino acid X_1 represents E, K or Q, and amino acid X_2 is such that it ensures that the structure of the viral protein is conserved, preferably X_2 represents A,

- or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of said ENV protein, and has an immunosuppressive activity,
- or a protein derived from said ENV protein presenting at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of the mutated ENV protein,

for the manufacture of a medicament or a vaccine intended for the prevention and/or the treatment of cancer, of a viral disease, or of a pathology requiring an inhibition of the immune system, such as an autoimmune disease, allergy or graft rejection.

44. The use according to claim 43, wherein the ENV protein is selected from:
HERV-T ENV, represented by SEQ ID NO: 84, or
HERV-R ENV, represented by SEQ ID NO: 86, or
HERV-V ENV, represented by SEQ ID NO: 88, or
HERV-R(b) ENV, represented by SEQ ID NO: 90, or

HTLV-1 ENV, represented by SEQ ID NO: 92, or
HTLV-2 ENV, represented by SEQ ID NO: 94, or
FeLV ENV, represented by SEQ ID NO: 96, or
PERV ENV, represented by SEQ ID NO: 98, or
STLV-1 ENV, represented by SEQ ID NO: 100, or
FV ENV, represented by SEQ ID NO: 102.

45. The use of an isolated polypeptide according to any one of claims 1 to 14, or of a protein according to any of claims 15 to 31, for the preparation of ligands of ENV proteins selected from:
- polyclonal or monoclonal antibodies, or fragments thereof, said fragments being Fab or $F(ab)'_2$ fragments,
- scFv polypeptides,
- aptamers,
- binding peptides.

46. An antibody or fragment thereof, scFv polypeptide, aptamer, or binding peptide, directed against mutated ENV proteins according to any one of claims 15 to 31 provided that said antibody or fragment thereof, scFv polypeptide, aptamer, or binding peptide does not bind to the corresponding wild-type ENV proteins.

47. The use of a polypeptide according to any one of claims 1 to 14, or of a protein according to any one of claims 15 to 31, for screening compounds liable to modulate the immunosuppressive activity of a virus or a tumor cell.

48. The use of an antibody or fragments thereof, scFv polypeptide, aptamer, or binding peptide according to claim 46, for screening compounds liable to modulate the immunosuppressive activity of a virus or a tumor cell.

49. The use according to claim 47 or claim 48, wherein the compounds to screen are peptides, in particular peptides comprising from 5 to 30 amino acids, such as peptides originating from combinatorial peptide libraries.

50. A method of preventing and/or treating a viral disease such as HTLV or FeLV infections said method comprising the step of administering to a subject in need thereof at least one protein comprising or constituted of an isolated mutated EMF protein or a fragment thereof according to any one of claims 18 to 22 or a nucleic acid coding for said protein.

51. A method of preventing and/or treating cancer said method comprising a step of administering to a subject in need thereof at least one protein comprising or constituted of an isolated mutated EMF protein or a fragment thereof according to any one of claims 21 to 25 or a nucleic acid coding for said protein.

52. A method of preventing and/or treating a pathology requiring an inhibition of the immune system including an autoimmune disease, allergy or graft rejection said method comprising the step of administering to a subject in need thereof at least one protein comprising or constituted of an isolated mutated EMF protein or a fragment thereof according to any one of claims 28 to 31 or a nucleic acid coding for said protein.

53. A method of preventing and/or treating cancer, a viral disease or a pathology requiring an inhibition of the immune system such as an autoimmune disease, allergy or graft rejection said method comprising the step of administering to a subject in need thereof at least one isolated polypeptide according to any one of claims 1 to 14 or a nucleic acid coding for said polypeptide.

54. A method of preventing and/or treating cancer, a viral disease or a pathology requiring an inhibition of the immune system such as an

autoimmune disease, allergy or graft rejection, said method comprising the step of administering to a subject in need thereof at least one protein or nucleic acid coding for said protein comprising or constituted of

- an immunosuppressive ENV protein essentially comprising the following sequence:

$$NY_1Y_2Y_3LY_4Y_5LY_6Y_7Y_8X_1Y_9Y_{10}Y_{11}CY_{12}X_2,$$

wherein amino acids Y_1 to Y_{12} represent any amino acid, amino acid X_1 represents E, K or Q, and amino acid X_2 is such that it ensures that the structure of the viral protein is conserved, preferably X_2 represents A,

- or a fragment thereof that is at least 7 amino acids long, provided that said fragment carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of said ENV protein, and has an immunosuppressive activity,
- or a protein derived from said ENV protein presenting at least 80% sequence identity, in particular 90% sequence identity with said mutated ENV, or fragments thereof, by insertion, deletion or substitution of at least one amino acid, provided that said derived protein carries amino acid X_1 and optionally X_2, and that it has an immunosuppressive activity similar to that of the mutated ENV protein.

55. An isolated polypeptide according to claim 1; an isolated mutated ENV protein according to claim 15 or 28; a eukaryotic or prokaryotic expression vector according to claim 34; a recombinant cell according to claim 37; a pharmaceutical or vaccine composition according to claim 38; a use according to any one of claims 39 to 43; an antibody or fragment thereof according to claim 46; or a method of preventing and/or treating a disease according to any one of claims 50 to 54, substantially as herein described with reference to any one or more of the examples but excluding comparative examples.

phCMV-envMoMLV -> Graphic Map

DNA sequence 6859 bp GCGGCCGCTCTA ... TCCACCGCGGTG circular

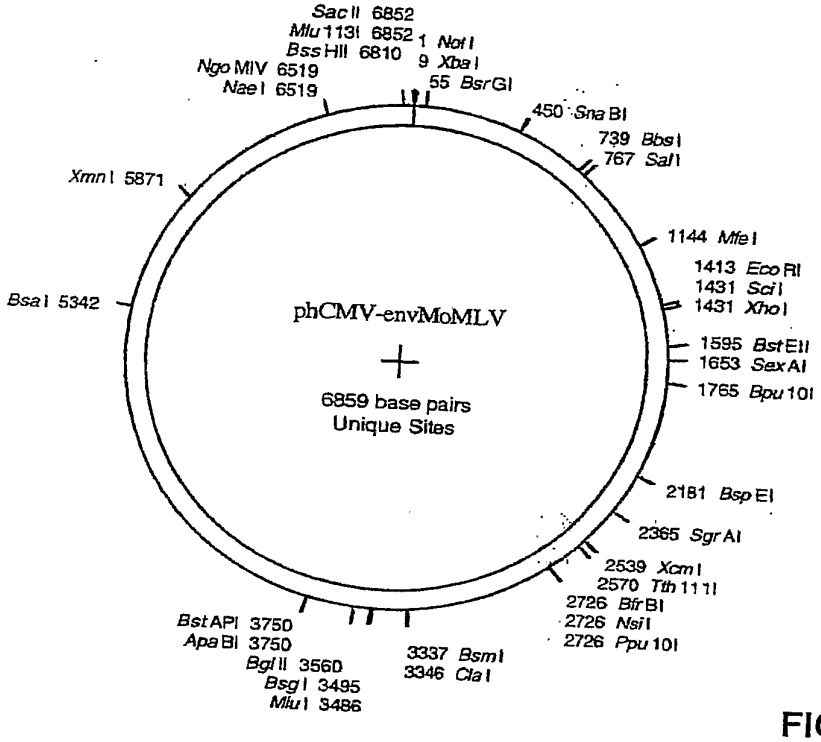

FIG 1A

pDFG-envMoMLV-iresHygro -> Graphic Map

DNA sequence 11787 bp GGATTAGTCCAA ... ACCGGATCCGCG circular

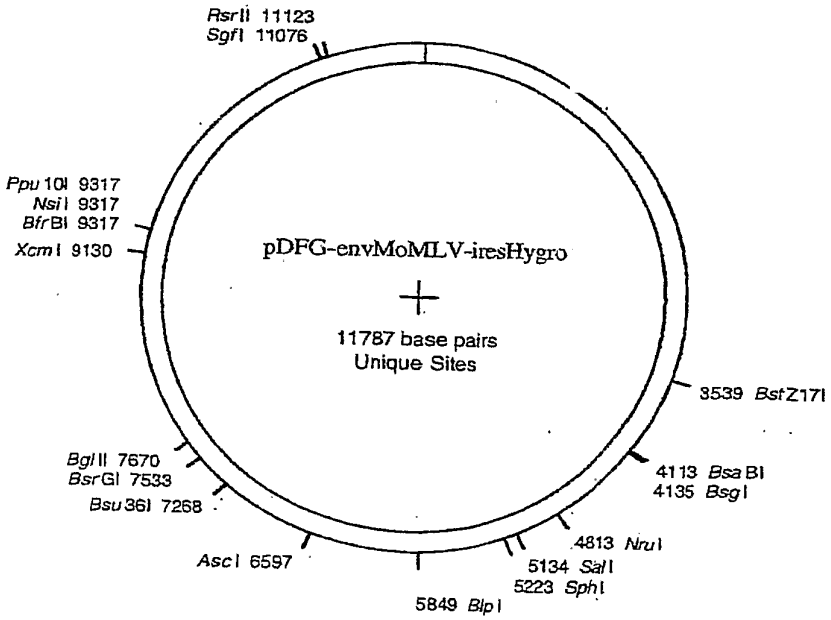

FIG 1B

phCMV-envMPMV -> Graphic Map

DNA sequence 6589 bp GCGGCCGCTCTA ... TCCACCGCGGTG circular

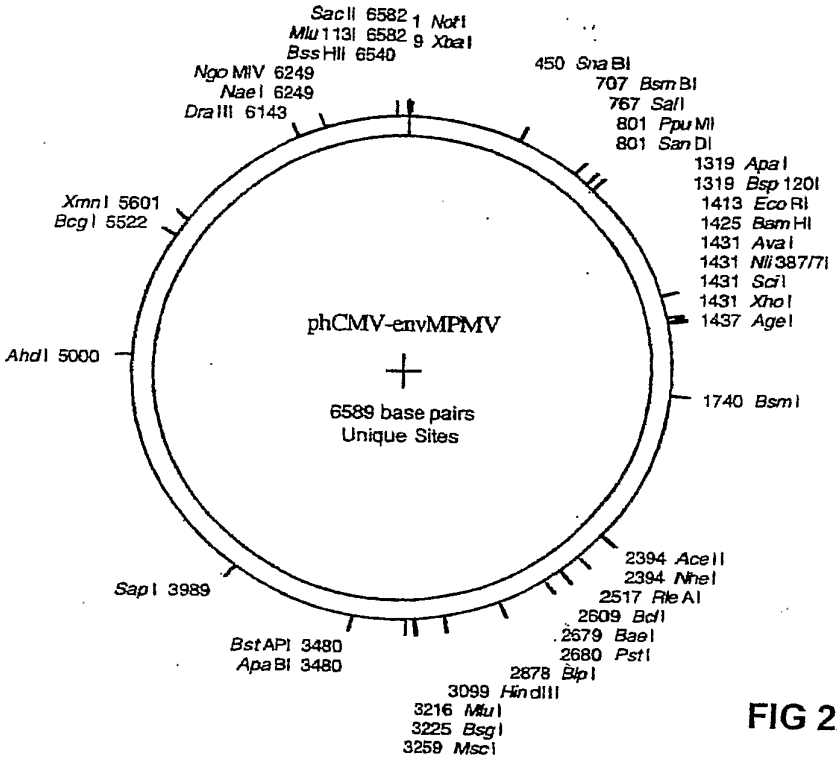

FIG 2A

pDFG-envMPMV-iresHygro -> Graphic Map

DNA sequence 11293 bp GGATCCGCGGGA ... GGAGACAATACC circular

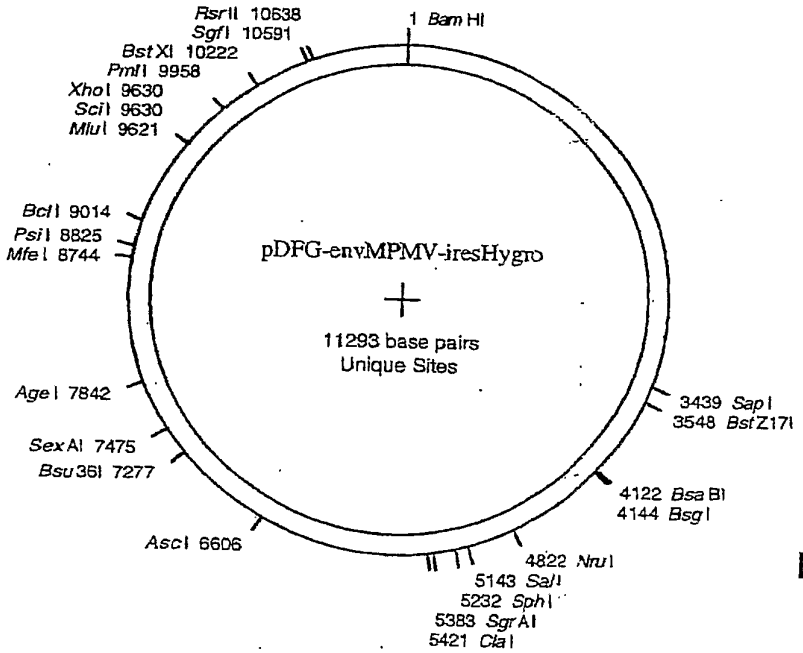

FIG 2B

phCMV-EnvW -> Graphic Map

DNA sequence 6570 bp GCGGCCGCTCTA ... TCCACCGCGGTG circular

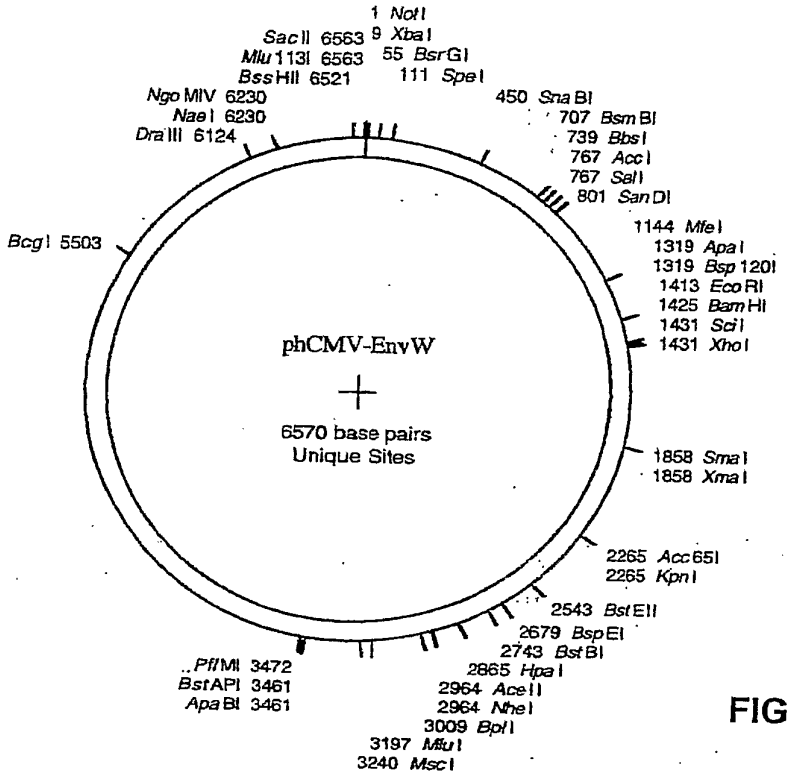

FIG 3A

pDFG-envW-iresHygro -> Graphic Map

DNA sequence 11383 bp GGATCCGCGGGA ... GGAGACAATACC circular

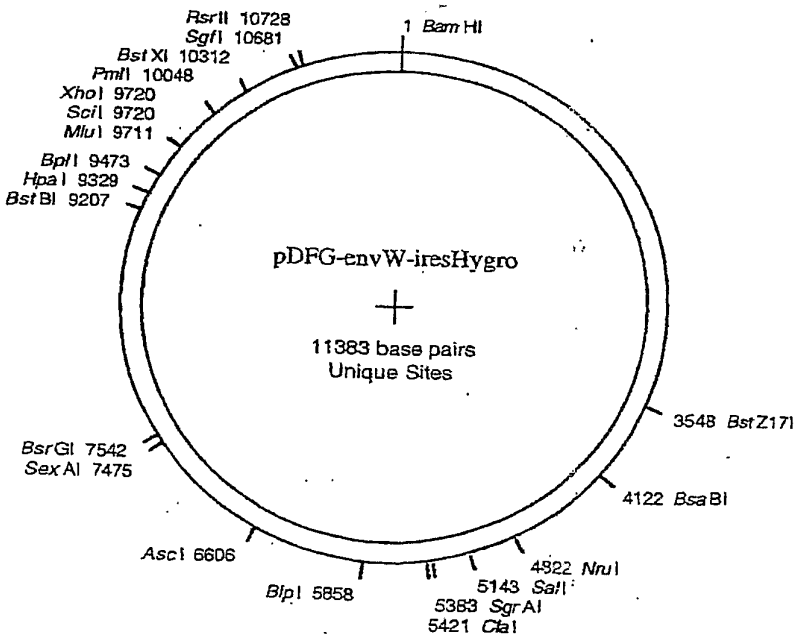

FIG 3B

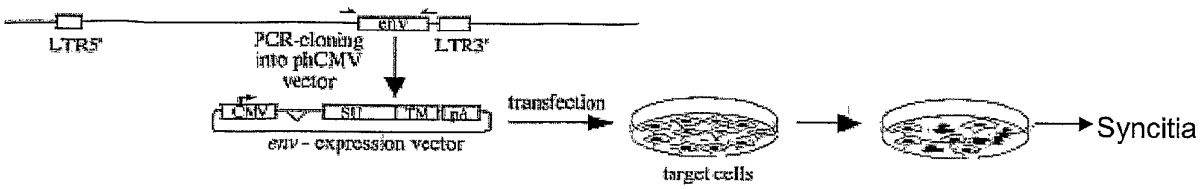

Figure 4

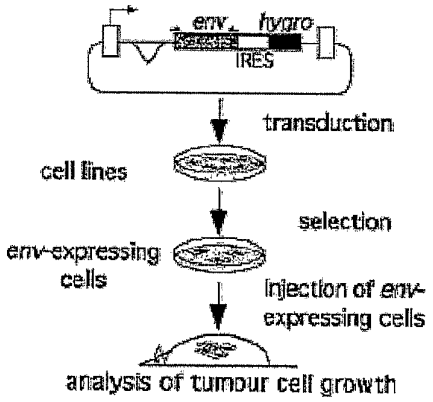

Figure 5

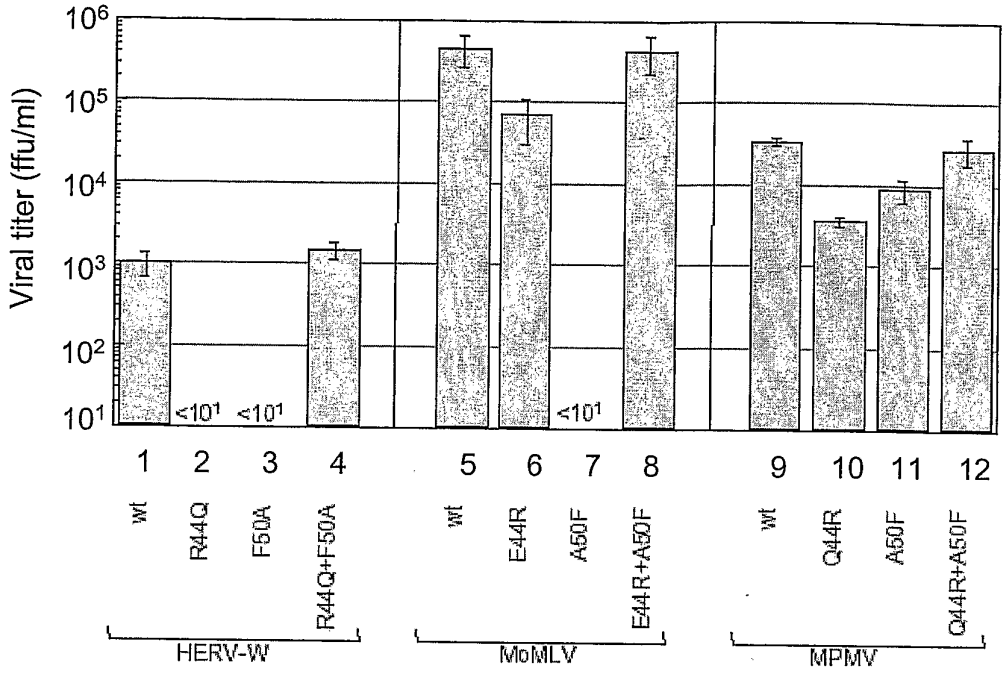

Figure 6

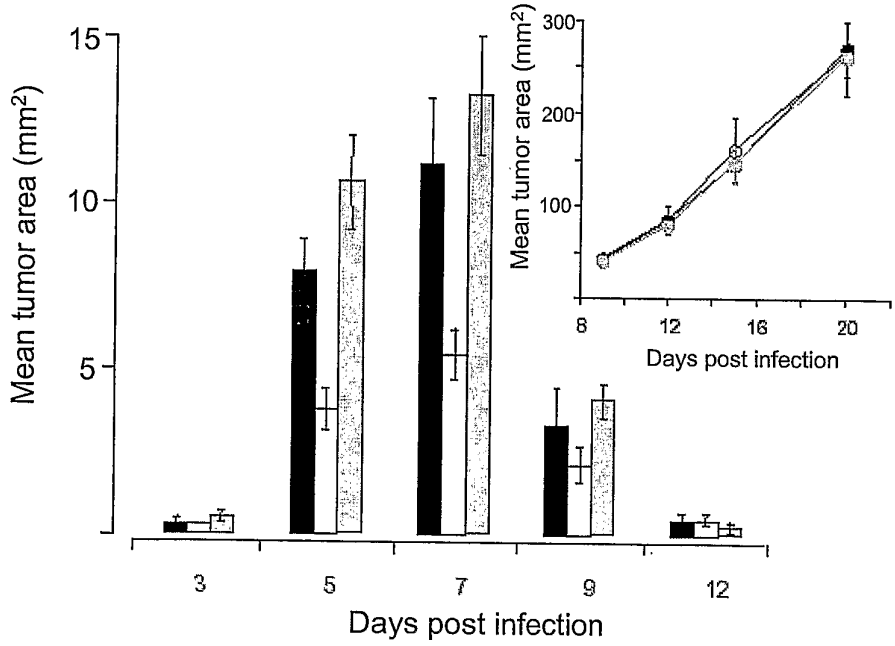

Figure 7

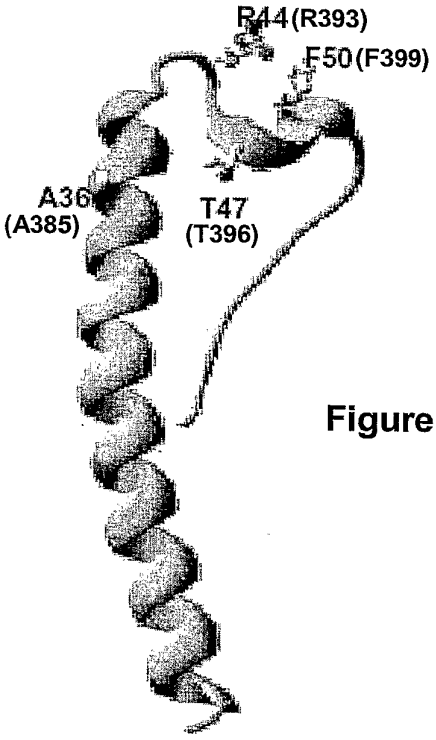

Figure 8

Name	Origin	Nucleotide sequence	Accession Number
HERV-T	Human endogenous	LQNCRCLDLLFLS**Q**GGLCA**A**	AC 078 899
HTLV-1	Human retrovirus	AQNRRGLDLLFWE**Q**GGLCK**A**	AY 324 800
STLV-1	Simian retrovirus	AQNRRGLDLLFWE**Q**GGLCK**A**	AY 324 800
HERV-FRD	Human endogenous	LQNRRGLDMLTAA**Q**GGLCL**A**	AL 136 139
MPMV	Human retrovirus	LQNRRGLDLLTAE**Q**GGICL**A**	AF 033 815
Fowlpox	Poxvirus	LQNRRGLDLLTAE**Q**GGICL**A**	NC_002 188
MoMLV	Human retrovirus	LQNRRGLDLLFLK**E**GGLCA**A**	AF 033 811
Friend	Human retrovirus	LQNRRGLDLLFLK**E**GGLCA**A**	M 90 673
PyERV	python endogenous	LQNRRGLDLLFLK**E**GGLCV**A**	AF 500 297
PERV	porcine endogenous	LQNRRGLDLLFLK**E**GGLCV**A**	AY 364 236
FeLV	feline leukaemia virus	LQNRRGLDILFLQ**E**GGLCA**A**	M 18248
SSAV	Simian Sarcoma-associated virus	LQNRRGLDLLFLK**E**GGLCA**A**	J 02396
GLV-X	Gibbon leukemia virus X	LQNRRGLDLLFLK**E**GGLCA**A**	U 60065
EBOLA	Filovirus	ILNRKAIDFLLQR**W**GGTCH**I**	EVU 31033
Marburg	Filovirus	LINRHAIDFLLTR**W**GGTCK**V**	MVVIRPR
HERV-W	Human endogenous	LQNRRALDLLTAE**R**GGTCL**F**	AF 072 503
HERV-W	Human endogenous	LQNWRALDLLTAK**R**GGTCL**F**	
HERV-W	Human endogenous	LQNWRALDLLIAK**R**GGTCV**F**	
HERV-H1	Human endogenous	LQNRRGLDLLTAE**K**GGLCI**F**	AJ 289 709
HERV-F(c)1	Human endogenous	MQNRRALDLLTAD**K**GGTCM**F**	AL 354 685
HERV-F(c)2	Human endogenous	AQNRQALDLLMAE**K**GRTCL**F**	AC 016 222

Figure 9

Figure 10

A. Nucleotide sequence encoding envMoMLV

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AGGCCCCCTAATCCCCTTAATTCTTCTGATGCTCAGAGGGGTCAGTACTG
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ACCAATGGAGATCGGGAGACGGTATGGGCAACTTCTGGCAACCACCCTCT
GTGGACCTGGTGGCCTGACCTTACCCCAGATTTATGTATGTTAGCCCACC
ATGGACCATCTTATTGGGGGCTAGAATATCAATCCCCTTTTTCTTCTCCC
CCGGGGCCCCCTTGTTGCTCAGGGGGCAGCAGCCCAGGCTGTTCCAGAGA
CTGCGAAGAACCTTTAACCTCCCTCACCCCTCGGTGCAACACTGCCTGGA
ACAGACTCAAGCTAGACCAGACAACTCATAAATCAAATGAGGGATTTTAT
GTTTGCCCCGGGCCCCACCGCCCCCGAGAATCCAAGTCATGTGGGGGTCC
AGACTCCTTCTACTGTGCCTATTGGGGCTGTGAGACAACCGGTAGAGCTT
ACTGGAAGCCCTCCTCATCATGGGATTTCATCACAGTAAACAACAATCTC
ACCTCTGACCAGGCTGTCCAGGTATGCAAAGATAATAAGTGGTGCAACCC
CTTAGTTATTCGGTTTACAGACGCCGGGAGACGGGTTACTTCCTGGACCA
CAGGACATTACTGGGGCTTACGTTTGTATGTCTCCGGACAAGATCCAGGG
CTTACATTTGGGATCCGACTCAGATACCAAAATCTAGGACCCCGCGTCCC
AATAGGGCCAAACCCCGTTCTGGCAGACCAACAGCCACTCTCCAAGCCCA
AACCTGTTAAGTCGCCTTCAGTCACCAAACCACCCAGTGGGACTCCTCTC
TCCCCTACCCAACTTCCACCGGCGGGAACGGAAAATAGGCTGCTAAACTT
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AAGAGTGCTGGTTGTGTCTAGTAGCGGGACCCCCCTACTACGAAGGGGTT
GCCGTCCTGGGTACCTACTCCAACCATACCTCTGCTCCAGCCAACTGCTC
CGTGGCCTCCCAACACAAGTTGACCCTGTCCGAAGTGACCGGACAGGGAC
TCTGCATAGGAGCAGTTCCCAAAACACATCAGGCCCTATGTAATACCACC
CAGACAAGCAGTCGAGGGTCCTATTATCTAGTTGCCCCTACAGGTACCAT
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ACCTTACCACTGATTATTGTGTTCTTGTCGAACTCTGGCCAAGAGTCACC
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CTGAAGTTGTCCTACAGAATCGAAGGGGCCTAGACTTGTTATTTCTAAAA
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CCACACAGGACTAGTGAGAGACAGCATGGCCAAATTGAGAGAGAGGCTTA
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TTGACTCAACAATATCACCAGCTGAAGCCTATAGAGTACGAGCCATAG

B. Protein sequence of envMoMLV

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VCPGPHRPRESKSCGGPDSFYCAYWGCETTGRAYWKPSSSWDFITVNNNL
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C. Nucleotide sequence encoding envMPMV

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D. Protein sequence of envMPMV

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DSLAEVVLQNRRGLDLLTAEQGGICLALQEKCCFYANKSGIVRDKIKNLQ
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MTFIKHQIESIQAKPIQVHYHRLEQEDSGGSYLTLT*

E. Nucleotide sequence encoding envHERV-W (envW)

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CAGCAGGAAGCAGTTAG

F. Protein sequence of envHERV-W (envW)

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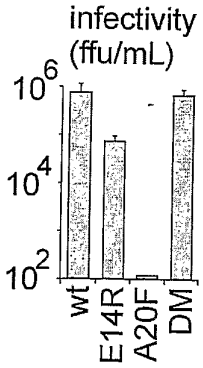


Figure 11A

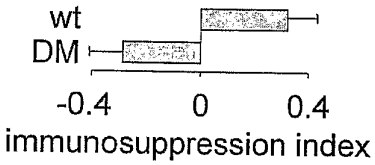


Figure 11B

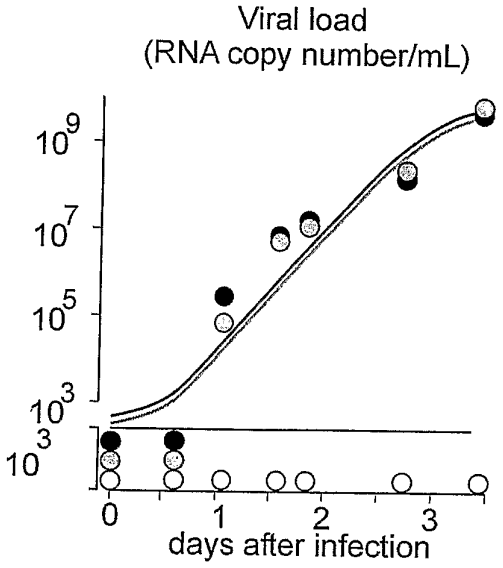


Figure 11C

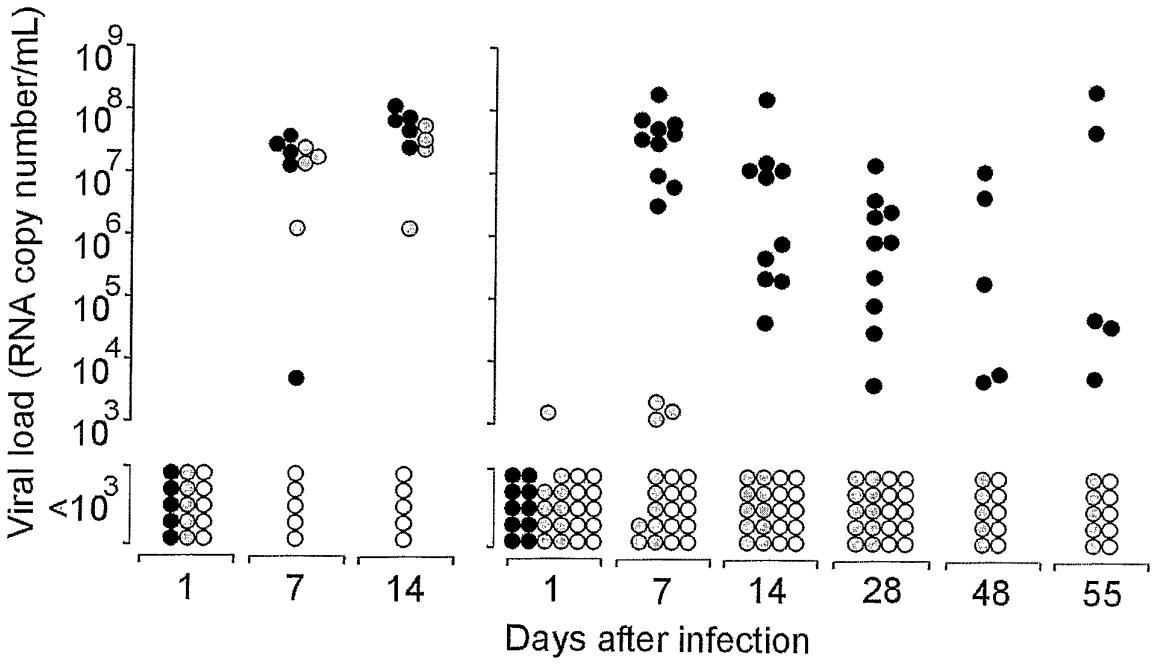


Figure 12A

Figure 12B

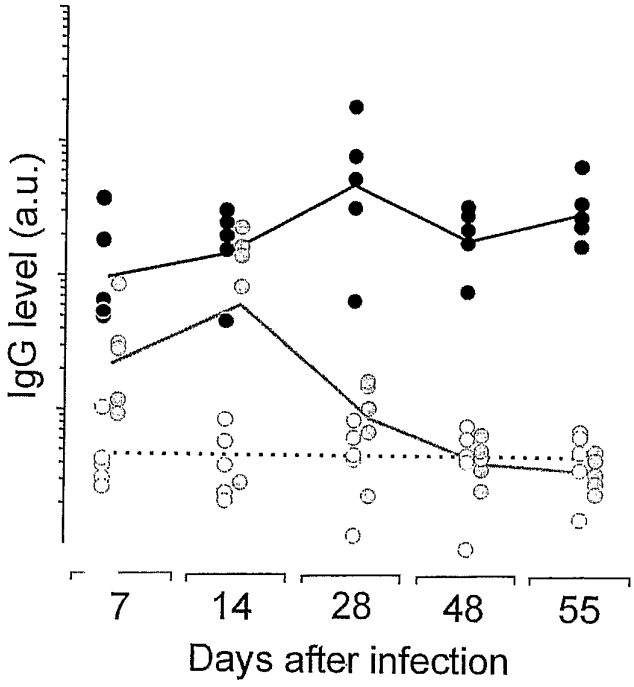


Figure 13

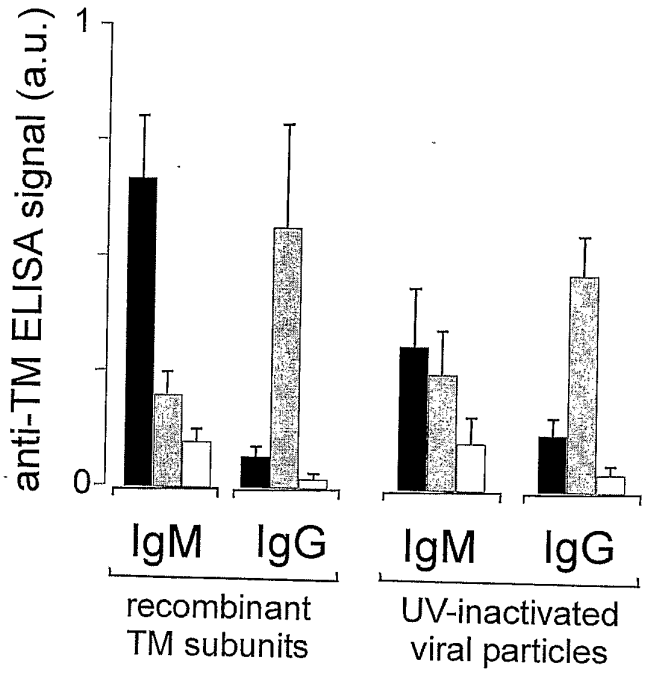


Figure 14A

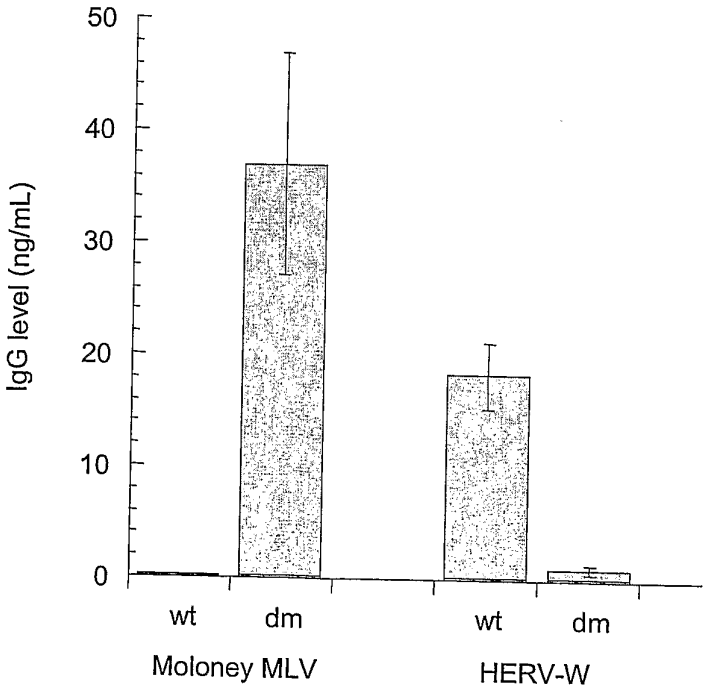


Figure 14B

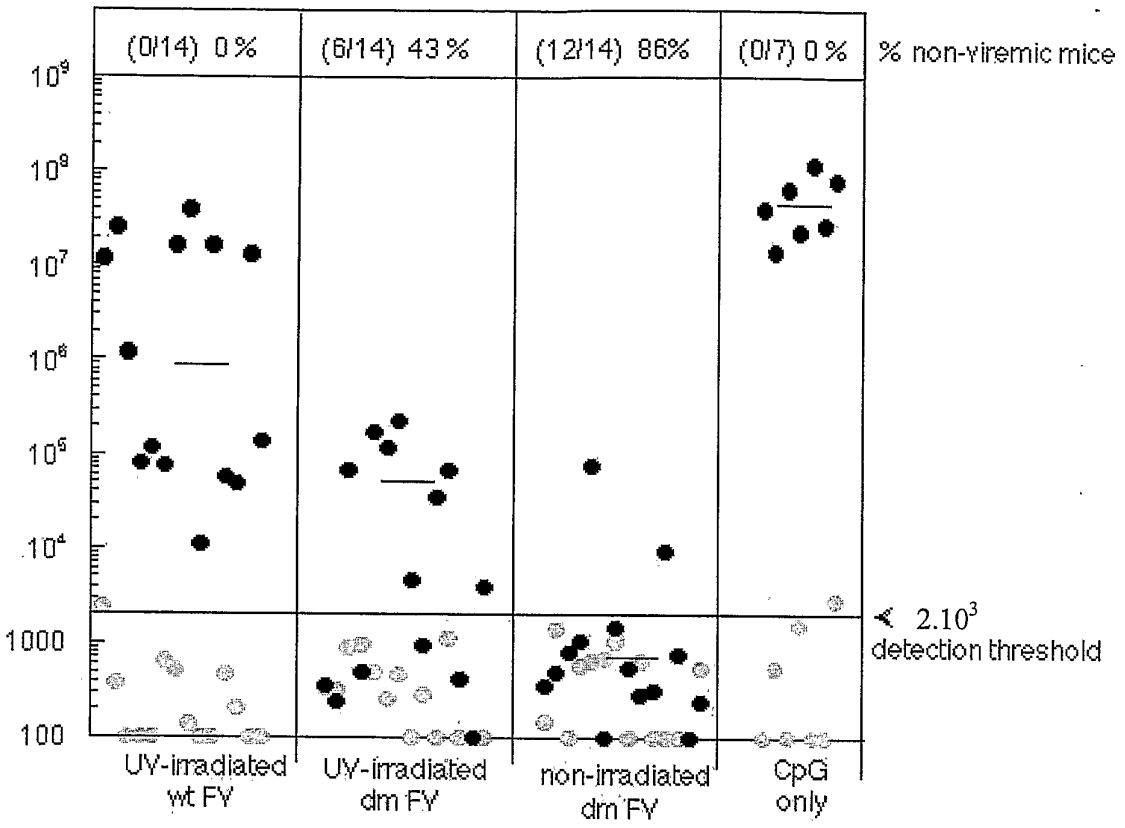

(0/14) 0 %
(6/14) 43 %
(12/14) 86%
(0/7) 0 %
% non-viremic mice
10^9
10^8
10^7
10^6
10^5
10^4
1000
100
< 2.10^3
detection threshold
UV-irradiated wt FV
UV-irradiated dm FV
non-irradiated dm FV
CpG only

Figure 15

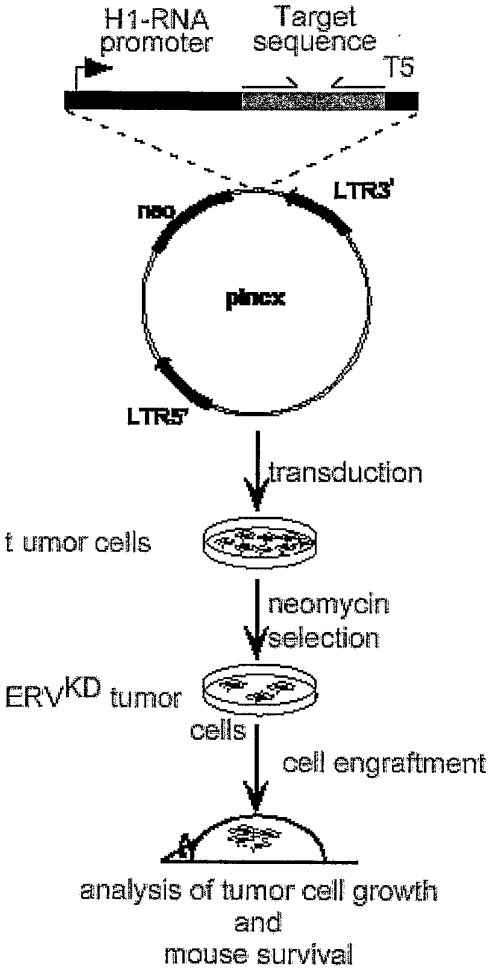


Figure 16A

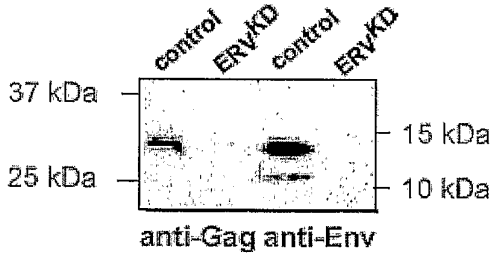
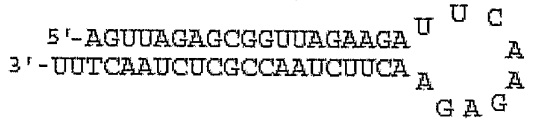


Figure 16C

predicted transcripts against ERV (1220-1238)



predicted control transcripts against GFP (215-233)

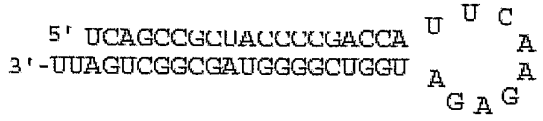


Figure 16B

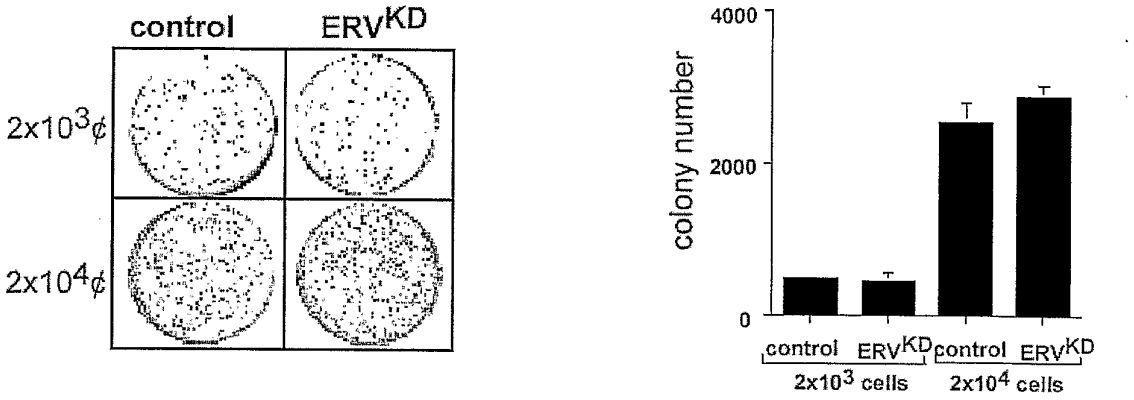


Figure 17A

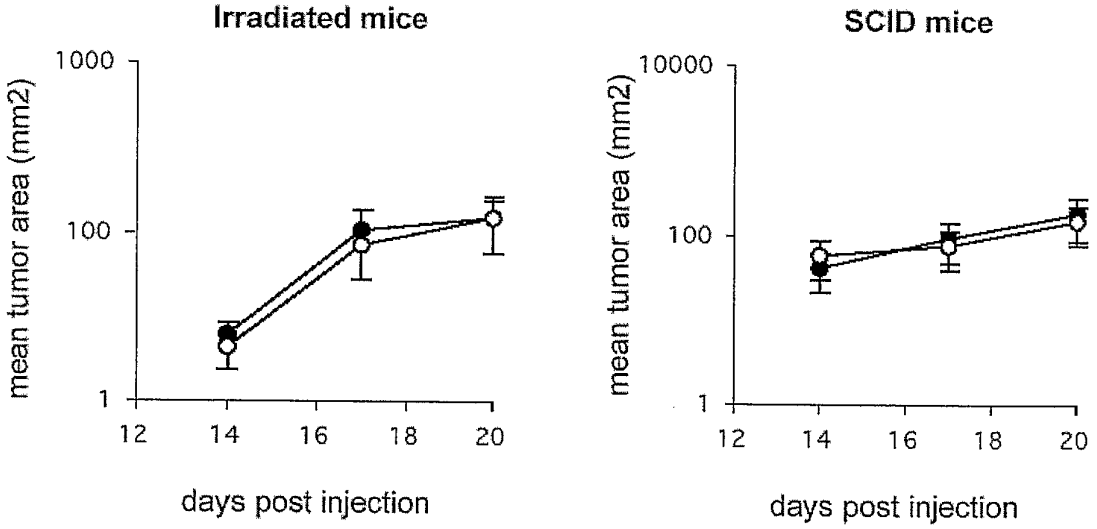


Figure 17B

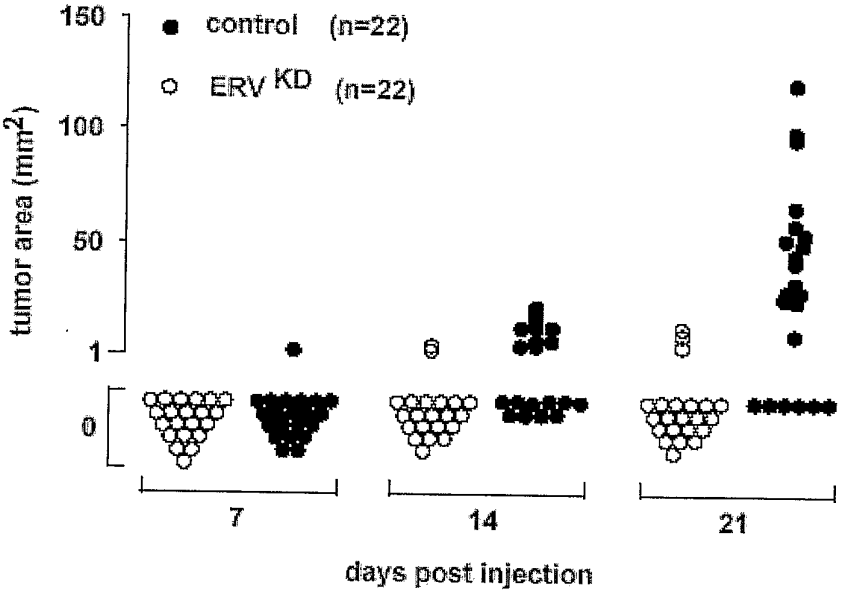


Figure 18A

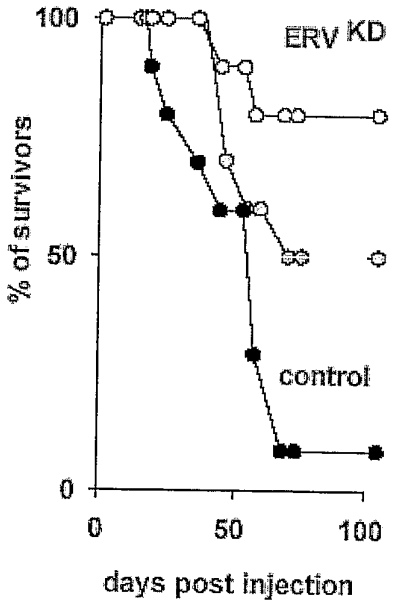


Figure 18B

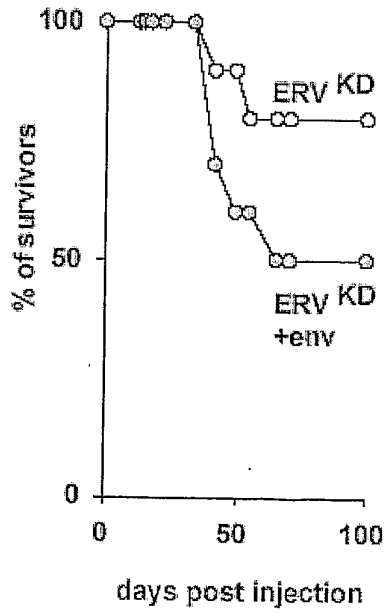


Figure 18C

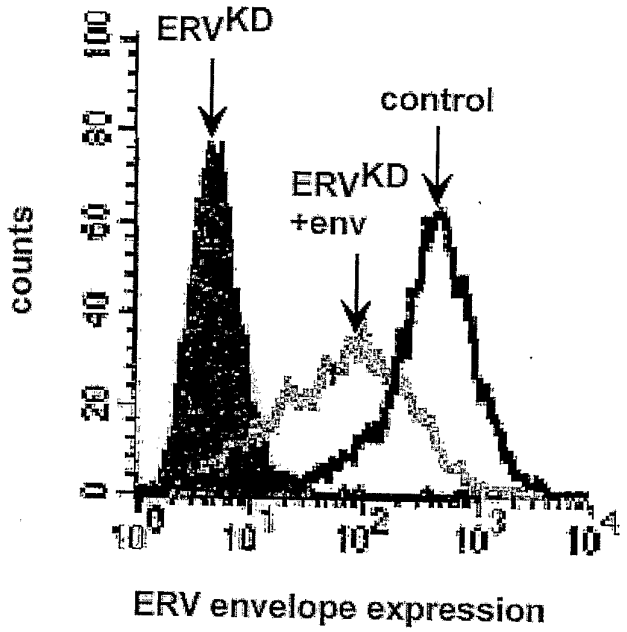


Figure 19

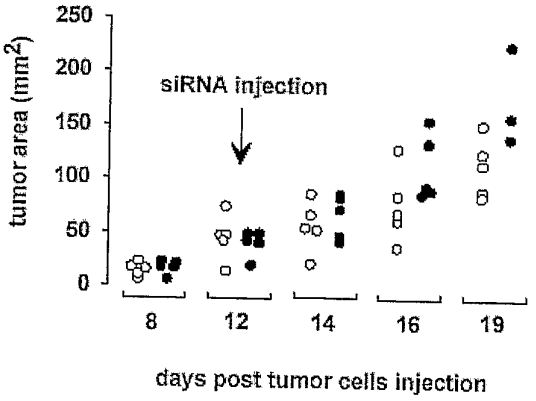


Figure 20A

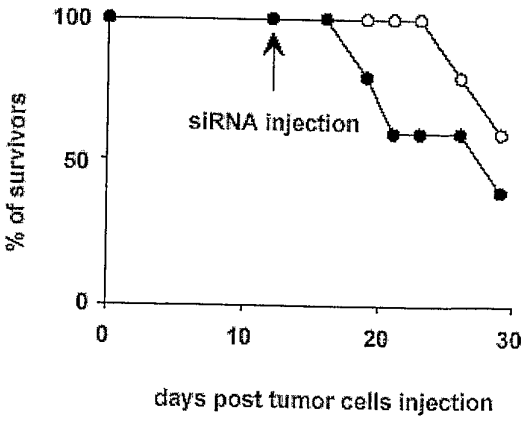


Figure 20B

SEQUENCE LISTING

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CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE

UNIVERSITE PARIS XI

<120> POLYPEPTIDE SEQUENCE INVOLVED IN THE MODULATION OF THE IMMUNOSUPPRESSIVE EFFECT OR VIRAL PROTEINS

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Glu Gly Gly Leu Cys Ala Ala
1 5

<210> 22
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 22
Glu Gly Gly Leu Cys Val Ala
1 5

<210> 23
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 23
Arg Gly Gly Thr Cys Leu Phe
1 5

<210> 24
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 24
Lys Gly Gly Thr Cys Met Phe
1 5

<210> 25
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 25
Lys Gly Arg Thr Cys Leu Phe
1 5

<210> 26
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 26
Lys Gly Gly Leu Cys Ile Phe
1 5

<210> 27
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 27
Arg Gly Gly Leu Cys Lys Phe
1 5

<210> 28
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 28
Arg Gly Gly Leu Cys Ala Phe
1 5

<210> 29
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 29
Arg Gly Gly Leu Cys Leu Phe
1 5

<210> 30
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 30
Arg Gly Gly Ile Cys Leu Phe
1 5

<210> 31
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic

peptide

<400> 31
Arg Gly Gly Leu Cys Val Phe
1 5

<210> 32
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 32
Arg Gly Gly Thr Cys Val Phe
1 5

<210> 33
<211> 20
<212> PRT
<213> human T-cell leukaemia virus type 1

<400> 33
Ala Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Trp Glu Gln Gly Gly
1 5 10 15

Leu Cys Lys Ala
20

<210> 34
<211> 20
<212> PRT
<213> human endogenous retrovirus T

<400> 34
Leu Gln Asn Cys Arg Cys Leu Asp Leu Leu Phe Leu Ser Gln Gly Gly
1 5 10 15

Leu Cys Ala Ala
20

<210> 35
<211> 20
<212> PRT
<213> Human endogenous retrovirus FRD

<400> 35
Leu Gln Asn Arg Arg Gly Leu Asp Met Leu Thr Ala Ala Gln Gly Gly
1 5 10 15

Leu Cys Leu Ala
20

<210> 36
<211> 20
<212> PRT
<213> Mason-Pfizer monkey virus

<400> 36
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Thr Ala Glu Gln Gly Gly
1 5 10 15

Ile Cys Leu Ala
20

<210> 37
<211> 20
<212> PRT
<213> Feline leukemia virus

<400> 37
Leu Gln Asn Arg Arg Gly Leu Asp Ile Leu Phe Leu Gln Glu Gly Gly
1 5 10 15

Leu Cys Ala Ala
20

<210> 38
<211> 20
<212> PRT
<213> Moloney murine leukaemia virus

<400> 38
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly
1 5 10 15

Leu Cys Ala Ala
20

<210> 39
<211> 20
<212> PRT
<213> Porcine endogenous retrovirus

<400> 39
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly
1 5 10 15

Leu Cys Val Ala
20

<210> 40
<211> 20
<212> PRT
<213> Human endogenous retrovirus W

<400> 40
Leu Gln Asn Arg Arg Ala Leu Asp Leu Leu Thr Ala Glu Arg Gly Gly
1 5 10 15

Thr Cys Leu Phe
20

<210> 41
<211> 20
<212> PRT
<213> Human endogenous retrovirus W

<400> 41
Leu Gln Asn Trp Arg Ala Leu Asp Leu Leu Thr Ala Lys Arg Gly Gly
1 5 10 15

Thr Cys Leu Phe
20

<210> 42
<211> 20
<212> PRT
<213> Human endogenous retrovirus W

<400> 42
Leu Gln Asn Trp Arg Ala Leu Asp Leu Leu Ile Ala Lys Arg Gly Gly
1 5 10 15

Thr Cys Val Phe
20

<210> 43
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 43
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Thr Ala Glu Arg Gly Gly
1 5 10 15

Thr Cys Leu Phe
20

<210> 44
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 44
Leu Gln Asn Arg Arg Ala Leu Asp Leu Leu Thr Ala Glu Arg Gly Gly
1 5 10 15

Ile Cys Leu Phe
20

<210> 45
<211> 20
<212> PRT
<213> Human endogenous retrovirus H1

<400> 45
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Thr Ala Glu Lys Gly Gly
1 5 10 15

Leu Cys Ile Phe

20

<210> 46
<211> 20
<212> PRT
<213> Human endogenous retrovirus Fc(1)

<400> 46
Met Gln Asn Arg Arg Ala Leu Asp Leu Leu Thr Ala Asp Lys Gly Gly
1 5 10 15

Thr Cys Met Phe
20

<210> 47
<211> 20
<212> PRT
<213> Human endogenous retrovirus Fc(2)

<400> 47
Ala Gln Asn Arg Gln Ala Leu Asp Leu Leu Met Ala Glu Lys Gly Arg
1 5 10 15

Thr Cys Leu Phe
20

<210> 48
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 48
Ala Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Trp Glu Arg Gly Gly
1 5 10 15

Leu Cys Lys Phe
20

<210> 49
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 49
Leu Gln Asn Cys Arg Cys Leu Asp Leu Leu Phe Leu Ser Arg Gly Gly
1 5 10 15

Leu Cys Ala Phe
20

<210> 50
<211> 20

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 50
Leu Gln Asn Arg Arg Gly Leu Asp Met Leu Thr Ala Ala Arg Gly Gly
1 5 10 15

Leu Cys Leu Phe
20

<210> 51
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 51
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Thr Ala Glu Arg Gly Gly
1 5 10 15

Ile Cys Leu Phe
20

<210> 52
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 52
Leu Gln Asn Arg Arg Gly Leu Asp Ile Leu Phe Leu Gln Arg Gly Gly
1 5 10 15

Leu Cys Ala Phe
20

<210> 53
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 53
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Arg Gly Gly
1 5 10 15

Leu Cys Ala Phe
20

<210> 54
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 54
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Arg Gly Gly
1 5 10 15

Leu Cys Val Phe
20

<210> 55
<211> 58
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: oligonucleotide

<400> 55
atacatctcg agaccggtcc aactagaacc atgaacttca ttatcattt catctgga 58

<210> 56
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: oligonucleotide

<400> 56
atacatacgc gtctatgtta aggtcaaata tgagccacc 39

<210> 57
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: oligonucleotide

<400> 57
tagtccttca aatcgccgcg gtttagactt gctaa 35

<210> 58
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: oligonucleotide

<400> 58
acaaggggggt acctgtttat ttttagggga aga 33

<210> 59
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:
oligonucleotide

<400> 59
ccgctgaaag agggggcata tgtttatttt tagggga 37

<210> 60
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:
oligonucleotide

<400> 60
aaccgctgaa agaggggggta cctgtttagc tttaggggaa ga 42

<210> 61
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:
oligonucleotide

<400> 61
aaccgctgaa caaggggggta cctgtttagc tttaggggaa ga 42

<210> 62
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 62
cttcggcgtc tctcgagaga cgccgaag 28

<210> 63
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 63

caaaacagaa gaggattaga tctacttaca gc 32

<210> 64
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 64
tacttacagc agagagagga ggtatctgct tag 33

<210> 65
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 65
gggaggtatc tgcttatttt tacaggaaaa atgtt 35

<210> 66
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 66
acttacagca gagagaggag gtatctgctt atttttacag gaaaaatg 48

<210> 67
<211> 20
<212> PRT
<213> Ebola virus

<400> 67
Ile Leu Asn Arg Lys Ala Ile Asp Phe Leu Leu Gln Arg Trp Gly Gly
1 5 10 15

Thr Cys His Ile
20

<210> 68
<211> 20
<212> PRT
<213> Marburg virus

<400> 68
Leu Ile Asn Arg His Ala Ile Asp Phe Leu Leu Thr Arg Trp Gly Gly
1 5 10 15

Thr Cys Lys Val
20

<210> 69
<211> 1998
<212> DNA
<213> Moloney murine leukaemia virus

<220>
<221> CDS
<222> (1)..(1998)
<223> coding sequence of envelope protein

<400> 69

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atg gcg cgt tca acg ctc tca aaa ccc ctt aaa aat aag gtt aac ccg   48
Met Ala Arg Ser Thr Leu Ser Lys Pro Leu Lys Asn Lys Val Asn Pro
  1               5                  10                  15

cga ggc ccc cta atc ccc tta att ctt ctg atg ctc aga ggg gtc agt   96
Arg Gly Pro Leu Ile Pro Leu Ile Leu Leu Met Leu Arg Gly Val Ser
            20                  25                  30

act gct tcg ccc ggc tcc agt cct cat caa gtc tat aat atc acc tgg   144
Thr Ala Ser Pro Gly Ser Ser Pro His Gln Val Tyr Asn Ile Thr Trp
        35                  40                  45

gag gta acc aat gga gat cgg gag acg gta tgg gca act tct ggc aac   192
Glu Val Thr Asn Gly Asp Arg Glu Thr Val Trp Ala Thr Ser Gly Asn
    50                  55                  60

cac cct ctg tgg acc tgg tgg cct gac ctt acc cca gat tta tgt atg   240
His Pro Leu Trp Thr Trp Trp Pro Asp Leu Thr Pro Asp Leu Cys Met
65                  70                  75                  80

tta gcc cac cat gga cca tct tat tgg ggg cta gaa tat caa tcc cct   288
Leu Ala His His Gly Pro Ser Tyr Trp Gly Leu Glu Tyr Gln Ser Pro
                85                  90                  95

ttt tct tct ccc ccg ggg ccc cct tgt tgc tca ggg ggc agc agc cca   336
Phe Ser Ser Pro Pro Gly Pro Pro Cys Cys Ser Gly Gly Ser Ser Pro
            100                 105                 110

ggc tgt tcc aga gac tgc gaa gaa cct tta acc tcc ctc acc cct cgg   384
Gly Cys Ser Arg Asp Cys Glu Glu Pro Leu Thr Ser Leu Thr Pro Arg
        115                 120                 125

tgc aac act gcc tgg aac aga ctc aag cta gac cag aca act cat aaa   432
Cys Asn Thr Ala Trp Asn Arg Leu Lys Leu Asp Gln Thr Thr His Lys
    130                 135                 140

tca aat gag gga ttt tat gtt tgc ccc ggg ccc cac cgc ccc cga gaa   480
Ser Asn Glu Gly Phe Tyr Val Cys Pro Gly Pro His Arg Pro Arg Glu
145                 150                 155                 160

tcc aag tca tgt ggg ggt cca gac tcc ttc tac tgt gcc tat tgg ggc   528
Ser Lys Ser Cys Gly Gly Pro Asp Ser Phe Tyr Cys Ala Tyr Trp Gly
                165                 170                 175

tgt gag aca acc ggt aga gct tac tgg aag ccc tcc tca tca tgg gat   576
Cys Glu Thr Thr Gly Arg Ala Tyr Trp Lys Pro Ser Ser Ser Trp Asp
            180                 185                 190

ttc atc aca gta aac aac aat ctc acc tct gac cag gct gtc cag gta   624
Phe Ile Thr Val Asn Asn Asn Leu Thr Ser Asp Gln Ala Val Gln Val
        195                 200                 205

tgc aaa gat aat aag tgg tgc aac ccc tta gtt att cgg ttt aca gac   672
Cys Lys Asp Asn Lys Trp Cys Asn Pro Leu Val Ile Arg Phe Thr Asp
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    210                 215                 220

gcc ggg aga cgg gtt act tcc tgg acc aca gga cat tac tgg ggc tta   720
Ala Gly Arg Arg Val Thr Ser Trp Thr Thr Gly His Tyr Trp Gly Leu
225                 230                 235                 240

cgt ttg tat gtc tcc gga caa gat cca ggg ctt aca ttt ggg atc cga   768
Arg Leu Tyr Val Ser Gly Gln Asp Pro Gly Leu Thr Phe Gly Ile Arg
                245                 250                 255

ctc aga tac caa aat cta gga ccc cgc gtc cca ata ggg cca aac ccc   816
Leu Arg Tyr Gln Asn Leu Gly Pro Arg Val Pro Ile Gly Pro Asn Pro
            260                 265                 270

gtt ctg gca gac caa cag cca ctc tcc aag ccc aaa cct gtt aag tcg   864
Val Leu Ala Asp Gln Gln Pro Leu Ser Lys Pro Lys Pro Val Lys Ser
        275                 280                 285

cct tca gtc acc aaa cca ccc agt ggg act cct ctc tcc cct acc caa   912
Pro Ser Val Thr Lys Pro Pro Ser Gly Thr Pro Leu Ser Pro Thr Gln
    290                 295                 300

ctt cca ccg gcg gga acg gaa aat agg ctg cta aac tta gta gac gga   960
Leu Pro Pro Ala Gly Thr Glu Asn Arg Leu Leu Asn Leu Val Asp Gly
305                 310                 315                 320

gcc tac caa gcc ctc aac ctc acc agt cct gac aaa acc caa gag tgc  1008
Ala Tyr Gln Ala Leu Asn Leu Thr Ser Pro Asp Lys Thr Gln Glu Cys
                325                 330                 335

tgg ttg tgt cta gta gcg gga ccc ccc tac tac gaa ggg gtt gcc gtc  1056
Trp Leu Cys Leu Val Ala Gly Pro Pro Tyr Tyr Glu Gly Val Ala Val
            340                 345                 350

ctg ggt acc tac tcc aac cat acc tct gct cca gcc aac tgc tcc gtg  1104
Leu Gly Thr Tyr Ser Asn His Thr Ser Ala Pro Ala Asn Cys Ser Val
        355                 360                 365

gcc tcc caa cac aag ttg acc ctg tcc gaa gtg acc gga cag gga ctc  1152
Ala Ser Gln His Lys Leu Thr Leu Ser Glu Val Thr Gly Gln Gly Leu
    370                 375                 380

tgc ata gga gca gtt ccc aaa aca cat cag gcc cta tgt aat acc acc  1200
Cys Ile Gly Ala Val Pro Lys Thr His Gln Ala Leu Cys Asn Thr Thr
385                 390                 395                 400

cag aca agc agt cga ggg tcc tat tat cta gtt gcc cct aca ggt acc  1248
Gln Thr Ser Ser Arg Gly Ser Tyr Tyr Leu Val Ala Pro Thr Gly Thr
                405                 410                 415

atg tgg gct tgt agt acc ggg ctt act cca tgc atc tcc acc acc ata  1296
Met Trp Ala Cys Ser Thr Gly Leu Thr Pro Cys Ile Ser Thr Thr Ile
            420                 425                 430

ctg aac ctt acc act gat tat tgt gtt ctt gtc gaa ctc tgg cca aga  1344
Leu Asn Leu Thr Thr Asp Tyr Cys Val Leu Val Glu Leu Trp Pro Arg
        435                 440                 445

gtc acc tat cat tcc ccc agc tat gtt tac ggc ctg ttt gag aga tcc  1392
Val Thr Tyr His Ser Pro Ser Tyr Val Tyr Gly Leu Phe Glu Arg Ser
    450                 455                 460

aac cga cac aaa aga gaa ccg gtg tcg tta acc ctg gcc cta tta ttg  1440
Asn Arg His Lys Arg Glu Pro Val Ser Leu Thr Leu Ala Leu Leu Leu
465                 470                 475                 480
```

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ggt gga cta acc atg ggg gga att gcc gct gga ata gga aca ggg act   1488
Gly Gly Leu Thr Met Gly Gly Ile Ala Ala Gly Ile Gly Thr Gly Thr
                485                 490                 495

act gct cta atg gcc act cag caa ttc cag cag ctc caa gcc gca gta   1536
Thr Ala Leu Met Ala Thr Gln Gln Phe Gln Gln Leu Gln Ala Ala Val
            500                 505                 510

cag gat gat ctc agg gag gtt gaa aaa tca atc tct aac cta gaa aag   1584
Gln Asp Asp Leu Arg Glu Val Glu Lys Ser Ile Ser Asn Leu Glu Lys
        515                 520                 525

tct ctc act tcc ctg tct gaa gtt gtc cta cag aat cga agg ggc cta   1632
Ser Leu Thr Ser Leu Ser Glu Val Val Leu Gln Asn Arg Arg Gly Leu
    530                 535                 540

gac ttg tta ttt cta aaa gaa gga ggg ctg tgt gct gct cta aaa gaa   1680
Asp Leu Leu Phe Leu Lys Glu Gly Gly Leu Cys Ala Ala Leu Lys Glu
545                 550                 555                 560

gaa tgt tgc ttc tat gcg gac cac aca gga cta gtg aga gac agc atg   1728
Glu Cys Cys Phe Tyr Ala Asp His Thr Gly Leu Val Arg Asp Ser Met
                565                 570                 575

gcc aaa ttg aga gag agg ctt aat cag aga cag aaa ctg ttt gag tca   1776
Ala Lys Leu Arg Glu Arg Leu Asn Gln Arg Gln Lys Leu Phe Glu Ser
            580                 585                 590

act caa gga tgg ttt gag gga ctg ttt aac aga tcc cct tgg ttt acc   1824
Thr Gln Gly Trp Phe Glu Gly Leu Phe Asn Arg Ser Pro Trp Phe Thr
        595                 600                 605

acc ttg ata tct acc att atg gga ccc ctc att gta ctc cta atg att   1872
Thr Leu Ile Ser Thr Ile Met Gly Pro Leu Ile Val Leu Leu Met Ile
    610                 615                 620

ttg ctc ttc gga ccc tgc att ctt aat cga tta gtc caa ttt gtt aaa   1920
Leu Leu Phe Gly Pro Cys Ile Leu Asn Arg Leu Val Gln Phe Val Lys
625                 630                 635                 640

gac agg ata tca gtg gtc cag gct cta gtt ttg act caa caa tat cac   1968
Asp Arg Ile Ser Val Val Gln Ala Leu Val Leu Thr Gln Gln Tyr His
                645                 650                 655

cag ctg aag cct ata gag tac gag cca tag                          1998
Gln Leu Lys Pro Ile Glu Tyr Glu Pro
            660                 665
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<210> 70
<211> 665
<212> PRT
<213> Moloney murine leukaemia virus

<400> 70

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

```
 65                  70                  75                  80
Leu Ala His His Gly Pro Ser Tyr Trp Gly Leu Glu Tyr Gln Ser Pro
                85                  90                  95
Phe Ser Ser Pro Pro Gly Pro Pro Cys Cys Ser Gly Gly Ser Ser Pro
            100                 105                 110
Gly Cys Ser Arg Asp Cys Glu Glu Pro Leu Thr Ser Leu Thr Pro Arg
        115                 120                 125
Cys Asn Thr Ala Trp Asn Arg Leu Lys Leu Asp Gln Thr Thr His Lys
    130                 135                 140
Ser Asn Glu Gly Phe Tyr Val Cys Pro Gly Pro His Arg Pro Arg Glu
145                 150                 155                 160
Ser Lys Ser Cys Gly Gly Pro Asp Ser Phe Tyr Cys Ala Tyr Trp Gly
                165                 170                 175
Cys Glu Thr Thr Gly Arg Ala Tyr Trp Lys Pro Ser Ser Ser Trp Asp
            180                 185                 190
Phe Ile Thr Val Asn Asn Asn Leu Thr Ser Asp Gln Ala Val Gln Val
        195                 200                 205
Cys Lys Asp Asn Lys Trp Cys Asn Pro Leu Val Ile Arg Phe Thr Asp
    210                 215                 220
Ala Gly Arg Arg Val Thr Ser Trp Thr Thr Gly His Tyr Trp Gly Leu
225                 230                 235                 240
Arg Leu Tyr Val Ser Gly Gln Asp Pro Gly Leu Thr Phe Gly Ile Arg
                245                 250                 255
Leu Arg Tyr Gln Asn Leu Gly Pro Arg Val Pro Ile Gly Pro Asn Pro
            260                 265                 270
Val Leu Ala Asp Gln Gln Pro Leu Ser Lys Pro Lys Pro Val Lys Ser
        275                 280                 285
Pro Ser Val Thr Lys Pro Pro Ser Gly Thr Pro Leu Ser Pro Thr Gln
    290                 295                 300
Leu Pro Pro Ala Gly Thr Glu Asn Arg Leu Leu Asn Leu Val Asp Gly
305                 310                 315                 320
Ala Tyr Gln Ala Leu Asn Leu Thr Ser Pro Asp Lys Thr Gln Glu Cys
                325                 330                 335
Trp Leu Cys Leu Val Ala Gly Pro Pro Tyr Tyr Glu Gly Val Ala Val
            340                 345                 350
Leu Gly Thr Tyr Ser Asn His Thr Ser Ala Pro Ala Asn Cys Ser Val
        355                 360                 365
Ala Ser Gln His Lys Leu Thr Leu Ser Glu Val Thr Gly Gln Gly Leu
    370                 375                 380
Cys Ile Gly Ala Val Pro Lys Thr His Gln Ala Leu Cys Asn Thr Thr
385                 390                 395                 400
Gln Thr Ser Ser Arg Gly Ser Tyr Tyr Leu Val Ala Pro Thr Gly Thr
                405                 410                 415
Met Trp Ala Cys Ser Thr Gly Leu Thr Pro Cys Ile Ser Thr Thr Ile
            420                 425                 430
Leu Asn Leu Thr Thr Asp Tyr Cys Val Leu Val Glu Leu Trp Pro Arg
        435                 440                 445
Val Thr Tyr His Ser Pro Ser Tyr Val Tyr Gly Leu Phe Glu Arg Ser
    450                 455                 460
Asn Arg His Lys Arg Glu Pro Val Ser Leu Thr Leu Ala Leu Leu Leu
465                 470                 475                 480
Gly Gly Leu Thr Met Gly Gly Ile Ala Ala Gly Ile Gly Thr Gly Thr
                485                 490                 495
Thr Ala Leu Met Ala Thr Gln Gln Phe Gln Gln Leu Gln Ala Ala Val
            500                 505                 510
Gln Asp Asp Leu Arg Glu Val Glu Lys Ser Ile Ser Asn Leu Glu Lys
        515                 520                 525
Ser Leu Thr Ser Leu Ser Glu Val Val Leu Gln Asn Arg Arg Gly Leu
    530                 535                 540
Asp Leu Leu Phe Leu Lys Glu Gly Gly Leu Cys Ala Ala Leu Lys Glu
545                 550                 555                 560
Glu Cys Cys Phe Tyr Ala Asp His Thr Gly Leu Val Arg Asp Ser Met
                565                 570                 575
Ala Lys Leu Arg Glu Arg Leu Asn Gln Arg Gln Lys Leu Phe Glu Ser
            580                 585                 590
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Thr Gln Gly Trp Phe Glu Gly Leu Phe Asn Arg Ser Pro Trp Phe Thr
        595                 600                 605
Thr Leu Ile Ser Thr Ile Met Gly Pro Leu Ile Val Leu Leu Met Ile
    610                 615                 620
Leu Leu Phe Gly Pro Cys Ile Leu Asn Arg Leu Val Gln Phe Val Lys
625                 630                 635                 640
Asp Arg Ile Ser Val Val Gln Ala Leu Val Leu Thr Gln Gln Tyr His
                645                 650                 655
Gln Leu Lys Pro Ile Glu Tyr Glu Pro
            660                 665
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<210> 71
<211> 1761
<212> DNA
<213> Mason-Pfizer monkey virus

<220>
<221> CDS
<222> (1)..(1761)
<223> coding sequence of envelope protein

<400> 71

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atg aac ttc aat tat cat ttc atc tgg agc tta gtg ata cta tct caa   48
Met Asn Phe Asn Tyr His Phe Ile Trp Ser Leu Val Ile Leu Ser Gln
  1               5                  10                  15

ata tct caa gtt caa gcc ggt ttt gga gat ccg cgt gaa gcc ctg gca   96
Ile Ser Gln Val Gln Ala Gly Phe Gly Asp Pro Arg Glu Ala Leu Ala
             20                  25                  30

gaa ata caa caa aaa cat ggt aaa cct tgt gac tgt gct gga gga tat   144
Glu Ile Gln Gln Lys His Gly Lys Pro Cys Asp Cys Ala Gly Gly Tyr
         35                  40                  45

gtt tcc tcc cca ccg att aac tct ctt aca act gtt tct tgc tct act   192
Val Ser Ser Pro Pro Ile Asn Ser Leu Thr Thr Val Ser Cys Ser Thr
     50                  55                  60

cat act gct tat tca gtg aca aac tcc cta aaa tgg cag tgt gtg tca   240
His Thr Ala Tyr Ser Val Thr Asn Ser Leu Lys Trp Gln Cys Val Ser
 65                  70                  75                  80

act ccc act acc cct agc aat aca cat ata gga agt tgt ccc ggt gaa   288
Thr Pro Thr Thr Pro Ser Asn Thr His Ile Gly Ser Cys Pro Gly Glu
                85                  90                  95

tgc aac acg atc tca tat gat tct gta cat gcc tct tgc tat aac cac   336
Cys Asn Thr Ile Ser Tyr Asp Ser Val His Ala Ser Cys Tyr Asn His
            100                 105                 110

tat caa caa tgt aac att ggt aat aaa aca tat ctc act gcc act ata   384
Tyr Gln Gln Cys Asn Ile Gly Asn Lys Thr Tyr Leu Thr Ala Thr Ile
        115                 120                 125

act gga gat aga act cct gcc att ggt gac ggg aat gtc cct aca gta   432
Thr Gly Asp Arg Thr Pro Ala Ile Gly Asp Gly Asn Val Pro Thr Val
    130                 135                 140

cta ggg act agt cac aac ctc att aca gca ggc tgt ccc aat ggt aaa   480
Leu Gly Thr Ser His Asn Leu Ile Thr Ala Gly Cys Pro Asn Gly Lys
145                 150                 155                 160

aag ggc caa gtg gtc tgt tgg aat agc cga cct tct gtt cat ata tct   528
```

```
Lys Gly Gln Val Val Cys Trp Asn Ser Arg Pro Ser Val His Ile Ser
                165                 170                 175

gat gga gga ggg cct caa gat aag gcc cgc gac att ata gta aat aaa   576
Asp Gly Gly Gly Pro Gln Asp Lys Ala Arg Asp Ile Ile Val Asn Lys
            180                 185                 190

aag ttt gag gaa ttg cac agg tcg ctg ttc cca gaa ctt tct tac cat   624
Lys Phe Glu Glu Leu His Arg Ser Leu Phe Pro Glu Leu Ser Tyr His
        195                 200                 205

cct ctg gcc ttg ccc gaa gcc cgt ggt aaa gaa aaa att gac gca cac   672
Pro Leu Ala Leu Pro Glu Ala Arg Gly Lys Glu Lys Ile Asp Ala His
    210                 215                 220

act ctt gat ctc ctt gcc act gta cat agt tta ctc aat gct tcc caa   720
Thr Leu Asp Leu Leu Ala Thr Val His Ser Leu Leu Asn Ala Ser Gln
225                 230                 235                 240

ccc agt tta gcc gaa gat tgc tgg ctg tgc tta cag tca gga gat ccc   768
Pro Ser Leu Ala Glu Asp Cys Trp Leu Cys Leu Gln Ser Gly Asp Pro
                245                 250                 255

gtt cct ctt gcc ctg ccc tat aat gat aca ctc tgc tct aac ttt gcc   816
Val Pro Leu Ala Leu Pro Tyr Asn Asp Thr Leu Cys Ser Asn Phe Ala
            260                 265                 270

tgt tta tct aat cac tcc tgc cct tta acc ccc cct ttt tta gta cag   864
Cys Leu Ser Asn His Ser Cys Pro Leu Thr Pro Pro Phe Leu Val Gln
        275                 280                 285

ccc ttt aac ttc act gat tcc aat tgc ctt tac gct cat tat caa aac   912
Pro Phe Asn Phe Thr Asp Ser Asn Cys Leu Tyr Ala His Tyr Gln Asn
    290                 295                 300

aac tca ttt gac ata gat gta ggt cta gct agc ttt act aat tgc tct   960
Asn Ser Phe Asp Ile Asp Val Gly Leu Ala Ser Phe Thr Asn Cys Ser
305                 310                 315                 320

agc tat tat aac gtt tct aca gcc tcc aaa ccc tct aat tcc cta tgc   1008
Ser Tyr Tyr Asn Val Ser Thr Ala Ser Lys Pro Ser Asn Ser Leu Cys
                325                 330                 335

gcc cca aac agc tcg gtt ttt gta tgc ggt aac aat aag gca tac act   1056
Ala Pro Asn Ser Ser Val Phe Val Cys Gly Asn Asn Lys Ala Tyr Thr
            340                 345                 350

tat cta ccc aca aat tgg acg gga agt tgt gta ctt gct act ctt ttg   1104
Tyr Leu Pro Thr Asn Trp Thr Gly Ser Cys Val Leu Ala Thr Leu Leu
        355                 360                 365

ccc gat ata gac atc att cca ggt agt gag cct gtc ccc att cca gct   1152
Pro Asp Ile Asp Ile Ile Pro Gly Ser Glu Pro Val Pro Ile Pro Ala
    370                 375                 380

att gat cat ttt tta ggc aaa gcc aaa aga gca atc caa ctt atc ccc   1200
Ile Asp His Phe Leu Gly Lys Ala Lys Arg Ala Ile Gln Leu Ile Pro
385                 390                 395                 400

ctg ttc gta ggg tta ggt ata act act gca gta tct act ggg gct gct   1248
Leu Phe Val Gly Leu Gly Ile Thr Thr Ala Val Ser Thr Gly Ala Ala
                405                 410                 415

ggt cta ggg gtt tcc atc act caa tat aca aaa tta tct cat caa cta   1296
Gly Leu Gly Val Ser Ile Thr Gln Tyr Thr Lys Leu Ser His Gln Leu
```

```
            420                 425                 430

ata tca gat gtt caa gct att tct agc act ata caa gat ctc caa gat   1344
Ile Ser Asp Val Gln Ala Ile Ser Ser Thr Ile Gln Asp Leu Gln Asp
        435                 440                 445

cag gta gac tct cta gca gaa gta gta ctg caa aac aga aga gga tta   1392
Gln Val Asp Ser Leu Ala Glu Val Val Leu Gln Asn Arg Arg Gly Leu
    450                 455                 460

gat cta ctt aca gca gag cag gga ggt atc tgc tta gcc tta cag gaa   1440
Asp Leu Leu Thr Ala Glu Gln Gly Gly Ile Cys Leu Ala Leu Gln Glu
465                 470                 475                 480

aaa tgt tgt ttc tac gcc aat aaa tct gga atc gtc aga gac aag att   1488
Lys Cys Cys Phe Tyr Ala Asn Lys Ser Gly Ile Val Arg Asp Lys Ile
                485                 490                 495

aaa aac cta caa gac gac tta gaa aga cgc cga aga caa ctg atc gac   1536
Lys Asn Leu Gln Asp Asp Leu Glu Arg Arg Arg Arg Gln Leu Ile Asp
            500                 505                 510

aac cca ttt tgg acc agt ttt cat gga ttc ctc cct tat gtt atg ccc   1584
Asn Pro Phe Trp Thr Ser Phe His Gly Phe Leu Pro Tyr Val Met Pro
        515                 520                 525

cta tta ggc cct ttg ctt tgc tta ttg ctt gtg tta tct ttc ggt cca   1632
Leu Leu Gly Pro Leu Leu Cys Leu Leu Leu Val Leu Ser Phe Gly Pro
    530                 535                 540

att att ttc aac aag ctt atg acc ttt att aaa cat caa att gag agc   1680
Ile Ile Phe Asn Lys Leu Met Thr Phe Ile Lys His Gln Ile Glu Ser
545                 550                 555                 560

atc cag gcc aaa cct ata caa gtc cat tat cat cgc ctt gaa caa gaa   1728
Ile Gln Ala Lys Pro Ile Gln Val His Tyr His Arg Leu Glu Gln Glu
                565                 570                 575

gac agt ggt ggc tca tat ttg acc tta aca tag                       1761
Asp Ser Gly Gly Ser Tyr Leu Thr Leu Thr
            580                 585
```

<210> 72
<211> 586
<212> PRT
<213> Mason-Pfizer monkey virus

<400> 72

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

```
Thr Gly Asp Arg Thr Pro Ala Ile Gly Asp Gly Asn Val Pro Thr Val
    130                 135                 140
Leu Gly Thr Ser His Asn Leu Ile Thr Ala Gly Cys Pro Asn Gly Lys
145                 150                 155                 160
Lys Gly Gln Val Val Cys Trp Asn Ser Arg Pro Ser Val His Ile Ser
                165                 170                 175
Asp Gly Gly Gly Pro Gln Asp Lys Ala Arg Asp Ile Ile Val Asn Lys
            180                 185                 190
Lys Phe Glu Glu Leu His Arg Ser Leu Phe Pro Glu Leu Ser Tyr His
        195                 200                 205
Pro Leu Ala Leu Pro Glu Ala Arg Gly Lys Glu Lys Ile Asp Ala His
    210                 215                 220
Thr Leu Asp Leu Leu Ala Thr Val His Ser Leu Leu Asn Ala Ser Gln
225                 230                 235                 240
Pro Ser Leu Ala Glu Asp Cys Trp Leu Cys Leu Gln Ser Gly Asp Pro
                245                 250                 255
Val Pro Leu Ala Leu Pro Tyr Asn Asp Thr Leu Cys Ser Asn Phe Ala
            260                 265                 270
Cys Leu Ser Asn His Ser Cys Pro Leu Thr Pro Pro Phe Leu Val Gln
        275                 280                 285
Pro Phe Asn Phe Thr Asp Ser Asn Cys Leu Tyr Ala His Tyr Gln Asn
    290                 295                 300
Asn Ser Phe Asp Ile Asp Val Gly Leu Ala Ser Phe Thr Asn Cys Ser
305                 310                 315                 320
Ser Tyr Tyr Asn Val Ser Thr Ala Ser Lys Pro Ser Asn Ser Leu Cys
                325                 330                 335
Ala Pro Asn Ser Ser Val Phe Val Cys Gly Asn Asn Lys Ala Tyr Thr
            340                 345                 350
Tyr Leu Pro Thr Asn Trp Thr Gly Ser Cys Val Leu Ala Thr Leu Leu
        355                 360                 365
Pro Asp Ile Asp Ile Ile Pro Gly Ser Glu Pro Val Pro Ile Pro Ala
    370                 375                 380
Ile Asp His Phe Leu Gly Lys Ala Lys Arg Ala Ile Gln Leu Ile Pro
385                 390                 395                 400
Leu Phe Val Gly Leu Gly Ile Thr Thr Ala Val Ser Thr Gly Ala Ala
                405                 410                 415
Gly Leu Gly Val Ser Ile Thr Gln Tyr Thr Lys Leu Ser His Gln Leu
            420                 425                 430
Ile Ser Asp Val Gln Ala Ile Ser Ser Thr Ile Gln Asp Leu Gln Asp
        435                 440                 445
Gln Val Asp Ser Leu Ala Glu Val Val Leu Gln Asn Arg Arg Gly Leu
    450                 455                 460
Asp Leu Leu Thr Ala Glu Gln Gly Gly Ile Cys Leu Ala Leu Gln Glu
465                 470                 475                 480
Lys Cys Cys Phe Tyr Ala Asn Lys Ser Gly Ile Val Arg Asp Lys Ile
                485                 490                 495
Lys Asn Leu Gln Asp Asp Leu Glu Arg Arg Arg Arg Gln Leu Ile Asp
            500                 505                 510
Asn Pro Phe Trp Thr Ser Phe His Gly Phe Leu Pro Tyr Val Met Pro
        515                 520                 525
Leu Leu Gly Pro Leu Leu Cys Leu Leu Leu Val Leu Ser Phe Gly Pro
    530                 535                 540
Ile Ile Phe Asn Lys Leu Met Thr Phe Ile Lys His Gln Ile Glu Ser
545                 550                 555                 560
Ile Gln Ala Lys Pro Ile Gln Val His Tyr His Arg Leu Glu Gln Glu
                565                 570                 575
Asp Ser Gly Gly Ser Tyr Leu Thr Leu Thr
            580                 585
```

<210> 73
<211> 1617
<212> DNA
<213> Human endogenous retrovirus W

<220>
<221> CDS
<222> (1)..(1617)
<223> coding sequence of envelope protein

<400> 73

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atg gcc ctc cct tat cat att ttt ctc ttt act gtt ctt tta ccc tct   48
Met Ala Leu Pro Tyr His Ile Phe Leu Phe Thr Val Leu Leu Pro Ser
  1               5                  10                  15

ttc act ctc act gca ccc cct cca tgc cgc tgt atg acc agt agc tcc   96
Phe Thr Leu Thr Ala Pro Pro Pro Cys Arg Cys Met Thr Ser Ser Ser
             20                  25                  30

cct tac caa gag ttt cta tgg aga atg cag cgt ccc gga aat att gat   144
Pro Tyr Gln Glu Phe Leu Trp Arg Met Gln Arg Pro Gly Asn Ile Asp
         35                  40                  45

gcc cca tcg tat agg agt ctt tct aag gga acc ccc acc ttc act gcc   192
Ala Pro Ser Tyr Arg Ser Leu Ser Lys Gly Thr Pro Thr Phe Thr Ala
     50                  55                  60

cac acc cat atg ccc cgc aac tgc tat cac tct gcc act ctt tgc atg   240
His Thr His Met Pro Arg Asn Cys Tyr His Ser Ala Thr Leu Cys Met
 65                  70                  75                  80

cat gca aat act cat tat tgg aca gga aaa atg att aat cct agt tgt   288
His Ala Asn Thr His Tyr Trp Thr Gly Lys Met Ile Asn Pro Ser Cys
                 85                  90                  95

cct gga gga ctt gga gtc act gtc tgt tgg act tac ttc acc caa act   336
Pro Gly Gly Leu Gly Val Thr Val Cys Trp Thr Tyr Phe Thr Gln Thr
            100                 105                 110

ggt atg tct gat ggg ggt gga gtt caa gat cag gca aga gaa aaa cat   384
Gly Met Ser Asp Gly Gly Gly Val Gln Asp Gln Ala Arg Glu Lys His
        115                 120                 125

gta aaa gaa gta atc tcc caa ctc acc cgg gta cat ggc acc tct agc   432
Val Lys Glu Val Ile Ser Gln Leu Thr Arg Val His Gly Thr Ser Ser
    130                 135                 140

ccc tac aaa gga cta gat ctc tca aaa cta cat gaa acc ctc cgt acc   480
Pro Tyr Lys Gly Leu Asp Leu Ser Lys Leu His Glu Thr Leu Arg Thr
145                 150                 155                 160

cat act cgc ctg gta agc cta ttt aat acc acc ctc act ggg ctc cat   528
His Thr Arg Leu Val Ser Leu Phe Asn Thr Thr Leu Thr Gly Leu His
                165                 170                 175

gag gtc tcg gcc caa aac cct act aac tgt tgg ata tgc ctc ccc ctg   576
Glu Val Ser Ala Gln Asn Pro Thr Asn Cys Trp Ile Cys Leu Pro Leu
            180                 185                 190

aac ttc agg cca tat gtt tca atc cct gta cct gaa caa tgg aac aac   624
Asn Phe Arg Pro Tyr Val Ser Ile Pro Val Pro Glu Gln Trp Asn Asn
        195                 200                 205

ttc agc aca gaa ata aac acc act tcc gtt tta gta gga cct ctt gtt   672
Phe Ser Thr Glu Ile Asn Thr Thr Ser Val Leu Val Gly Pro Leu Val
    210                 215                 220

tcc aat ctg gaa ata acc cat acc tca aac ctc acc tgt gta aaa ttt   720
Ser Asn Leu Glu Ile Thr His Thr Ser Asn Leu Thr Cys Val Lys Phe
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225                 230                 235                 240

agc aat act aca tac aca acc aac tcc caa tgc atc agg tgg gta act   768
Ser Asn Thr Thr Tyr Thr Thr Asn Ser Gln Cys Ile Arg Trp Val Thr
                245                 250                 255

cct ccc aca caa ata gtc tgc cta ccc tca gga ata ttt ttt gtc tgt   816
Pro Pro Thr Gln Ile Val Cys Leu Pro Ser Gly Ile Phe Phe Val Cys
            260                 265                 270

ggt acc tca gcc tat cgt tgt ttg aat ggc tct tca gaa tct atg tgc   864
Gly Thr Ser Ala Tyr Arg Cys Leu Asn Gly Ser Ser Glu Ser Met Cys
        275                 280                 285

ttc ctc tca ttc tta gtg ccc cct atg acc atc tac act gaa caa gat   912
Phe Leu Ser Phe Leu Val Pro Pro Met Thr Ile Tyr Thr Glu Gln Asp
    290                 295                 300

tta tac agt tat gtc ata tct aag ccc cgc aac aaa aga gta ccc att   960
Leu Tyr Ser Tyr Val Ile Ser Lys Pro Arg Asn Lys Arg Val Pro Ile
305                 310                 315                 320

ctt cct ttt gtt ata gga gca gga gtg cta ggt gca cta ggt act ggc   1008
Leu Pro Phe Val Ile Gly Ala Gly Val Leu Gly Ala Leu Gly Thr Gly
                325                 330                 335

att ggc ggt atc aca acc tct act cag ttc tac tac aaa cta tct caa   1056
Ile Gly Gly Ile Thr Thr Ser Thr Gln Phe Tyr Tyr Lys Leu Ser Gln
            340                 345                 350

gaa cta aat ggg gac atg gaa cgg gtc gcc gac tcc ctg gtc acc ttg   1104
Glu Leu Asn Gly Asp Met Glu Arg Val Ala Asp Ser Leu Val Thr Leu
        355                 360                 365

caa gat caa ctt aac tcc cta gca gca gta gtc ctt caa aat cga aga   1152
Gln Asp Gln Leu Asn Ser Leu Ala Ala Val Val Leu Gln Asn Arg Arg
    370                 375                 380

gct tta gac ttg cta acc gct gaa aga ggg gga acc tgt tta ttt tta   1200
Ala Leu Asp Leu Leu Thr Ala Glu Arg Gly Gly Thr Cys Leu Phe Leu
385                 390                 395                 400

ggg gaa gaa tgc tgt tat tat gtt aat caa tcc gga atc gtc act gag   1248
Gly Glu Glu Cys Cys Tyr Tyr Val Asn Gln Ser Gly Ile Val Thr Glu
                405                 410                 415

aaa gtt aaa gaa att cga gat cga ata caa cgt aga gca gag gag ctt   1296
Lys Val Lys Glu Ile Arg Asp Arg Ile Gln Arg Arg Ala Glu Glu Leu
            420                 425                 430

cga aac act gga ccc tgg ggc ctc ctc agc caa tgg atg ccc tgg att   1344
Arg Asn Thr Gly Pro Trp Gly Leu Leu Ser Gln Trp Met Pro Trp Ile
        435                 440                 445

ctc ccc ttc tta gga cct cta gca gct ata ata ttg cta ctc ctc ttt   1392
Leu Pro Phe Leu Gly Pro Leu Ala Ala Ile Ile Leu Leu Leu Leu Phe
    450                 455                 460

gga ccc tgt atc ttt aac ctc ctt gtt aac ttt gtc tct tcc aga atc   1440
Gly Pro Cys Ile Phe Asn Leu Leu Val Asn Phe Val Ser Ser Arg Ile
465                 470                 475                 480

gaa gct gta aaa cta caa atg gag ccc aag atg cag tcc aag act aag   1488
Glu Ala Val Lys Leu Gln Met Glu Pro Lys Met Gln Ser Lys Thr Lys
                485                 490                 495
```

```
atc tac cgc aga ccc ctg gac cgg cct gct agc cca cga tct gat gtt   1536
Ile Tyr Arg Arg Pro Leu Asp Arg Pro Ala Ser Pro Arg Ser Asp Val
            500                 505                 510

aat gac atc aaa ggc acc cct cct gag gaa atc tca gct gca caa cct   1584
Asn Asp Ile Lys Gly Thr Pro Pro Glu Glu Ile Ser Ala Ala Gln Pro
        515                 520                 525

cta cta cgc ccc aat tca gca gga agc agt tag                      1617
Leu Leu Arg Pro Asn Ser Ala Gly Ser Ser
    530                 535
```

<210> 74
<211> 538
<212> PRT
<213> Human endogenous retrovirus W

<400> 74

```
Met Ala Leu Pro Tyr His Ile Phe Leu Phe Thr Val Leu Leu Pro Ser
  1               5                  10                  15
Phe Thr Leu Thr Ala Pro Pro Pro Cys Arg Cys Met Thr Ser Ser Ser
             20                  25                  30
Pro Tyr Gln Glu Phe Leu Trp Arg Met Gln Arg Pro Gly Asn Ile Asp
         35                  40                  45
Ala Pro Ser Tyr Arg Ser Leu Ser Lys Gly Thr Pro Thr Phe Thr Ala
     50                  55                  60
His Thr His Met Pro Arg Asn Cys Tyr His Ser Ala Thr Leu Cys Met
 65                  70                  75                  80
His Ala Asn Thr His Tyr Trp Thr Gly Lys Met Ile Asn Pro Ser Cys
                 85                  90                  95
Pro Gly Gly Leu Gly Val Thr Val Cys Trp Thr Tyr Phe Thr Gln Thr
            100                 105                 110
Gly Met Ser Asp Gly Gly Gly Val Gln Asp Gln Ala Arg Glu Lys His
        115                 120                 125
Val Lys Glu Val Ile Ser Gln Leu Thr Arg Val His Gly Thr Ser Ser
    130                 135                 140
Pro Tyr Lys Gly Leu Asp Leu Ser Lys Leu His Glu Thr Leu Arg Thr
145                 150                 155                 160
His Thr Arg Leu Val Ser Leu Phe Asn Thr Thr Leu Thr Gly Leu His
                165                 170                 175
Glu Val Ser Ala Gln Asn Pro Thr Asn Cys Trp Ile Cys Leu Pro Leu
            180                 185                 190
Asn Phe Arg Pro Tyr Val Ser Ile Pro Val Pro Glu Gln Trp Asn Asn
        195                 200                 205
Phe Ser Thr Glu Ile Asn Thr Thr Ser Val Leu Val Gly Pro Leu Val
    210                 215                 220
Ser Asn Leu Glu Ile Thr His Thr Ser Asn Leu Thr Cys Val Lys Phe
225                 230                 235                 240
Ser Asn Thr Thr Tyr Thr Thr Asn Ser Gln Cys Ile Arg Trp Val Thr
                245                 250                 255
Pro Pro Thr Gln Ile Val Cys Leu Pro Ser Gly Ile Phe Phe Val Cys
            260                 265                 270
Gly Thr Ser Ala Tyr Arg Cys Leu Asn Gly Ser Ser Glu Ser Met Cys
        275                 280                 285
Phe Leu Ser Phe Leu Val Pro Pro Met Thr Ile Tyr Thr Glu Gln Asp
    290                 295                 300
Leu Tyr Ser Tyr Val Ile Ser Lys Pro Arg Asn Lys Arg Val Pro Ile
305                 310                 315                 320
Leu Pro Phe Val Ile Gly Ala Gly Val Leu Gly Ala Leu Gly Thr Gly
                325                 330                 335
Ile Gly Gly Ile Thr Thr Ser Thr Gln Phe Tyr Tyr Lys Leu Ser Gln
            340                 345                 350
Glu Leu Asn Gly Asp Met Glu Arg Val Ala Asp Ser Leu Val Thr Leu
```

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

<210> 75
<211> 20
<212> PRT
<213> Fowlpox virus

<400> 75
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Thr Ala Glu Gln Gly Gly
1 5 10 15

Ile Cys Leu Ala
20

<210> 76
<211> 20
<212> PRT
<213> Simian sarcoma-associated virus

<400> 76
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly
1 5 10 15

Leu Cys Ala Ala
20

<210> 77
<211> 20
<212> PRT
<213> Friend virus

<400> 77
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly
1 5 10 15

Leu Cys Ala Ala
20

<210> 78
<211> 20
<212> PRT
<213> python endogenous retrovirus

<400> 78
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly
1 5 10 15

Leu Cys Val Ala
20

<210> 79
<211> 20
<212> PRT
<213> Gibbon leukemia virus X

<400> 79
Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys Glu Gly Gly
1 5 10 15

Leu Cys Ala Ala
20

<210> 80
<211> 20
<212> PRT
<213> Simian T-cell leukaemia virus type 1

<400> 80
Ala Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Trp Glu Gln Gly Gly
1 5 10 15

Leu Cys Lys Ala
20

<210> 81

<211> 1615

<212> DNA

<213> Human endogenous retrovirus FRD

<400> 81
atgggcctgc tcctgctggt tctcattctc acgccttcac tagcagccta ccgccatcct 60

gatttcccgt tattggaaaa agctcagcaa ctgctccaaa gtacaggatc cccttactcc 120

accaattgct ggttatgtac tagctcttcc actgaaacac cagggacagc ttatccagcc 180

tcgcccagag aatggacaag catagaggcg gaattacata tttcctatcg atgggaccct 240

aatctgaaag gactgatgag gcctgcaaat agtcttcttt caacagtaaa gcaagatttc 300

cctgatatcc gccagaaacc tcccattttc ggacccatct ttactaatat caacctaatg 360

ggaatagccc ctatttgtgt tatggccaaa aggaaaaatg gaacaaatgt aggcactctt 420

ccaagtacag tctgtaatgt tactttcact gtagattcta accaacagac ttaccaaaca 480

tacacccaca accaattccg ccatcaacca agattcccca aacctccaaa tattactttt 540

cctcagggaa ctttgctaga taaatccagc cggttttgcc agggacgccc aagctcatgc 600

agtactcgaa acttctggtt ccggcctgct gattataacc aatgtctgca aatttccaac 660

ctcagctcta cagcggaatg ggttctattg gaccaaactc gaaattctct tttttgggaa 720

aataaaacca agggagctaa ccagagccaa acaccctgcg tccaagtctt agcaggcatg 780

actatagcca ccagctacct gggcatatca gcagtctcag aatttttttgg aacctccctc 840

acccccttat ttcatttcca tatctctaca tgccttaaaa ctcaaggagc cttttatatt 900

tgtggccagt cgattcacca atgcctcccc agtaactgga ctggaacttg taccataggc 960

tatgtaaccc cagacatctt catagcccct ggcaatctct ctcttccaat accaatctat 1020

gggaattccc cgttgcccag ggtgaggagg gcaatccatt tcattcccct tctcgcggga 1080

ctcggcattc tagctggtac gggaaccgga attgctggaa tcacaaaagc ttccctcacc 1140

tatagccagc tctcaaagga aatagccaac aacattgaca ccatggctaa agccttaacg 1200

accatgcaag aacaaatcga ctctttagca gccgtagtcc ttcaaaatcg tcgaggacta 1260

gacatgttaa cggcagcaca gggaggaatt tgtttggcct tagatgaaaa atgttgcttt 1320

tgggtaaatc aatcaggaaa agtacaagac aacatcagac aactcctaaa tcaagcctcc 1380

agtttacggg aacgagccac tcagggttgg ttaaattggg aaggaacttg gaaatggttc 1440

tcttgggttc ttccccttac aggcccactt gttagtctcc tacttttgct ccttttttggt 1500

ccatgtctcc taaatctaat aacccaattt gtctcctctc gccttcaggc cataaagctc 1560

cagacgaatc tcagtgcagg acgccatcct cgcaatattc aagagtcacc cttct 1615

<210> 82

<211> 538

<212> PRT

<213> Human endogenous retrovirus FRD

<400> 82

Met Gly Leu Leu Leu Leu Val Leu Ile Leu Thr Pro Ser Leu Ala Ala
1 5 10 15

Tyr Arg His Pro Asp Phe Pro Leu Leu Glu Lys Ala Gln Gln Leu Leu
20 25 30

Gln Ser Thr Gly Ser Pro Tyr Ser Thr Asn Cys Trp Leu Cys Thr Ser
35 40 45

Ser Ser Thr Glu Thr Pro Gly Thr Ala Tyr Pro Ala Ser Pro Arg Glu
50 55 60

```
Trp Thr Ser Ile Glu Ala Glu Leu His Ile Ser Tyr Arg Trp Asp Pro
65                  70                  75                  80

Asn Leu Lys Gly Leu Met Arg Pro Ala Asn Ser Leu Leu Ser Thr Val
                85                  90                  95

Lys Gln Asp Phe Pro Asp Ile Arg Gln Lys Pro Pro Ile Phe Gly Pro
            100                 105                 110

Ile Phe Thr Asn Ile Asn Leu Met Gly Ile Ala Pro Ile Cys Val Met
        115                 120                 125

Ala Lys Arg Lys Asn Gly Thr Asn Val Gly Thr Leu Pro Ser Thr Val
    130                 135                 140

Cys Asn Val Thr Phe Thr Val Asp Ser Asn Gln Gln Thr Tyr Gln Thr
145                 150                 155                 160

Tyr Thr His Asn Gln Phe Arg His Gln Pro Arg Phe Pro Lys Pro Pro
                165                 170                 175

Asn Ile Thr Phe Pro Gln Gly Thr Leu Leu Asp Lys Ser Ser Arg Phe
            180                 185                 190

Cys Gln Gly Arg Pro Ser Ser Cys Ser Thr Arg Asn Phe Trp Phe Arg
        195                 200                 205

Pro Ala Asp Tyr Asn Gln Cys Leu Gln Ile Ser Asn Leu Ser Ser Thr
    210                 215                 220

Ala Glu Trp Val Leu Leu Asp Gln Thr Arg Asn Ser Leu Phe Trp Glu
225                 230                 235                 240

Asn Lys Thr Lys Gly Ala Asn Gln Ser Gln Thr Pro Cys Val Gln Val
                245                 250                 255

Leu Ala Gly Met Thr Ile Ala Thr Ser Tyr Leu Gly Ile Ser Ala Val
            260                 265                 270

Ser Glu Phe Phe Gly Thr Ser Leu Thr Pro Leu Phe His Phe His Ile
        275                 280                 285

Ser Thr Cys Leu Lys Thr Gln Gly Ala Phe Tyr Ile Cys Gly Gln Ser
    290                 295                 300

Ile His Gln Cys Leu Pro Ser Asn Trp Thr Gly Thr Cys Thr Ile Gly
305                 310                 315                 320
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Tyr Val Thr Pro Asp Ile Phe Ile Ala Pro Gly Asn Leu Ser Leu Pro
325 330 335

Ile Pro Ile Tyr Gly Asn Ser Pro Leu Pro Arg Val Arg Arg Ala Ile
340 345 350

His Phe Ile Pro Leu Leu Ala Gly Leu Gly Ile Leu Ala Gly Thr Gly
355 360 365

Thr Gly Ile Ala Gly Ile Thr Lys Ala Ser Leu Thr Tyr Ser Gln Leu
370 375 380

Ser Lys Glu Ile Ala Asn Asn Ile Asp Thr Met Ala Lys Ala Leu Thr
385 390 395 400

Thr Met Gln Glu Gln Ile Asp Ser Leu Ala Ala Val Val Leu Gln Asn
405 410 415

Arg Arg Gly Leu Asp Met Leu Thr Ala Ala Gln Gly Gly Ile Cys Leu
420 425 430

Ala Leu Asp Glu Lys Cys Cys Phe Trp Val Asn Gln Ser Gly Lys Val
435 440 445

Gln Asp Asn Ile Arg Gln Leu Leu Asn Gln Ala Ser Ser Leu Arg Glu
450 455 460

Arg Ala Thr Gln Gly Trp Leu Asn Trp Glu Gly Thr Trp Lys Trp Phe
465 470 475 480

Ser Trp Val Leu Pro Leu Thr Gly Pro Leu Val Ser Leu Leu Leu Leu
485 490 495

Leu Leu Phe Gly Pro Cys Leu Leu Asn Leu Ile Thr Gln Phe Val Ser
500 505 510

Ser Arg Leu Gln Ala Ile Lys Leu Gln Thr Asn Leu Ser Ala Gly Arg
515 520 525

His Pro Arg Asn Ile Gln Glu Ser Pro Phe
530 535

<210> 83

<211> 1878

<212> DNA

<213> Human endogenous retrovirus T

<400> 83
atgggtcccg aagcctgggt caggcccctt aaaactgcgc ctaagccggg tgaagccatt 60
agattaattc tttttattta cctctcttgt ttctttttgc ctgttatgtc ctctgagcct 120
tcctactcct ttctcctcac ctctttcaca acaggacgtg tattcgcaaa cactacttgg 180
agggccggta cctccaagga agtctccttt gcagttgatt tatgtgtact gttcccagag 240
ccagctcgta cccatgaaga gcaacataat ttgccggtca taggagcagg aagtgtcgac 300
cttgcagcag gatttggaca ctctgggagc caaactggat gtggaagctc caaaggtgca 360
gaaaaagggc tccaaaatgt tgacttttac ctctgtcctg gaaatcaccc tgacgctagc 420
tgtagagata cttaccagtt tttctgccct gattggacat gtgtaacttt agccacctac 480
tctgggggat caactagatc ttcaactctt tccataagtc gtgttcctca tcctaaatta 540
tgtactagaa aaaattgtaa tcctcttact ataactgtcc atgaccctaa tgcagctcaa 600
tggtattatg gcatgtcatg gggattaaga ctttatatcc caggatttga tgttgggact 660
atgttcacca tccaaaagaa aatcttggtc tcatggagct cccccaagcc aatcgggcct 720
ttaactgatc taggtgaccc tatattccag aaacaccctg acaaagttga tttaactgtt 780
cctctgccat tcttagttcc tagaccccag ctacaacaac aacatcttca acccagccta 840
atgtctatac taggtggagt acaccatctc cttaacctca cccagcctaa actagcccaa 900
gattgttggc tatgtttaaa agcaaaaccc ccttattatg taggattagg agtagaagcc 960
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gtgtctggaa atgcttcctg tctgattagt accgggtata acttatctgc ttctcctttt 1080
caggctactt gtaatcagtc cctgcttact tccataagca cctcagtctc ttaccaagca 1140
cccaacaata cctggttggc ctgcacctca ggtctcactc gctgcattaa tggaactgaa 1200
ccaggacctc tcctgtgcgt gttagttcat gtacttcccc aggtatatgt gtacagtgga 1260
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ccacttctgg ttcccctatt ggctggtctt agcatagctg gatcagcagc cattggtacg 1380
gctgccctgg ttcaaggaga aactggacta atatccctgt ctcaacaggt ggatgctgat 1440
tttagtaacc tccagtctgc catagatata ctacattccc aggtagagtc tctggctgaa 1500
gtagttcttc aaaactgccg atgcttagat ctgctattcc tctctcaagg aggtttatgt 1560
gcagctctag gagaaagttg ttgcttctat gccaatcaat ctggagtcat aaaaggtaca 1620
gtaaaaaaag ttcgagaaaa tctagatagg caccaacaag aacgagaaaa taacatcccc 1680
tggtatcaaa gcatgtttaa ctggaaccca tggctaacta ctttaatcac tgggttagct 1740
ggacctctcc tcatcctact attaagttta atttttgggc cttgtatatt aaattcgttt 1800
cttaatttta taaaacaacg catagcttct gtcaaactta cgtatcttaa gactcaatat 1860

gacacccttg ttaataac 1878

<210> 84

<211> 626

<212> PRT

<213> Human endogenous retrovirus T

<400> 84

Met Gly Pro Glu Ala Trp Val Arg Pro Leu Lys Thr Ala Pro Lys Pro
1 5 10 15

Gly Glu Ala Ile Arg Leu Ile Leu Phe Ile Tyr Leu Ser Cys Phe Phe
20 25 30

Leu Pro Val Met Ser Ser Glu Pro Ser Tyr Ser Phe Leu Leu Thr Ser
35 40 45

Phe Thr Thr Gly Arg Val Phe Ala Asn Thr Thr Trp Arg Ala Gly Thr
50 55 60

Ser Lys Glu Val Ser Phe Ala Val Asp Leu Cys Val Leu Phe Pro Glu
65 70 75 80

Pro Ala Arg Thr His Glu Glu Gln His Asn Leu Pro Val Ile Gly Ala
85 90 95

Gly Ser Val Asp Leu Ala Ala Gly Phe Gly His Ser Gly Ser Gln Thr
100 105 110

Gly Cys Gly Ser Ser Lys Gly Ala Glu Lys Gly Leu Gln Asn Val Asp
115 120 125

Phe Tyr Leu Cys Pro Gly Asn His Pro Asp Ala Ser Cys Arg Asp Thr
130 135 140

Tyr Gln Phe Phe Cys Pro Asp Trp Thr Cys Val Thr Leu Ala Thr Tyr
145 150 155 160

Ser Gly Gly Ser Thr Arg Ser Ser Thr Leu Ser Ile Ser Arg Val Pro
165 170 175

His Pro Lys Leu Cys Thr Arg Lys Asn Cys Asn Pro Leu Thr Ile Thr
180 185 190

Val His Asp Pro Asn Ala Ala Gln Trp Tyr Tyr Gly Met Ser Trp Gly
195 200 205

Leu Arg Leu Tyr Ile Pro Gly Phe Asp Val Gly Thr Met Phe Thr Ile
210 215 220

Gln Lys Lys Ile Leu Val Ser Trp Ser Ser Pro Lys Pro Ile Gly Pro
225 230 235 240

Leu Thr Asp Leu Gly Asp Pro Ile Phe Gln Lys His Pro Asp Lys Val
245 250 255

Asp Leu Thr Val Pro Leu Pro Phe Leu Val Pro Arg Pro Gln Leu Gln
260 265 270

Gln Gln His Leu Gln Pro Ser Leu Met Ser Ile Leu Gly Gly Val His
275 280 285

His Leu Leu Asn Leu Thr Gln Pro Lys Leu Ala Gln Asp Cys Trp Leu
290 295 300

Cys Leu Lys Ala Lys Pro Pro Tyr Tyr Val Gly Leu Gly Val Glu Ala
305 310 315 320

Thr Leu Lys Arg Gly Pro Leu Ser Cys His Thr Arg Pro Arg Ala Leu
325 330 335

Thr Ile Gly Asp Val Ser Gly Asn Ala Ser Cys Leu Ile Ser Thr Gly
340 345 350

Tyr Asn Leu Ser Ala Ser Pro Phe Gln Ala Thr Cys Asn Gln Ser Leu
355 360 365

Leu Thr Ser Ile Ser Thr Ser Val Ser Tyr Gln Ala Pro Asn Asn Thr
370 375 380

Trp Leu Ala Cys Thr Ser Gly Leu Thr Arg Cys Ile Asn Gly Thr Glu
385 390 395 400

Pro Gly Pro Leu Leu Cys Val Leu Val His Val Leu Pro Gln Val Tyr
405 410 415

Val Tyr Ser Gly Pro Glu Gly Arg Gln Leu Ile Ala Pro Pro Glu Leu
420 425 430

His Pro Arg Leu His Gln Ala Val Pro Leu Leu Val Pro Leu Leu Ala
435 440 445

Gly Leu Ser Ile Ala Gly Ser Ala Ala Ile Gly Thr Ala Ala Leu Val
450 455 460

Gln Gly Glu Thr Gly Leu Ile Ser Leu Ser Gln Gln Val Asp Ala Asp
465 470 475 480

Phe Ser Asn Leu Gln Ser Ala Ile Asp Ile Leu His Ser Gln Val Glu
485 490 495

Ser Leu Ala Glu Val Val Leu Gln Asn Cys Arg Cys Leu Asp Leu Leu
500 505 510

Phe Leu Ser Gln Gly Gly Leu Cys Ala Ala Leu Gly Glu Ser Cys Cys
515 520 525

Phe Tyr Ala Asn Gln Ser Gly Val Ile Lys Gly Thr Val Lys Lys Val
530 535 540

Arg Glu Asn Leu Asp Arg His Gln Gln Glu Arg Glu Asn Asn Ile Pro
545 550 555 560

Trp Tyr Gln Ser Met Phe Asn Trp Asn Pro Trp Leu Thr Thr Leu Ile
565 570 575

Thr Gly Leu Ala Gly Pro Leu Leu Ile Leu Leu Leu Ser Leu Ile Phe
580 585 590

Gly Pro Cys Ile Leu Asn Ser Phe Leu Asn Phe Ile Lys Gln Arg Ile
595 600 605

Ala Ser Val Lys Leu Thr Tyr Leu Lys Thr Gln Tyr Asp Thr Leu Val
610 615 620

Asn Asn
625

<210> 85

<211> 1812

<212> DNA

<213> Human endogenous retrovirus R

<400> 85

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aaaggagaac cctgggaggg atgcctccac tgcacccaca ctacgtggtc ggggaacatc 120

atgactaaaa ccctgttgta tcacacttat tatgagtgtg ctgggacctg cctaggaact 180

tgtactcaca accagacaac ctactcagtc tgtgacccag gaaggggcca gccttatgtg 240

tgttatgacc ctaagtcttc acctgggatc tggtttgaaa ttcatgtcgg gtcaaaggaa 300

ggggatcttc taaaccaaac caaggtattt ccctctggca aggatgtcgt atccttatac 360

tttgatgttt gccagatagt atccatgggc tcactctttc ccgtaatctt cagttccatg 420

gagtactata gtagctgcca taaaaatagg tatgcacacc ctgcttgttc caccgattcc 480

ccagtaacaa cttgctggga ctgcacaacg tggtccacta accaacaatc actagggcca 540

attatgctta ccaaaatacc attagaacca gattgtaaaa caagcacttg caattctgta 600

aatcttacca tcttagagcc agatcagccc atatggacaa caggtttaaa agcaccgcta 660

ggggcacgag tcagcggtga agaaattggc ccaggagcct atgtctatct atatatcata 720

aagaaaactc ggacccgctc aacccaacag ttccgagttt ttgagtcatt ctatgagcat 780

gttaaccaga aattgcctga gccccctccc ttggccagta atttattcgc ccaactggct 840

gaaaacatag ccagcagcct gcacgttgct tcatgttatg tctgtggggg aatgaacatg 900

ggagaccaat ggccatggga agcaagggaa ctaatgcccc aagataattt cacactaacc 960

gcctcttccc tcgaacctgc accatcaagt cagagcatct ggttcttaaa aacctccatt 1020

attggaaaat tctgtattgc tcgctgggga aaggccttta cagacccagt aggagagtta 1080

acttgcctag gacaacaata ttacaacgag acactaggaa agactttatg gaggggcaaa 1140

agcaataatt ctgaatcacc acacccaagc ccattctctc gtttcccatc tttaaaccat 1200

tcttggtacc aacttgaagc tccaaatacc tggcaggcac cctctggcct ctactggatc 1260

tgtgggccac aagcatatcg acaactgcca gctaaatggt caggggcctg tgtactgggg 1320

acaattaggc cgtccttctt cctaatgccc ctaaaacagg gagaagcctt aggatacccc 1380

atctatgatg aaactaaaag gaaaagcaaa agaggcataa ctataggaga ttggaaggac 1440

agtgaatggc ctcctgaaag aataattcaa tattatggcc cagccacctg ggcagaagat 1500

ggaatgtggg gataccgcac cccagtttac atgcttaacc gcattataag attgcaggca 1560

gtactagaaa tcattaccaa tgaaactgca ggggccttga atctgcttgc ccagcaagcc 1620

acaaaaatga gaaatgtcat ttatcaaaat agactggcct tagactacct cctagcccag 1680

gaagagggag tatgcggaaa gttcagcctt actaactgct gcctggaact tgatgacgaa 1740

ggaaaggtta tcaaagaaat aactgctaaa atccaaaagt tagctcacat cccagttcag 1800

acttggaaag ga 1812

<210> 86

<211> 604

<212> PRT

<213> Human endogenous retrovirus R

<400> 86

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Met Leu Gly Met Asn Met Leu Leu Ile Thr Leu Phe Leu Leu Leu Pro
1               5                  10                  15

Leu Ser Met Leu Lys Gly Glu Pro Trp Glu Gly Cys Leu His Cys Thr
            20                  25                  30

His Thr Thr Trp Ser Gly Asn Ile Met Thr Lys Thr Leu Leu Tyr His
        35                  40                  45

Thr Tyr Tyr Glu Cys Ala Gly Thr Cys Leu Gly Thr Cys Thr His Asn
    50                  55                  60

Gln Thr Thr Tyr Ser Val Cys Asp Pro Gly Arg Gly Gln Pro Tyr Val
65                  70                  75                  80

Cys Tyr Asp Pro Lys Ser Ser Pro Gly Ile Trp Phe Glu Ile His Val
                85                  90                  95

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

Gly Lys Asp Val Val Ser Leu Tyr Phe Asp Val Cys Gln Ile Val Ser
        115                 120                 125

Met Gly Ser Leu Phe Pro Val Ile Phe Ser Ser Met Glu Tyr Tyr Ser
    130                 135                 140

Ser Cys His Lys Asn Arg Tyr Ala His Pro Ala Cys Ser Thr Asp Ser
145                 150                 155                 160

Pro Val Thr Thr Cys Trp Asp Cys Thr Thr Trp Ser Thr Asn Gln Gln
                165                 170                 175

Ser Leu Gly Pro Ile Met Leu Thr Lys Ile Pro Leu Glu Pro Asp Cys
            180                 185                 190

Lys Thr Ser Thr Cys Asn Ser Val Asn Leu Thr Ile Leu Glu Pro Asp
        195                 200                 205

Gln Pro Ile Trp Thr Thr Gly Leu Lys Ala Pro Leu Gly Ala Arg Val
    210                 215                 220

Ser Gly Glu Glu Ile Gly Pro Gly Ala Tyr Val Tyr Leu Tyr Ile Ile
225                 230                 235                 240

Lys Lys Thr Arg Thr Arg Ser Thr Gln Gln Phe Arg Val Phe Glu Ser
                245                 250                 255
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Phe Tyr Glu His Val Asn Gln Lys Leu Pro Glu Pro Pro Pro Leu Ala
            260                 265                 270

Ser Asn Leu Phe Ala Gln Leu Ala Glu Asn Ile Ala Ser Ser Leu His
        275                 280                 285

Val Ala Ser Cys Tyr Val Cys Gly Gly Met Asn Met Gly Asp Gln Trp
    290                 295                 300

Pro Trp Glu Ala Arg Glu Leu Met Pro Gln Asp Asn Phe Thr Leu Thr
305                 310                 315                 320

Ala Ser Ser Leu Glu Pro Ala Pro Ser Ser Gln Ser Ile Trp Phe Leu
                325                 330                 335

Lys Thr Ser Ile Ile Gly Lys Phe Cys Ile Ala Arg Trp Gly Lys Ala
            340                 345                 350

Phe Thr Asp Pro Val Gly Glu Leu Thr Cys Leu Gly Gln Gln Tyr Tyr
        355                 360                 365

Asn Glu Thr Leu Gly Lys Thr Leu Trp Arg Gly Lys Ser Asn Asn Ser
    370                 375                 380

Glu Ser Pro His Pro Ser Pro Phe Ser Arg Phe Pro Ser Leu Asn His
385                 390                 395                 400

Ser Trp Tyr Gln Leu Glu Ala Pro Asn Thr Trp Gln Ala Pro Ser Gly
                405                 410                 415

Leu Tyr Trp Ile Cys Gly Pro Gln Ala Tyr Arg Gln Leu Pro Ala Lys
            420                 425                 430

Trp Ser Gly Ala Cys Val Leu Gly Thr Ile Arg Pro Ser Phe Phe Leu
        435                 440                 445

Met Pro Leu Lys Gln Gly Glu Ala Leu Gly Tyr Pro Ile Tyr Asp Glu
    450                 455                 460

Thr Lys Arg Lys Ser Lys Arg Gly Ile Thr Ile Gly Asp Trp Lys Asp
465                 470                 475                 480

Ser Glu Trp Pro Pro Glu Arg Ile Ile Gln Tyr Tyr Gly Pro Ala Thr
                485                 490                 495

Trp Ala Glu Asp Gly Met Trp Gly Tyr Arg Thr Pro Val Tyr Met Leu
            500                 505                 510

Asn Arg Ile Ile Arg Leu Gln Ala Val Leu Glu Ile Ile Thr Asn Glu
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515 520 525

Thr Ala Gly Ala Leu Asn Leu Leu Ala Gln Gln Ala Thr Lys Met Arg
530 535 540

Asn Val Ile Tyr Gln Asn Arg Leu Ala Leu Asp Tyr Leu Leu Ala Gln
545 550 555 560

Glu Glu Gly Val Cys Gly Lys Phe Ser Leu Thr Asn Cys Cys Leu Glu
565 570 575

Leu Asp Asp Glu Gly Lys Val Ile Lys Glu Ile Thr Ala Lys Ile Gln
580 585 590

Lys Leu Ala His Ile Pro Val Gln Thr Trp Lys Gly
595 600

<210> 87

<211> 1563

<212> DNA

<213> Human endogenous retrovirus V

<400> 87
atgcccctac tctcacaggc acagtggaat gaaaattccc ttgtcagttt ttccaaaata 60

attgcttcgg gaaaccatct aagcaactgt tggatctgcc acaacttcat caccaggtcc 120

tcatcttacc aatatatttt ggtaagaaat ttttctttaa acctaacatt tggttcagga 180

atccctgaag gccaacataa atctgttccg ctccaggttt cgcttgctaa ctcagcgcac 240

caagtcccct gcctggatct cactccacct ttcaatcaaa gctctaaaac ttctttctat 300

ttctacaact gctcttctct aaaccaaacc tgttgtccat gccctgaagg acactgtgac 360

aggaagaaca cctctgagga gggattcccc agtcccacca tccatcccat gagcttctcc 420

ccagcaggct gccaccctaa cttgactcac tggtgtccag ctaaacaaat gaacgattat 480

cgagacaagt caccccaaaa ccgctgtgca gcttgggaag gaaaagagct aatcacatgg 540

agggttctat attcgcttcc caaggcacac actgtcccca catggccaaa atctactgtt 600

cccctgggag ggcctctatc ccctgcatgc aatcaaacta ttccagcagg gtggaaatcg 660

cagttacaca agtggttcga cagccacatc ccccggtggg cctgtacccc tcctggctat 720

gtatttttat gtgggccaca aaaaaataaa ctgccctttg atggaagtcc taagataacc 780

tattcaaccc cccctgtggc aaacctctac acttgcatta ataacatcca acatacggga 840

gaatgtgctg tgggactttt gggaccacgg gggataggtg tgaccattta taacaccacc 900

caacccagac agaaaagagc tctgggtcta atactggcag ggatgggtgc ggccatagga 960

atgatcgccc catggggagg gttcacttat catgatgtca ccctcagaaa tctctccaga 1020

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gattctctag caaatgtagt catggacaac agattggcct tagattacct cttagcagag 1140

cagggtggag tctgtgcagt gatcaataaa tcctgttgcg tttatgtcaa taacagtggg 1200

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ccttgtttct ttaatttact gattaagtgt gtctcttcta ggataaagca atttcacatg 1440

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cacatctccc ccttggatgc cagtgggcaa agattccggg aaactatgga ggaattttct 1560

ctc 1563

<210> 88

<211> 521

<212> PRT

<213> Human endogneous retrovirus V

<400> 88

Met Pro Leu Leu Ser Gln Ala Gln Trp Asn Glu Asn Ser Leu Val Ser
1 5 10 15

Phe Ser Lys Ile Ile Ala Ser Gly Asn His Leu Ser Asn Cys Trp Ile
20 25 30

Cys His Asn Phe Ile Thr Arg Ser Ser Ser Tyr Gln Tyr Ile Leu Val
35 40 45

Arg Asn Phe Ser Leu Asn Leu Thr Phe Gly Ser Gly Ile Pro Glu Gly
50 55 60

Gln His Lys Ser Val Pro Leu Gln Val Ser Leu Ala Asn Ser Ala His
65 70 75 80

Gln Val Pro Cys Leu Asp Leu Thr Pro Pro Phe Asn Gln Ser Ser Lys
85 90 95

Thr Ser Phe Tyr Phe Tyr Asn Cys Ser Ser Leu Asn Gln Thr Cys Cys
100 105 110

Pro Cys Pro Glu Gly His Cys Asp Arg Lys Asn Thr Ser Glu Glu Gly

115 120 125

Phe Pro Ser Pro Thr Ile His Pro Met Ser Phe Ser Pro Ala Gly Cys
130 135 140

His Pro Asn Leu Thr His Trp Cys Pro Ala Lys Gln Met Asn Asp Tyr
145 150 155 160

Arg Asp Lys Ser Pro Gln Asn Arg Cys Ala Ala Trp Glu Gly Lys Glu
165 170 175

Leu Ile Thr Trp Arg Val Leu Tyr Ser Leu Pro Lys Ala His Thr Val
180 185 190

Pro Thr Trp Pro Lys Ser Thr Val Pro Leu Gly Gly Pro Leu Ser Pro
195 200 205

Ala Cys Asn Gln Thr Ile Pro Ala Gly Trp Lys Ser Gln Leu His Lys
210 215 220

Trp Phe Asp Ser His Ile Pro Arg Trp Ala Cys Thr Pro Pro Gly Tyr
225 230 235 240

Val Phe Leu Cys Gly Pro Gln Lys Asn Lys Leu Pro Phe Asp Gly Ser
245 250 255

Pro Lys Ile Thr Tyr Ser Thr Pro Pro Val Ala Asn Leu Tyr Thr Cys
260 265 270

Ile Asn Asn Ile Gln His Thr Gly Glu Cys Ala Val Gly Leu Leu Gly
275 280 285

Pro Arg Gly Ile Gly Val Thr Ile Tyr Asn Thr Thr Gln Pro Arg Gln
290 295 300

Lys Arg Ala Leu Gly Leu Ile Leu Ala Gly Met Gly Ala Ala Ile Gly
305 310 315 320

Met Ile Ala Pro Trp Gly Gly Phe Thr Tyr His Asp Val Thr Leu Arg
325 330 335

Asn Leu Ser Arg Gln Ile Asp Asn Ile Ala Lys Ser Thr Arg Asp Ser
340 345 350

Ile Ser Lys Leu Lys Ala Ser Ile Asp Ser Leu Ala Asn Val Val Met
355 360 365

Asp Asn Arg Leu Ala Leu Asp Tyr Leu Leu Ala Glu Gln Gly Gly Val
370 375 380

Cys Ala Val Ile Asn Lys Ser Cys Cys Val Tyr Val Asn Asn Ser Gly
385 390 395 400

Ala Ile Glu Glu Asp Ile Lys Lys Ile Tyr Asp Glu Ala Thr Trp Leu
405 410 415

His Asp Phe Gly Lys Gly Gly Ala Ser Ala Arg Ala Ile Trp Glu Ala
420 425 430

Val Lys Ser Ala Leu Pro Ser Leu Asn Trp Phe Val Pro Leu Leu Gly
435 440 445

Pro Ala Thr Val Ile Leu Leu Leu Phe Leu Phe Gly Pro Cys Phe Phe
450 455 460

Asn Leu Leu Ile Lys Cys Val Ser Ser Arg Ile Lys Gln Phe His Met
465 470 475 480

Lys Ser Pro Gln Met Glu Arg Tyr Gln Leu Ser Val Ile Gly Gly Pro
485 490 495

Ser Thr Tyr Lys His Ile Ser Pro Leu Asp Ala Ser Gly Gln Arg Phe
500 505 510

Arg Glu Thr Met Glu Glu Phe Ser Leu
515 520

<210> 89

<211> 1542

<212> DNA

<213> Human endogenous retrovirus R(b)

<400> 89
atggatccac tacacacgat tgaaaaagtt cctgcaagaa gaaacatcca cgacagagga 60

caccaaggcc accgaatggg agatggaacc cctggaaggc ctaagatttc tgttcaacaa 120

atgacaagat tttcccttat aatatttttc ctttctgctc cttttgttgt taatgcctct 180

acctctaacg ttttcctaca atgggcacac agttatgcag atggcttaca acaaggagac 240

ccttgctggg tctgtggttc gttacccgtc actaacacca tggagctacc ttggtgggtc 300

tccccgctac aagggaaaga ctgggttttt tttcaaagct ttatagggga tcttaaacaa 360

tggacagggg cacagatgac tggggtaact agaaaaaaca tttcagaatg gcctataaat 420

aaaactttaa atgagccagg gcatgataaa ccattctcag taaatgagac aagggataaa 480

gtaatagcct ttgccatccc cttgttggat accaaggtgt ttgtccagac ttccagacct 540

cagaacactc aatatagaaa tgggtttctc cagatatggg acgggttcat ttggctgaca 600

gccactaagg gacacttaag ccagatagct cccttatgct gggagcaaag aaatcactcc 660

cttgataact ggccaaacac aactcgtgtt atgggatgga ttccacctgg acagtgccga 720

catactatac tgttacaaca gagggaccta tttgccacag actggtctca gcaacctggc 780

ttgaattggt atgctcccaa cggaacccag tggctctgca gcccaaactt atggccttgg 840

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gtaaaaacca tggaagtcta tccttatctt ccacatgtgg ttaaccaagg gactagggcc 960

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gtaatacagc acatagaggc tctagccaat tttacccaac gggccctaaa tgacagcctc 1080

caaagtattt ctctcatgaa tgctgaagtg tattatatgc acgaggacat cttacaaaac 1140

cgaatggccc tagatatttt aactgcggct gaaggaggaa cctgtgccct catcaaaact 1200

gaatgttgtg tgtatattcc caataactct agaaacattt ccttggcctt agaggataca 1260

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cagtttagtg gaagaccttc ctggtggcag aaaatcctca ttgtccttgc caccctctgg 1380

agcgtaggca tagcactgtg ttgtggactg tatttttgtc gcatgttttc ccaacacatt 1440

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<210> 90

<211> 514

<212> PRT

<213> Human endogenous retrovirus R(b)

<400> 90

Met Asp Pro Leu His Thr Ile Glu Lys Val Pro Ala Arg Arg Asn Ile
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His Asp Arg Gly His Gln Gly His Arg Met Gly Asp Gly Thr Pro Gly
20 25 30

Arg Pro Lys Ile Ser Val Gln Gln Met Thr Arg Phe Ser Leu Ile Ile
35 40 45

Phe Phe Leu Ser Ala Pro Phe Val Val Asn Ala Ser Thr Ser Asn Val
50 55 60

Phe Leu Gln Trp Ala His Ser Tyr Ala Asp Gly Leu Gln Gln Gly Asp
65 70 75 80

Pro Cys Trp Val Cys Gly Ser Leu Pro Val Thr Asn Thr Met Glu Leu
85 90 95

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

Ser Phe Ile Gly Asp Leu Lys Gln Trp Thr Gly Ala Gln Met Thr Gly
115 120 125

Val Thr Arg Lys Asn Ile Ser Glu Trp Pro Ile Asn Lys Thr Leu Asn
130 135 140

Glu Pro Gly His Asp Lys Pro Phe Ser Val Asn Glu Thr Arg Asp Lys
145 150 155 160

Val Ile Ala Phe Ala Ile Pro Leu Leu Asp Thr Lys Val Phe Val Gln
165 170 175

Thr Ser Arg Pro Gln Asn Thr Gln Tyr Arg Asn Gly Phe Leu Gln Ile
180 185 190

Trp Asp Gly Phe Ile Trp Leu Thr Ala Thr Lys Gly His Leu Ser Gln
195 200 205

Ile Ala Pro Leu Cys Trp Glu Gln Arg Asn His Ser Leu Asp Asn Trp
210 215 220

Pro Asn Thr Thr Arg Val Met Gly Trp Ile Pro Pro Gly Gln Cys Arg
225 230 235 240

His Thr Ile Leu Leu Gln Gln Arg Asp Leu Phe Ala Thr Asp Trp Ser
245 250 255

Gln Gln Pro Gly Leu Asn Trp Tyr Ala Pro Asn Gly Thr Gln Trp Leu
260 265 270

Cys Ser Pro Asn Leu Trp Pro Trp Leu Pro Ser Gly Trp Leu Gly Cys
275 280 285

Cys Thr Leu Gly Ile Pro Trp Ala Gln Gly Arg Trp Val Lys Thr Met
290 295 300

Glu Val Tyr Pro Tyr Leu Pro His Val Val Asn Gln Gly Thr Arg Ala
305 310 315 320

Ile Val His Arg Asn Asp His Leu Pro Thr Ile Phe Met Pro Ser Val

325 330 335

Gly Leu Gly Thr Val Ile Gln His Ile Glu Ala Leu Ala Asn Phe Thr
340 345 350

Gln Arg Ala Leu Asn Asp Ser Leu Gln Ser Ile Ser Leu Met Asn Ala
355 360 365

Glu Val Tyr Tyr Met His Glu Asp Ile Leu Gln Asn Arg Met Ala Leu
370 375 380

Asp Ile Leu Thr Ala Ala Glu Gly Gly Thr Cys Ala Leu Ile Lys Thr
385 390 395 400

Glu Cys Cys Val Tyr Ile Pro Asn Asn Ser Arg Asn Ile Ser Leu Ala
405 410 415

Leu Glu Asp Thr Cys Arg Gln Ile Gln Val Ile Ser Ser Ser Ala Leu
420 425 430

Ser Leu His Asp Trp Ile Ala Ser Gln Phe Ser Gly Arg Pro Ser Trp
435 440 445

Trp Gln Lys Ile Leu Ile Val Leu Ala Thr Leu Trp Ser Val Gly Ile
450 455 460

Ala Leu Cys Cys Gly Leu Tyr Phe Cys Arg Met Phe Ser Gln His Ile
465 470 475 480

Pro Gln Thr His Ser Ile Ile Phe Gln Gln Glu Leu Pro Leu Ser Pro
485 490 495

Pro Ser Gln Glu His Tyr Gln Ser Gln Arg Asp Ile Phe His Ser Asn
500 505 510

Ala Pro

<210> 91

<211> 1464

<212> DNA

<213> Human T-cell lymphotropic virus type 1

<400> 91
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tgcaatcctg cccagccagt ttgttcgtgg accctcgacc tgctggccct ttcagcagat 180

caggccctac agccccccctg ccctaaccta gtaagttact ccagctacca tgccacctat 240

tccctatatc tattccctca ttggactaag aagccaaacc gaaatggcgg aggctattat 300

tcagcctctt attcagaccc ttgttcctta aagtgcccat acctggggtg ccaatcatgg 360

acctgccccct atacaggagc cgtctccagc ccctactgga agtttcaaca cgatgtcaat 420

tttactcaag aagtttcacg cctcaatatt aatctccatt tttcaaaatg cggttttccc 480

ttctcccttc tagtcgacgc tccaggatat gaccccatct ggttccttaa taccgaaccc 540

agccaactgc ctcccaccgc ccctcctcta ctcccccact ctaacctaga ccacatcctc 600

gagccctcta taccatggaa atcaaaactc ctgacccttg tccagttaac cctacaaagc 660

actaattata cttgcattgt ctgtatcgat cgtgccagcc tctccacttg gcacgtccta 720

tactctccca acgtctctgt tccatcctct tcttctaccc ccctccttta cccatcgtta 780

gcgcttccag ccccccacct gacgttacca tttaactgga cccactgctt tgacccccag 840

attcaagcta tagtctcctc cccctgtcat aactccctca tcctgccccc cttttccttg 900

tcacctgttc ccaccctagg atcccgctcc cgccgagcgg taccggtggc ggtctggctt 960

gtctccgccc tggccatggg agccggagtg gctggcggga ttaccggctc catgtccctc 1020

gcctcaggaa agagcctcct acatgaggtg gacaaagata tttcccagtt aactcaagca 1080

atagtcaaaa accacaaaaa tctactcaaa attgcgcagt atgctgccca gaacagacga 1140

ggccttgatc tcctgttctg ggagcaagga ggattatgca aagcattaca agaacagtgc 1200

cgttttccga atattaccaa ttcccatgtc ccaatactac aagaaagacc ccccccttgag 1260

aatcgagtcc tgactggctg gggccttaac tgggaccttg gcctctcaca gtgggctcga 1320

gaggccttac aaactggaat cacccttgtt gcgctactcc ttcttgttat ccttgcagga 1380

ccatgcatcc tccgtcagct acgacacctc ccctcgcgcg tcagataccc ccattactct 1440

cttataaacc ctgagtcatc cctg 1464

<210> 92

<211> 488

<212> PRT

<213> Human T-cell lymphotropic virus type 1

<400> 92

Met Gly Lys Phe Leu Ala Thr Leu Ile Leu Phe Phe Gln Phe Cys Pro
1 5 10 15

Leu Ile Phe Gly Asp Tyr Ser Pro Ser Cys Cys Thr Leu Thr Ile Gly

```
            20                  25                  30

Val Ser Ser Tyr His Ser Lys Pro Cys Asn Pro Ala Gln Pro Val Cys
        35                  40                  45

Ser Trp Thr Leu Asp Leu Leu Ala Leu Ser Ala Asp Gln Ala Leu Gln
    50                  55                  60

Pro Pro Cys Pro Asn Leu Val Ser Tyr Ser Ser Tyr His Ala Thr Tyr
65                  70                  75                  80

Ser Leu Tyr Leu Phe Pro His Trp Thr Lys Lys Pro Asn Arg Asn Gly
                85                  90                  95

Gly Gly Tyr Tyr Ser Ala Ser Tyr Ser Asp Pro Cys Ser Leu Lys Cys
            100                 105                 110

Pro Tyr Leu Gly Cys Gln Ser Trp Thr Cys Pro Tyr Thr Gly Ala Val
        115                 120                 125

Ser Ser Pro Tyr Trp Lys Phe Gln His Asp Val Asn Phe Thr Gln Glu
    130                 135                 140

Val Ser Arg Leu Asn Ile Asn Leu His Phe Ser Lys Cys Gly Phe Pro
145                 150                 155                 160

Phe Ser Leu Leu Val Asp Ala Pro Gly Tyr Asp Pro Ile Trp Phe Leu
                165                 170                 175

Asn Thr Glu Pro Ser Gln Leu Pro Pro Thr Ala Pro Pro Leu Leu Pro
            180                 185                 190

His Ser Asn Leu Asp His Ile Leu Glu Pro Ser Ile Pro Trp Lys Ser
        195                 200                 205

Lys Leu Leu Thr Leu Val Gln Leu Thr Leu Gln Ser Thr Asn Tyr Thr
    210                 215                 220

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

Tyr Ser Pro Asn Val Ser Val Pro Ser Ser Ser Ser Thr Pro Leu Leu
                245                 250                 255

Tyr Pro Ser Leu Ala Leu Pro Ala Pro His Leu Thr Leu Pro Phe Asn
            260                 265                 270

Trp Thr His Cys Phe Asp Pro Gln Ile Gln Ala Ile Val Ser Ser Pro
        275                 280                 285
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Cys His Asn Ser Leu Ile Leu Pro Pro Phe Ser Leu Ser Pro Val Pro
290 295 300

Thr Leu Gly Ser Arg Ser Arg Arg Ala Val Pro Val Ala Val Trp Leu
305 310 315 320

Val Ser Ala Leu Ala Met Gly Ala Gly Val Ala Gly Gly Ile Thr Gly
325 330 335

Ser Met Ser Leu Ala Ser Gly Lys Ser Leu Leu His Glu Val Asp Lys
340 345 350

Asp Ile Ser Gln Leu Thr Gln Ala Ile Val Lys Asn His Lys Asn Leu
355 360 365

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

Leu Phe Trp Glu Gln Gly Gly Leu Cys Lys Ala Leu Gln Glu Gln Cys
385 390 395 400

Arg Phe Pro Asn Ile Thr Asn Ser His Val Pro Ile Leu Gln Glu Arg
405 410 415

Pro Pro Leu Glu Asn Arg Val Leu Thr Gly Trp Gly Leu Asn Trp Asp
420 425 430

Leu Gly Leu Ser Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr
435 440 445

Leu Val Ala Leu Leu Leu Leu Val Ile Leu Ala Gly Pro Cys Ile Leu
450 455 460

Arg Gln Leu Arg His Leu Pro Ser Arg Val Arg Tyr Pro His Tyr Ser
465 470 475 480

Leu Ile Asn Pro Glu Ser Ser Leu
485

<210> 93

<211> 1458

<212> DNA

<213> Human T-cell lymphotropic virus type 2

<400> 93

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caacccgtct gcacgtggaa cctcgacctt aattccctaa caacggacca acgactacac 180

ccccccctgcc ctaacctaat tacttactct ggcttccata agacttattc cttatactta 240

ttcccacatt ggataaaaaa gccaaacaga cagggcctag ggtactactc gccttcctac 300

aatgaccctt gctcgctaca atgcccctac ttgggctgcc aagcatggac atccgcatac 360

acgggccccg tctccagtcc atcctggaag tttcattcag atgtaaattt cacccaggaa 420

gtcagccaag tgtcccttcg actacacttc tctaagtgcg gctcctccat gaccctccta 480

gtagatgccc ctggatatga tcctttatgg ttcatcacct cagaacccac tcagcctcca 540

ccaacttctc ccccattggt ccatgactcc gaccttgaac atgtcctaac cccctccacg 600

tcctggacga ccaaaatact caaatttatc cagctgacct tacagagcac caattactcc 660

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gctcctccat cccaaccctt cccttggacc cattgctacc aacctcgcct acaggcgata 840

acaacagata actgcaacaa ctccattatc ctccccccctt tttccctcgc tcccgtacct 900

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catcaaaaca tcctccgggt tgcacagtat gcagcccaaa atagacgagg attagacctc 1140

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aacccagaaa ccatgcta 1458

<210> 94

<211> 486

<212> PRT

<213> Human T-cell lymphotropic virus type 2

<400> 94

Met Gly Asn Val Phe Phe Leu Leu Leu Phe Ser Leu Thr His Phe Pro
1 5 10 15

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

His Ser Ser Pro Cys Ser Pro Thr Gln Pro Val Cys Thr Trp Asn Leu
        35                  40                  45

Asp Leu Asn Ser Leu Thr Thr Asp Gln Arg Leu His Pro Pro Cys Pro
    50                  55                  60

Asn Leu Ile Thr Tyr Ser Gly Phe His Lys Thr Tyr Ser Leu Tyr Leu
65                  70                  75                  80

Phe Pro His Trp Ile Lys Lys Pro Asn Arg Gln Gly Leu Gly Tyr Tyr
                85                  90                  95

Ser Pro Ser Tyr Asn Asp Pro Cys Ser Leu Gln Cys Pro Tyr Leu Gly
            100                 105                 110

Cys Gln Ala Trp Thr Ser Ala Tyr Thr Gly Pro Val Ser Ser Pro Ser
        115                 120                 125

Trp Lys Phe His Ser Asp Val Asn Phe Thr Gln Glu Val Ser Gln Val
    130                 135                 140

Ser Leu Arg Leu His Phe Ser Lys Cys Gly Ser Ser Met Thr Leu Leu
145                 150                 155                 160

Val Asp Ala Pro Gly Tyr Asp Pro Leu Trp Phe Ile Thr Ser Glu Pro
                165                 170                 175

Thr Gln Pro Pro Pro Thr Ser Pro Pro Leu Val His Asp Ser Asp Leu
            180                 185                 190

Glu His Val Leu Thr Pro Ser Thr Ser Trp Thr Thr Lys Ile Leu Lys
        195                 200                 205

Phe Ile Gln Leu Thr Leu Gln Ser Thr Asn Tyr Ser Cys Met Val Cys
    210                 215                 220

Val Asp Arg Ser Ser Leu Ser Ser Trp His Val Leu Tyr Thr Pro Asn
225                 230                 235                 240

Ile Ser Ile Pro Gln Gln Thr Ser Ser Arg Thr Ile Leu Phe Pro Ser
                245                 250                 255

Leu Ala Leu Pro Ala Pro Pro Ser Gln Pro Phe Pro Trp Thr His Cys
            260                 265                 270
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Tyr Gln Pro Arg Leu Gln Ala Ile Thr Thr Asp Asn Cys Asn Asn Ser
275 280 285

Ile Ile Leu Pro Pro Phe Ser Leu Ala Pro Val Pro Pro Pro Ala Thr
290 295 300

Arg Arg Arg Arg Ala Val Pro Ile Ala Val Trp Leu Val Ser Ala Leu
305 310 315 320

Ala Ala Gly Thr Gly Ile Ala Gly Gly Val Thr Gly Ser Leu Ser Leu
325 330 335

Ala Ser Ser Lys Ser Leu Leu Leu Glu Val Asp Lys Asp Ile Ser His
340 345 350

Leu Thr Gln Ala Ile Val Lys Asn His Gln Asn Ile Leu Arg Val Ala
355 360 365

Gln Tyr Ala Ala Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Trp Glu
370 375 380

Gln Gly Gly Leu Cys Lys Ala Ile Gln Glu Gln Cys Cys Phe Leu Asn
385 390 395 400

Ile Ser Asn Thr His Val Ser Val Leu Gln Glu Arg Pro Pro Leu Glu
405 410 415

Lys Arg Val Ile Thr Gly Trp Gly Leu Asn Trp Asp Leu Gly Leu Ser
420 425 430

Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr Ile Leu Ala Leu
435 440 445

Leu Leu Leu Val Ile Leu Phe Gly Pro Cys Ile Leu Arg Gln Ile Gln
450 455 460

Ala Leu Pro Gln Arg Leu Gln Asn Arg His Asn Gln Tyr Ser Leu Ile
465 470 475 480

Asn Pro Glu Thr Met Leu
485

<210> 95

<211> 1926

<212> DNA

<213> Feline leukemia virus

<400> 95

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ggggcacaag atgggttttg tgccgcatgg ggatgtgaaa ccaccggaga agcttggtgg 480

aagccctcct cctcatggga ctatatcaca gtaaaaagag ggagtagtca ggacaataac 540

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ctcctcttcg gcccatgcat ccttaacaga ttagtacaat tcgtaaaaga cagaatatct 1860

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cgacca 1926

<210> 96

<211> 642

<212> PRT

<213> Feline leukemia virus

<400> 96

Met Glu Ser Pro Thr His Pro Lys Pro Ser Lys Asp Lys Thr Leu Ser
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Trp Asn Leu Val Phe Leu Val Gly Ile Leu Phe Thr Ile Asp Ile Gly
20 25 30

Met Ala Asn Pro Ser Pro His Gln Ile Tyr Asn Val Thr Trp Val Ile
35 40 45

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

Thr Leu Thr Asp Val Tyr Pro Thr Leu His Val Asp Leu Cys Asp Leu
65 70 75 80

Val Gly Asp Thr Trp Glu Pro Ile Val Leu Ser Pro Thr Asn Val Lys
85 90 95

His Gly Ala Arg Tyr Pro Ser Ser Lys Tyr Gly Cys Lys Thr Thr Asp
100 105 110

Arg Lys Lys Gln Gln Gln Thr Tyr Pro Phe Tyr Val Cys Pro Gly His
115 120 125

Ala Pro Ser Leu Gly Pro Lys Gly Thr His Cys Gly Gly Ala Gln Asp
130 135 140

Gly Phe Cys Ala Ala Trp Gly Cys Glu Thr Thr Gly Glu Ala Trp Trp
145 150 155 160

Lys Pro Ser Ser Ser Trp Asp Tyr Ile Thr Val Lys Arg Gly Ser Ser
165 170 175

Gln Asp Asn Asn Cys Glu Gly Lys Cys Asn Pro Leu Ile Leu Gln Phe
180 185 190

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Thr Gln Lys Gly Lys Gln Ala Ser Trp Asp Gly Pro Lys Met Trp Gly
        195                 200                 205

Leu Arg Leu Tyr Arg Thr Gly Tyr Asp Pro Ile Ala Leu Phe Thr Val
    210                 215                 220

Ser Arg Gln Val Ser Thr Ile Thr Pro Pro Gln Ala Met Gly Pro Asn
225                 230                 235                 240

Leu Val Leu Pro Asp Gln Lys Pro Pro Ser Arg Gln Ser Gln Thr Gly
                245                 250                 255

Ser Lys Val Ala Thr Gln Arg Pro Gln Thr Asn Glu Ser Ala Pro Arg
            260                 265                 270

Ser Val Ala Pro Thr Thr Val Gly Pro Lys Arg Ile Gly Thr Gly Asp
        275                 280                 285

Arg Leu Ile Asn Leu Val Gln Gly Thr Tyr Leu Ala Leu Asn Ala Thr
    290                 295                 300

Asp Pro Asn Lys Thr Lys Asp Cys Trp Leu Cys Leu Val Ser Arg Pro
305                 310                 315                 320

Pro Tyr Tyr Glu Gly Ile Ala Ile Leu Gly Asn Tyr Ser Asn Gln Thr
                325                 330                 335

Asn Pro Pro Pro Ser Cys Leu Ser Ile Pro Gln His Lys Leu Thr Ile
            340                 345                 350

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

His Gln Ala Leu Cys Asn Lys Thr Gln Gln Gly His Thr Gly Ala His
    370                 375                 380

Tyr Leu Ala Ala Pro Asn Gly Thr Tyr Trp Ala Cys Asn Thr Gly Leu
385                 390                 395                 400

Thr Pro Cys Ile Ser Met Ala Val Leu Asn Trp Thr Ser Asp Phe Cys
                405                 410                 415

Val Leu Ile Glu Leu Trp Pro Arg Val Thr Tyr His Gln Pro Glu Tyr
            420                 425                 430

Val Tyr Thr His Phe Ala Lys Ala Val Arg Phe Arg Arg Glu Pro Ile
        435                 440                 445

Ser Leu Thr Val Ala Leu Met Leu Gly Gly Leu Thr Val Gly Gly Ile
```

450 455 460

Ala Ala Gly Val Gly Thr Gly Thr Lys Ala Leu Leu Glu Thr Ala Gln
465 470 475 480

Phe Arg Gln Leu Gln Met Ala Met His Thr Asp Ile Gln Ala Leu Glu
485 490 495

Glu Ser Ile Ser Ala Leu Glu Lys Ser Leu Thr Ser Leu Ser Glu Val
500 505 510

Val Leu Gln Asn Arg Arg Gly Leu Asp Ile Leu Phe Leu Gln Glu Gly
515 520 525

Gly Leu Cys Ala Ala Leu Lys Glu Glu Cys Cys Phe Tyr Ala Asp His
530 535 540

Thr Gly Leu Val Arg Asp Asn Met Ala Lys Leu Arg Glu Arg Leu Lys
545 550 555 560

Gln Arg Gln Gln Leu Phe Asp Ser Gln Gln Gly Trp Phe Glu Gly Trp
565 570 575

Phe Asn Arg Ser Pro Trp Phe Thr Thr Leu Ile Ser Ser Ile Met Gly
580 585 590

Pro Leu Leu Ile Leu Leu Leu Ile Leu Leu Phe Gly Pro Cys Ile Leu
595 600 605

Asn Arg Leu Val Gln Phe Val Lys Asp Arg Ile Ser Val Val Gln Ala
610 615 620

Leu Ile Leu Thr Gln Gln Tyr Gln Gln Ile Lys Gln Tyr Asp Pro Asp
625 630 635 640

Arg Pro

<210> 97

<211> 1977

<212> DNA

<213> Porcine endogenous retrovirus

<400> 97
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caggccacac cccccgatgt actccgtgct tacgggtttt acgtttgccc agggccccca 360

aataatgaag aatattgtgg aaatcctcag gatttctttt gcaagcaatg gagctgcgta 420

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ctagattact taaaaataag tttcactgaa aaaggaaaac aagaaaatat tcaaaagtgg 660

gtaaatggta tgtcttgggg aatagtgtac tatagaggct ctgggagaaa gaaaggatct 720

gttctgacta ttcgcctcag aatagaaact cagatggaac ctccggttgc tataggacca 780

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ggggcgaaac tttttaacct catccaggga gcttttcaag ctcttaactc cacgactcca 960

gaggctacct cttcttgttg gctttgctta gcttcgggcc caccttacta tgagggaatg 1020

gctagaggag ggaaattcaa tgtgacaaag gaacatagag accaatgtac atggggatcc 1080

caaaataagc ttacccttac tgaggtttct ggaaaaggca cctgcatagg gatggttccc 1140

ccatcccacc aacacctttg taaccacact gaagccttta atcgaacctc tgagagtcag 1200

tatctggtac ctggttatga caggtggtgg gcatgtaata ctggattaac cccttgtgtt 1260

tccaccttgg ttttcaacca aactaaagac ttttgcgtta tggtccaaat tgtcccccgg 1320

gtgtactact atcccgaaaa agcagtcctt gatgaatatg actatagata taatcggcca 1380

aaaagagagc ccatatccct gacactagct gtaatgctcg gattgggagt ggctgcaggc 1440

gtgggaacag gaacggctgc cctaatcaca ggaccgcaac agctggagaa aggacttagt 1500

aacctacatc gaattgtaac ggaaaatctc caagccctag aaaaatctgt cagtaacctg 1560

gaggaatccc taacctcctt atctgaagtg gttctacaga acagaagggg gttagatctg 1620

ttatttctaa aagaaggagg gttatgtgta gccttaaaag aggaatgctg cttctatgta 1680

gatcactcag gagccatcag agactccatg agcaagctta gagaaaggtt agagaggcgt 1740

cgaagggaaa gagaggctga ccaggggtgg tttgaaggat ggttcaacag gtctccttgg 1800

atggctaccc tactttctgc tttaacagga cccttaatag tcctcctcct gttactcaca 1860

gttgggccat gtattattaa caagttaatt gccttcatta gagaacgaat aagtgcagtc 1920

cagatcatgg tacttagaca acagtaccaa agcccgtcta gcagagaagc tggccgc 1977

<210> 98

<211> 659

<212> PRT

<213> Porcine endogenous retrovirus

<400> 98

Met His Pro Thr Leu Ser Arg Arg His Leu Pro Ile Arg Gly Gly Lys
1 5 10 15

Pro Lys Arg Leu Lys Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe
20 25 30

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

Ser Pro Asn Ser His Lys Pro Leu Ser Leu Thr Trp Leu Leu Thr Asp
50 55 60

Ser Gly Thr Gly Ile Asn Ile Asn Ser Thr Gln Gly Glu Ala Pro Leu
65 70 75 80

Gly Thr Trp Trp Pro Glu Leu Tyr Val Cys Leu Arg Ser Val Ile Pro
85 90 95

Gly Leu Asn Asp Gln Ala Thr Pro Pro Asp Val Leu Arg Ala Tyr Gly
100 105 110

Phe Tyr Val Cys Pro Gly Pro Pro Asn Asn Glu Glu Tyr Cys Gly Asn
115 120 125

Pro Gln Asp Phe Phe Cys Lys Gln Trp Ser Cys Val Thr Ser Asn Asp
130 135 140

Gly Asn Trp Lys Trp Pro Val Ser Gln Gln Asp Arg Val Ser Tyr Ser
145 150 155 160

Phe Val Asn Asn Pro Thr Ser Tyr Asn Gln Phe Asn Tyr Gly His Gly
165 170 175

Arg Trp Lys Asp Trp Gln Gln Arg Val Gln Lys Asp Val Arg Asn Lys
180 185 190

Gln Ile Ser Cys His Ser Leu Asp Leu Asp Tyr Leu Lys Ile Ser Phe
195 200 205

Thr Glu Lys Gly Lys Gln Glu Asn Ile Gln Lys Trp Val Asn Gly Met
210 215 220

Ser Trp Gly Ile Val Tyr Tyr Arg Gly Ser Gly Arg Lys Lys Gly Ser
225 230 235 240

Val Leu Thr Ile Arg Leu Arg Ile Glu Thr Gln Met Glu Pro Pro Val
245 250 255

Ala Ile Gly Pro Asn Lys Gly Leu Ala Glu Gln Gly Pro Pro Ile Gln
260 265 270

Glu Gln Arg Pro Ser Pro Asn Pro Ser Asp Tyr Asn Thr Thr Ser Gly
275 280 285

Ser Val Pro Thr Glu Pro Asn Ile Thr Ile Lys Thr Gly Ala Lys Leu
290 295 300

Phe Asn Leu Ile Gln Gly Ala Phe Gln Ala Leu Asn Ser Thr Thr Pro
305 310 315 320

Glu Ala Thr Ser Ser Cys Trp Leu Cys Leu Ala Ser Gly Pro Pro Tyr
325 330 335

Tyr Glu Gly Met Ala Arg Gly Gly Lys Phe Asn Val Thr Lys Glu His
340 345 350

Arg Asp Gln Cys Thr Trp Gly Ser Gln Asn Lys Leu Thr Leu Thr Glu
355 360 365

Val Ser Gly Lys Gly Thr Cys Ile Gly Met Val Pro Pro Ser His Gln
370 375 380

His Leu Cys Asn His Thr Glu Ala Phe Asn Arg Thr Ser Glu Ser Gln
385 390 395 400

Tyr Leu Val Pro Gly Tyr Asp Arg Trp Trp Ala Cys Asn Thr Gly Leu
405 410 415

Thr Pro Cys Val Ser Thr Leu Val Phe Asn Gln Thr Lys Asp Phe Cys
420 425 430

Val Met Val Gln Ile Val Pro Arg Val Tyr Tyr Tyr Pro Glu Lys Ala
435 440 445

Val Leu Asp Glu Tyr Asp Tyr Arg Tyr Asn Arg Pro Lys Arg Glu Pro
450 455 460

Ile Ser Leu Thr Leu Ala Val Met Leu Gly Leu Gly Val Ala Ala Gly
465 470 475 480

Val Gly Thr Gly Thr Ala Ala Leu Ile Thr Gly Pro Gln Gln Leu Glu
485 490 495

Lys Gly Leu Ser Asn Leu His Arg Ile Val Thr Glu Asn Leu Gln Ala
500 505 510

Leu Glu Lys Ser Val Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser
515 520 525

Glu Val Val Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys
530 535 540

Glu Gly Gly Leu Cys Val Ala Leu Lys Glu Glu Cys Cys Phe Tyr Val
545 550 555 560

Asp His Ser Gly Ala Ile Arg Asp Ser Met Ser Lys Leu Arg Glu Arg
565 570 575

Leu Glu Arg Arg Arg Arg Glu Arg Glu Ala Asp Gln Gly Trp Phe Glu
580 585 590

Gly Trp Phe Asn Arg Ser Pro Trp Met Ala Thr Leu Leu Ser Ala Leu
595 600 605

Thr Gly Pro Leu Ile Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys
610 615 620

Ile Ile Asn Lys Leu Ile Ala Phe Ile Arg Glu Arg Ile Ser Ala Val
625 630 635 640

Gln Ile Met Val Leu Arg Gln Gln Tyr Gln Ser Pro Ser Ser Arg Glu
645 650 655

Ala Gly Arg

<210> 99

<211> 1464

<212> DNA

<213> Simian T-cell lymphotropic virus type 1

<400> 99
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gattacagcc ccagctgctg tactctcacc attggagtct cctcatacca ttctaaaccc 120

tgcaatcctg cccagccggt ttgttcatgg actctcgacc tactggccct ttcagcagat 180

caagccctac agcccccctg ccctaatcta ataggttact ccagctacca tgccacctat 240

tccctatatc tatttcctca ttggattaaa aagccaaacc gaaacggtgg aggctactat 300

tcagcatctt attcagaccc ttgttcccta aagtgcccat acctagggtg ccaatcatgg 360

acctgccctt atacaggagc cgtctccagc ccctactgga aatttcaaca agatgtcaat 420

tttactcaag aagtctcacg cctcaatctt aatctccatt tttcaaaatg cggtttctcc 480

ttctcccttc tagttgacgc cccaggatat gaccccatct ggttccttaa caccgaaccc 540

aaccaactgc ctcccaccgc ccctcctcta ctccccccact ctaacctaga ccacatcctc 600

gagccctcta taccatggaa atcaaaactt ctgactcttg tccaactaac cctacagagc 660

actaactata cttgcattgt ctgtgtagat cgtgccagcc tatccacttg gcacgtcctg 720

tactctccca acgcctctgt tccatcctct tcttctaccc ccctccttta cccatcgtta 780

gcgcttccag ccccccacct gacgttacca tttaactgga cccactgctt tgacccccag 840

attcaagcta tagtctcctc cccctgtctt aactccctca tcctgccccc cttttccttg 900

tcacctgttc ccaccctagg atcccgttcc cgccgagcgg taccggtggc ggtctggctt 960

gtctccgccc tggccatggg agccgggatg gctggcggga ttaccggctc catgtccctt 1020

gcctcaggaa ggagcctcct acatgaggtg gacaaggata tttcccaatt aactcaagca 1080

atagtcaaaa accacaaaaa tctactcaaa attgcgcagt atgctgccca gaacagacga 1140

ggccttgatc tcctgttctg ggagcaagga ggattatgca aagcactaca agaacagtgc 1200

tgttttctaa atattaccaa ttcccatgtc tcaatactac aagaacgacc ccccccttgag 1260

aatcgagtcc tcaccggctg gggccttaac tgggaccttg gcctctcaca gtgggctcga 1320

gaggccttac aaactggaat cacccttgtt gcactactcc ttcttgttat ccttgcagga 1380

ccatgcatcc tccgtcaact acgacacctc ccctcgcgcg tcagataccc ccattattct 1440

cttataaacc ctgagtcatc cctg 1464

<210> 100

<211> 488

<212> PRT

<213> Simian T-cell lymphotropic virus type 1

<400> 100

Met Gly Lys Phe Leu Ala Ser Leu Thr Leu Phe Phe Gln Phe Cys Pro
1 5 10 15

Leu Ile Leu Gly Asp Tyr Ser Pro Ser Cys Cys Thr Leu Thr Ile Gly
20 25 30

```
Val Ser Ser Tyr His Ser Lys Pro Cys Asn Pro Ala Gln Pro Val Cys
        35                  40                  45

Ser Trp Thr Leu Asp Leu Leu Ala Leu Ser Ala Asp Gln Ala Leu Gln
    50                  55                  60

Pro Pro Cys Pro Asn Leu Ile Gly Tyr Ser Ser Tyr His Ala Thr Tyr
65                  70                  75                  80

Ser Leu Tyr Leu Phe Pro His Trp Ile Lys Lys Pro Asn Arg Asn Gly
                85                  90                  95

Gly Gly Tyr Tyr Ser Ala Ser Tyr Ser Asp Pro Cys Ser Leu Lys Cys
            100                 105                 110

Pro Tyr Leu Gly Cys Gln Ser Trp Thr Cys Pro Tyr Thr Gly Ala Val
        115                 120                 125

Ser Ser Pro Tyr Trp Lys Phe Gln Gln Asp Val Asn Phe Thr Gln Glu
    130                 135                 140

Val Ser Arg Leu Asn Leu Asn Leu His Phe Ser Lys Cys Gly Phe Ser
145                 150                 155                 160

Phe Ser Leu Leu Val Asp Ala Pro Gly Tyr Asp Pro Ile Trp Phe Leu
                165                 170                 175

Asn Thr Glu Pro Asn Gln Leu Pro Pro Thr Ala Pro Pro Leu Leu Pro
            180                 185                 190

His Ser Asn Leu Asp His Ile Leu Glu Pro Ser Ile Pro Trp Lys Ser
        195                 200                 205

Lys Leu Leu Thr Leu Val Gln Leu Thr Leu Gln Ser Thr Asn Tyr Thr
    210                 215                 220

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

Tyr Ser Pro Asn Ala Ser Val Pro Ser Ser Ser Ser Thr Pro Leu Leu
                245                 250                 255

Tyr Pro Ser Leu Ala Leu Pro Ala Pro His Leu Thr Leu Pro Phe Asn
            260                 265                 270

Trp Thr His Cys Phe Asp Pro Gln Ile Gln Ala Ile Val Ser Ser Pro
        275                 280                 285
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Cys Leu Asn Ser Leu Ile Leu Pro Pro Phe Ser Leu Ser Pro Val Pro
290 295 300

Thr Leu Gly Ser Arg Ser Arg Arg Ala Val Pro Val Ala Val Trp Leu
305 310 315 320

Val Ser Ala Leu Ala Met Gly Ala Gly Met Ala Gly Gly Ile Thr Gly
325 330 335

Ser Met Ser Leu Ala Ser Gly Arg Ser Leu Leu His Glu Val Asp Lys
340 345 350

Asp Ile Ser Gln Leu Thr Gln Ala Ile Val Lys Asn His Lys Asn Leu
355 360 365

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

Leu Phe Trp Glu Gln Gly Gly Leu Cys Lys Ala Leu Gln Glu Gln Cys
385 390 395 400

Cys Phe Leu Asn Ile Thr Asn Ser His Val Ser Ile Leu Gln Glu Arg
405 410 415

Pro Pro Leu Glu Asn Arg Val Leu Thr Gly Trp Gly Leu Asn Trp Asp
420 425 430

Leu Gly Leu Ser Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr
435 440 445

Leu Val Ala Leu Leu Leu Leu Val Ile Leu Ala Gly Pro Cys Ile Leu
450 455 460

Arg Gln Leu Arg His Leu Pro Ser Arg Val Arg Tyr Pro His Tyr Ser
465 470 475 480

Leu Ile Asn Pro Glu Ser Ser Leu
485

<210> 101

<211> 2025

<212> DNA

<213> Friend virus

<400> 101
atggcgtgtt caacgctccc aaaatcccct aaagataaga ttgacccgcg ggacctccta 60

atcccttaa ttctcttcct gtctctcaaa ggggccagat ccgcagcacc cggctccagc 120

cctcaccagg tctacaacat tacctgggaa gtgaccaatg gggatcggga gacagtatgg 180

gcaatatcag gcaaccaccc tctgtggact tggtggccag tcctcacccc agatttgtgt 240

atgttagctc tcagtgggcc gccccactgg gggctagagt atcaggcccc ctattcctcg 300

cccccggggc ccccttgttg ctcagggagc agcgggagca gtgcaggctg ttccagagac 360

tgcgacgagc ccttgacctc cctcacccct cggtgcaaca ctgcctggaa cagacttaag 420

ctagaccagg taactcataa atcaagtgag ggattttatg tctgccccgg gtcacatcgc 480

ccccgggaag ccaagtcctg tggaggtcca gactccttct actgtgcctc ttggggctgc 540

gagacaaccg gtagagtata ctggaagccc tcctcctctt gggactacat cacagtggac 600

aacaatctca ccactagcca ggctgtccag gtatgcaaag acaataagtg gtgcaatccc 660

ttggctatcc agtttacaaa cgccgggaaa caggtcacct catggacaac tggacactat 720

tggggtctac gtctttatgt ctctgggcgg gacccggggc ttactttcgg gatccgactc 780

agatatcaaa atctaggacc tcgggtcccg ataggaccga accccgtcct ggcagaccaa 840

ctttcgctcc cgcgacctaa tcccctaccc aaacctgcca agtctccccc cgcctctaat 900

tcgactccca cattgatttc cccgtccccc actcccactc agcccccgcc agcaggaacg 960

ggagacaggt tactaaatct agtacaggga gcttaccagg cactcaacct taccaaccct 1020

gataaaactc aagagtgctg gttatgccta gtgtctggac ccccctatta cgaaggggtt 1080

gccgtcctag gtacttattc caaccatacc tctgccccag ctaactgctc cgtggcctcc 1140

caacacaagt tgaccctgtc cgaagtgact ggacggggac tctgcatagg aacagtccca 1200

aaaactcacc aggccctgtg caacactacc cttaagatag acaaagggtc ttactatcta 1260

gttgccccca caggaactac gtgggcatgt aacactggac tcactccatg cctatctgcc 1320

accgtgctta atcgcaccac tgactattgc gttctcgtag agttatggcc cagggtcacc 1380

taccatcctc ccagttacgt ctatagccag tttgaaaaat cctatagaca taaaagagaa 1440

ccagtgtcct taaccttggc cctattatta ggtgggctaa ctatgggtgg catcgccgcg 1500

ggagtaggga caggaactac cgccctggtc gccacccagc agttccagca gctccatgct 1560

gccgtacaag atgatctcaa agaagtcgaa aagtcaatta ctaacctaga aaagtctctt 1620

acttcgttgt ctgaggttgt gctgcagaat cgacgaggcc tagacctgtt gttcctaaaa 1680

gaaggaggac tgtgtgctgc cctaaaagaa gaatgttgtt tctatgctga ccatacaggc 1740

ctagtaagag atagtatggc caaattaaga gagagactca ctcagagaca aaaactattt 1800

gagtcgagcc aaggatggtt cgaaggattg tttaacagat ccccctggtt taccacgtta 1860

atatccacca tcatggggcc tctcattata ctcctactaa ttctgctttt tggaccctgc 1920

attcttaatc gattagttca atttgttaaa gacaggatct cagtagtcca ggctttagtc 1980

ctgactcaac aataccacca gctaaaacca ctagaatacg agcca 2025

<210> 102

<211> 675

<212> PRT

<213> Friend virus

<400> 102

Met Ala Cys Ser Thr Leu Pro Lys Ser Pro Lys Asp Lys Ile Asp Pro
1 5 10 15

Arg Asp Leu Leu Ile Pro Leu Ile Leu Phe Leu Ser Leu Lys Gly Ala
20 25 30

Arg Ser Ala Ala Pro Gly Ser Ser Pro His Gln Val Tyr Asn Ile Thr
35 40 45

Trp Glu Val Thr Asn Gly Asp Arg Glu Thr Val Trp Ala Ile Ser Gly
50 55 60

Asn His Pro Leu Trp Thr Trp Trp Pro Val Leu Thr Pro Asp Leu Cys
65 70 75 80

Met Leu Ala Leu Ser Gly Pro Pro His Trp Gly Leu Glu Tyr Gln Ala
85 90 95

Pro Tyr Ser Ser Pro Pro Gly Pro Pro Cys Cys Ser Gly Ser Ser Gly
100 105 110

Ser Ser Ala Gly Cys Ser Arg Asp Cys Asp Glu Pro Leu Thr Ser Leu
115 120 125

Thr Pro Arg Cys Asn Thr Ala Trp Asn Arg Leu Lys Leu Asp Gln Val
130 135 140

Thr His Lys Ser Ser Glu Gly Phe Tyr Val Cys Pro Gly Ser His Arg
145 150 155 160

Pro Arg Glu Ala Lys Ser Cys Gly Gly Pro Asp Ser Phe Tyr Cys Ala
165 170 175

Ser Trp Gly Cys Glu Thr Thr Gly Arg Val Tyr Trp Lys Pro Ser Ser
180 185 190

Ser Trp Asp Tyr Ile Thr Val Asp Asn Asn Leu Thr Thr Ser Gln Ala
195 200 205

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Val Gln Val Cys Lys Asp Asn Lys Trp Cys Asn Pro Leu Ala Ile Gln
    210                 215                 220

Phe Thr Asn Ala Gly Lys Gln Val Thr Ser Trp Thr Thr Gly His Tyr
225                 230                 235                 240

Trp Gly Leu Arg Leu Tyr Val Ser Gly Arg Asp Pro Gly Leu Thr Phe
                245                 250                 255

Gly Ile Arg Leu Arg Tyr Gln Asn Leu Gly Pro Arg Val Pro Ile Gly
            260                 265                 270

Pro Asn Pro Val Leu Ala Asp Gln Leu Ser Leu Pro Arg Pro Asn Pro
        275                 280                 285

Leu Pro Lys Pro Ala Lys Ser Pro Pro Ala Ser Asn Ser Thr Pro Thr
    290                 295                 300

Leu Ile Ser Pro Ser Pro Thr Pro Thr Gln Pro Pro Pro Ala Gly Thr
305                 310                 315                 320

Gly Asp Arg Leu Leu Asn Leu Val Gln Gly Ala Tyr Gln Ala Leu Asn
                325                 330                 335

Leu Thr Asn Pro Asp Lys Thr Gln Glu Cys Trp Leu Cys Leu Val Ser
            340                 345                 350

Gly Pro Pro Tyr Tyr Glu Gly Val Ala Val Leu Gly Thr Tyr Ser Asn
        355                 360                 365

His Thr Ser Ala Pro Ala Asn Cys Ser Val Ala Ser Gln His Lys Leu
    370                 375                 380

Thr Leu Ser Glu Val Thr Gly Arg Gly Leu Cys Ile Gly Thr Val Pro
385                 390                 395                 400

Lys Thr His Gln Ala Leu Cys Asn Thr Thr Leu Lys Ile Asp Lys Gly
                405                 410                 415

Ser Tyr Tyr Leu Val Ala Pro Thr Gly Thr Thr Trp Ala Cys Asn Thr
            420                 425                 430

Gly Leu Thr Pro Cys Leu Ser Ala Thr Val Leu Asn Arg Thr Thr Asp
        435                 440                 445

Tyr Cys Val Leu Val Glu Leu Trp Pro Arg Val Thr Tyr His Pro Pro
    450                 455                 460
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Ser Tyr Val Tyr Ser Gln Phe Glu Lys Ser Tyr Arg His Lys Arg Glu
465 470 475 480

Pro Val Ser Leu Thr Leu Ala Leu Leu Leu Gly Gly Leu Thr Met Gly
485 490 495

Gly Ile Ala Ala Gly Val Gly Thr Gly Thr Thr Ala Leu Val Ala Thr
500 505 510

Gln Gln Phe Gln Gln Leu His Ala Ala Val Gln Asp Asp Leu Lys Glu
515 520 525

Val Glu Lys Ser Ile Thr Asn Leu Glu Lys Ser Leu Thr Ser Leu Ser
530 535 540

Glu Val Val Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys
545 550 555 560

Glu Gly Gly Leu Cys Ala Ala Leu Lys Glu Glu Cys Cys Phe Tyr Ala
565 570 575

Asp His Thr Gly Leu Val Arg Asp Ser Met Ala Lys Leu Arg Glu Arg
580 585 590

Leu Thr Gln Arg Gln Lys Leu Phe Glu Ser Ser Gln Gly Trp Phe Glu
595 600 605

Gly Leu Phe Asn Arg Ser Pro Trp Phe Thr Thr Leu Ile Ser Thr Ile
610 615 620

Met Gly Pro Leu Ile Ile Leu Leu Leu Ile Leu Leu Phe Gly Pro Cys
625 630 635 640

Ile Leu Asn Arg Leu Val Gln Phe Val Lys Asp Arg Ile Ser Val Val
645 650 655

Gln Ala Leu Val Leu Thr Gln Gln Tyr His Gln Leu Lys Pro Leu Glu
660 665 670

Tyr Glu Pro
675

<210> 103

<211> 1926

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated FeLV ENV

<220>

<221> misc_feature

<222> (1579)..(1581)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 103

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tttctggtgg ggatcttatt cacaatagac ataggaatgg ccaatcctag tccacaccaa 120

atatataatg taacttgggt aataaccaat gtacaaacta acacccaagc taatgccacc 180

tctatgttag gaaccttaac cgatgtctac cctaccctac atgttgactt atgtgaccta 240

gtgggagaca cctgggaacc tatagtccta agcccaacca atgtaaaaca cggggcacgt 300

taccttcct caaaatatgg atgtaaaact acagatagaa aaaaacagca acagacatac 360

ccctttacg tctgccccgg acatgccccc tcgctggggc caaagggaac acattgtgga 420

ggggcacaag atgggttttg tgccgcatgg ggatgtgaaa ccaccggaga agcttggtgg 480

aagccctcct cctcatggga ctatatcaca gtaaaaagag ggagtagtca ggacaataac 540

tgtgagggaa aatgcaaccc cctgattttg cagttcaccc agaaggggaa acaagcctct 600

tgggacggac ctaagatgtg gggattgcga ctataccgta caggatatga ccctatcgcc 660

ttattcacgg tatcccggca ggtgtcaacc attacgccgc ctcaggcaat gggaccaaac 720

ctagtcttac ctgatcaaaa acccccatcc cgacaatctc aaacagggtc caaagtggcg 780

acccagaggc cccaaacgaa tgaaagcgcc ccaaggtctg ttgcccccac caccgtgggt 840

cccaaacgga ttgggaccgg agataggtta ataaatttag tacaagggac atacctagcc 900

ttaaatgcca ccgaccccaa caaaactaaa gactgttggc tctgcctggt ttctcgacca 960

ccctattacg aagggattgc aatcttaggt aactacagca accaaacaaa ccctccccca 1020

tcctgcctat ctattccgca acacaagctg accatatctg aagtatcagg gcaaggactg 1080

tgcataggga ctgttcctaa gacccaccag gctttgtgca ataagacgca acagggacat 1140

acaggggcgc actatctagc cgcccccaat ggcacctatt gggcctgtaa cactggactc 1200

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ttatggccca gagtgactta ccatcaaccc gaatatgtgt acacacattt tgccaaagct 1320

gtcaggttcc gaagagaacc aatatcacta actgttgccc tcatgttggg aggactcact 1380

gtaggggcca tagccgcggg ggtcggaaca gggactaaag ccctccttga aacagcccag 1440

ttcagacaac tacaaatggc catgcacaca gacatccagg ccctagaaga gtcaattagt 1500

gccttagaaa agtccctgac ctccctttct gaagtagtct tacaaaacag acggggccta 1560

gatattctat tcctacaann nggagggctc tgtgccgcat taaaagaaga atgttgcttc 1620

tatgcggatc acaccggact cgtccgagac aatatggcta aattaagaga aagactaaaa 1680

cagcggcaac aactgtttga ctcccaacag ggatggtttg aaggatggtt caacaggtcc 1740

ccctggttta caaccctaat ttcctccatt atgggcccct tactaatcct actcctaatt 1800

ctcctcttcg gcccatgcat ccttaacaga ttagtacaat tcgtaaaaga cagaatatct 1860

gtggtacaag ccttaatttt aacccaacag taccaacaga taaagcaata cgatccggac 1920

cgacca 1926

<210> 104

<211> 642

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated FeLV ENV

<400> 104

Met Glu Ser Pro Thr His Pro Lys Pro Ser Lys Asp Lys Thr Leu Ser
1 5 10 15

Trp Asn Leu Val Phe Leu Val Gly Ile Leu Phe Thr Ile Asp Ile Gly
20 25 30

Met Ala Asn Pro Ser Pro His Gln Ile Tyr Asn Val Thr Trp Val Ile
35 40 45

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

Thr Leu Thr Asp Val Tyr Pro Thr Leu His Val Asp Leu Cys Asp Leu
65 70 75 80

Val Gly Asp Thr Trp Glu Pro Ile Val Leu Ser Pro Thr Asn Val Lys
85 90 95

His Gly Ala Arg Tyr Pro Ser Ser Lys Tyr Gly Cys Lys Thr Thr Asp
100 105 110

Arg Lys Lys Gln Gln Gln Thr Tyr Pro Phe Tyr Val Cys Pro Gly His
115 120 125

```
Ala Pro Ser Leu Gly Pro Lys Gly Thr His Cys Gly Gly Ala Gln Asp
    130                 135                 140

Gly Phe Cys Ala Ala Trp Gly Cys Glu Thr Thr Gly Glu Ala Trp Trp
145                 150                 155                 160

Lys Pro Ser Ser Ser Trp Asp Tyr Ile Thr Val Lys Arg Gly Ser Ser
                165                 170                 175

Gln Asp Asn Asn Cys Glu Gly Lys Cys Asn Pro Leu Ile Leu Gln Phe
            180                 185                 190

Thr Gln Lys Gly Lys Gln Ala Ser Trp Asp Gly Pro Lys Met Trp Gly
        195                 200                 205

Leu Arg Leu Tyr Arg Thr Gly Tyr Asp Pro Ile Ala Leu Phe Thr Val
    210                 215                 220

Ser Arg Gln Val Ser Thr Ile Thr Pro Pro Gln Ala Met Gly Pro Asn
225                 230                 235                 240

Leu Val Leu Pro Asp Gln Lys Pro Pro Ser Arg Gln Ser Gln Thr Gly
                245                 250                 255

Ser Lys Val Ala Thr Gln Arg Pro Gln Thr Asn Glu Ser Ala Pro Arg
            260                 265                 270

Ser Val Ala Pro Thr Thr Val Gly Pro Lys Arg Ile Gly Thr Gly Asp
        275                 280                 285

Arg Leu Ile Asn Leu Val Gln Gly Thr Tyr Leu Ala Leu Asn Ala Thr
    290                 295                 300

Asp Pro Asn Lys Thr Lys Asp Cys Trp Leu Cys Leu Val Ser Arg Pro
305                 310                 315                 320

Pro Tyr Tyr Glu Gly Ile Ala Ile Leu Gly Asn Tyr Ser Asn Gln Thr
                325                 330                 335

Asn Pro Pro Pro Ser Cys Leu Ser Ile Pro Gln His Lys Leu Thr Ile
            340                 345                 350

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

His Gln Ala Leu Cys Asn Lys Thr Gln Gln Gly His Thr Gly Ala His
    370                 375                 380
```

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Tyr Leu Ala Ala Pro Asn Gly Thr Tyr Trp Ala Cys Asn Thr Gly Leu
385                 390                 395                 400

Thr Pro Cys Ile Ser Met Ala Val Leu Asn Trp Thr Ser Asp Phe Cys
                405                 410                 415

Val Leu Ile Glu Leu Trp Pro Arg Val Thr Tyr His Gln Pro Glu Tyr
            420                 425                 430

Val Tyr Thr His Phe Ala Lys Ala Val Arg Phe Arg Arg Glu Pro Ile
        435                 440                 445

Ser Leu Thr Val Ala Leu Met Leu Gly Gly Leu Thr Val Gly Gly Ile
    450                 455                 460

Ala Ala Gly Val Gly Thr Gly Thr Lys Ala Leu Leu Glu Thr Ala Gln
465                 470                 475                 480

Phe Arg Gln Leu Gln Met Ala Met His Thr Asp Ile Gln Ala Leu Glu
                485                 490                 495

Glu Ser Ile Ser Ala Leu Glu Lys Ser Leu Thr Ser Leu Ser Glu Val
            500                 505                 510

Val Leu Gln Asn Arg Arg Gly Leu Asp Ile Leu Phe Leu Gln Arg Gly
        515                 520                 525

Gly Leu Cys Ala Ala Leu Lys Glu Glu Cys Cys Phe Tyr Ala Asp His
    530                 535                 540

Thr Gly Leu Val Arg Asp Asn Met Ala Lys Leu Arg Glu Arg Leu Lys
545                 550                 555                 560

Gln Arg Gln Gln Leu Phe Asp Ser Gln Gln Gly Trp Phe Glu Gly Trp
                565                 570                 575

Phe Asn Arg Ser Pro Trp Phe Thr Thr Leu Ile Ser Ser Ile Met Gly
            580                 585                 590

Pro Leu Leu Ile Leu Leu Leu Ile Leu Leu Phe Gly Pro Cys Ile Leu
        595                 600                 605

Asn Arg Leu Val Gln Phe Val Lys Asp Arg Ile Ser Val Val Gln Ala
    610                 615                 620

Leu Ile Leu Thr Gln Gln Tyr Gln Gln Ile Lys Gln Tyr Asp Pro Asp
625                 630                 635                 640

Arg Pro
```

<210> 105

<211> 1926

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated FeLV ENV

<220>

<221> misc_feature

<222> (1579)..(1581)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1597)..(1599)

<223> TTT or TTC

<400> 105

atggaaagtc caacgcaccc aaaaccctct aaagataaga ctctctcgtg gaacttagtg 60

tttctggtgg ggatcttatt cacaatagac ataggaatgg ccaatcctag tccacaccaa 120

atatataatg taacttgggt aataaccaat gtacaaacta acacccaagc taatgccacc 180

tctatgttag gaaccttaac cgatgtctac cctaccctac atgttgactt atgtgaccta 240

gtgggagaca cctgggaacc tatagtccta agcccaacca atgtaaaaca cggggcacgt 300

taccttcct caaaatatgg atgtaaaact acagatagaa aaaaacagca acagacatac 360

ccctttacg tctgccccgg acatgccccc tcgctggggc caaagggaac acattgtgga 420

ggggcacaag atgggttttg tgccgcatgg ggatgtgaaa ccaccggaga agcttggtgg 480

aagccctcct cctcatggga ctatatcaca gtaaaaagag ggagtagtca ggacaataac 540

tgtgagggaa aatgcaaccc cctgattttg cagttcaccc agaaggggaa acaagcctct 600

tgggacggac ctaagatgtg gggattgcga ctataccgta caggatatga ccctatcgcc 660

ttattcacgg tatcccggca ggtgtcaacc attacgccgc ctcaggcaat gggaccaaac 720

ctagtcttac ctgatcaaaa acccccatcc cgacaatctc aaacagggtc caaagtggcg 780

acccagaggc cccaaacgaa tgaaagcgcc ccaaggtctg ttgcccccac caccgtgggt 840

cccaaacgga ttgggaccgg agataggtta ataaatttag tacaagggac atacctagcc 900

ttaaatgcca ccgaccccaa caaaactaaa gactgttggc tctgcctggt ttctcgacca 960

ccctattacg aagggattgc aatcttaggt aactacagca accaaacaaa ccctccccca 1020

tcctgcctat ctattccgca acacaagctg accatatctg aagtatcagg gcaaggactg 1080

tgcataggga ctgttcctaa gacccaccag gctttgtgca ataagacgca acagggacat 1140

acaggggcgc actatctagc cgcccccaat ggcacctatt gggcctgtaa cactggactc 1200

accccatgca tttccatggc ggtgctcaat tggacctctg atttttgtgt cttaatcgaa 1260

ttatggccca gagtgactta ccatcaaccc gaatatgtgt acacacattt tgccaaagct 1320

gtcaggttcc gaagagaacc aatatcacta actgttgccc tcatgttggg aggactcact 1380

gtaggggcca tagccgcggg ggtcggaaca gggactaaag ccctccttga aacagcccag 1440

ttcagacaac tacaaatggc catgcacaca gacatccagg ccctagaaga gtcaattagt 1500

gccttagaaa agtccctgac ctccctttct gaagtagtct tacaaaacag acggggccta 1560

gatattctat tcctacaann nggagggctc tgtgccnnnt taaaagaaga atgttgcttc 1620

tatgcggatc acaccggact cgtccgagac aatatggcta aattaagaga aagactaaaa 1680

cagcggcaac aactgtttga ctcccaacag ggatggtttg aaggatggtt caacaggtcc 1740

ccctggttta caaccctaat ttcctccatt atgggccccc tactaatcct actcctaatt 1800

ctcctcttcg gcccatgcat ccttaacaga ttagtacaat tcgtaaaaga cagaatatct 1860

gtggtacaag ccttaatttt aacccaacag taccaacaga taaagcaata cgatccggac 1920

cgacca 1926

<210> 106

<211> 642

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated FeLV ENV

<400> 106

Met Glu Ser Pro Thr His Pro Lys Pro Ser Lys Asp Lys Thr Leu Ser
1 5 10 15

Trp Asn Leu Val Phe Leu Val Gly Ile Leu Phe Thr Ile Asp Ile Gly
20 25 30

Met Ala Asn Pro Ser Pro His Gln Ile Tyr Asn Val Thr Trp Val Ile

35 40 45

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

Thr Leu Thr Asp Val Tyr Pro Thr Leu His Val Asp Leu Cys Asp Leu
65 70 75 80

Val Gly Asp Thr Trp Glu Pro Ile Val Leu Ser Pro Thr Asn Val Lys
85 90 95

His Gly Ala Arg Tyr Pro Ser Ser Lys Tyr Gly Cys Lys Thr Thr Asp
100 105 110

Arg Lys Lys Gln Gln Gln Thr Tyr Pro Phe Tyr Val Cys Pro Gly His
115 120 125

Ala Pro Ser Leu Gly Pro Lys Gly Thr His Cys Gly Gly Ala Gln Asp
130 135 140

Gly Phe Cys Ala Ala Trp Gly Cys Glu Thr Thr Gly Glu Ala Trp Trp
145 150 155 160

Lys Pro Ser Ser Ser Trp Asp Tyr Ile Thr Val Lys Arg Gly Ser Ser
165 170 175

Gln Asp Asn Asn Cys Glu Gly Lys Cys Asn Pro Leu Ile Leu Gln Phe
180 185 190

Thr Gln Lys Gly Lys Gln Ala Ser Trp Asp Gly Pro Lys Met Trp Gly
195 200 205

Leu Arg Leu Tyr Arg Thr Gly Tyr Asp Pro Ile Ala Leu Phe Thr Val
210 215 220

Ser Arg Gln Val Ser Thr Ile Thr Pro Pro Gln Ala Met Gly Pro Asn
225 230 235 240

Leu Val Leu Pro Asp Gln Lys Pro Pro Ser Arg Gln Ser Gln Thr Gly
245 250 255

Ser Lys Val Ala Thr Gln Arg Pro Gln Thr Asn Glu Ser Ala Pro Arg
260 265 270

Ser Val Ala Pro Thr Thr Val Gly Pro Lys Arg Ile Gly Thr Gly Asp
275 280 285

Arg Leu Ile Asn Leu Val Gln Gly Thr Tyr Leu Ala Leu Asn Ala Thr
290 295 300

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Asp Pro Asn Lys Thr Lys Asp Cys Trp Leu Cys Leu Val Ser Arg Pro
305                 310                 315                 320

Pro Tyr Tyr Glu Gly Ile Ala Ile Leu Gly Asn Tyr Ser Asn Gln Thr
                325                 330                 335

Asn Pro Pro Pro Ser Cys Leu Ser Ile Pro Gln His Lys Leu Thr Ile
            340                 345                 350

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

His Gln Ala Leu Cys Asn Lys Thr Gln Gln Gly His Thr Gly Ala His
    370                 375                 380

Tyr Leu Ala Ala Pro Asn Gly Thr Tyr Trp Ala Cys Asn Thr Gly Leu
385                 390                 395                 400

Thr Pro Cys Ile Ser Met Ala Val Leu Asn Trp Thr Ser Asp Phe Cys
                405                 410                 415

Val Leu Ile Glu Leu Trp Pro Arg Val Thr Tyr His Gln Pro Glu Tyr
            420                 425                 430

Val Tyr Thr His Phe Ala Lys Ala Val Arg Phe Arg Arg Glu Pro Ile
        435                 440                 445

Ser Leu Thr Val Ala Leu Met Leu Gly Gly Leu Thr Val Gly Gly Ile
    450                 455                 460

Ala Ala Gly Val Gly Thr Gly Thr Lys Ala Leu Leu Glu Thr Ala Gln
465                 470                 475                 480

Phe Arg Gln Leu Gln Met Ala Met His Thr Asp Ile Gln Ala Leu Glu
                485                 490                 495

Glu Ser Ile Ser Ala Leu Glu Lys Ser Leu Thr Ser Leu Ser Glu Val
            500                 505                 510

Val Leu Gln Asn Arg Arg Gly Leu Asp Ile Leu Phe Leu Gln Arg Gly
        515                 520                 525

Gly Leu Cys Ala Phe Leu Lys Glu Glu Cys Cys Phe Tyr Ala Asp His
    530                 535                 540

Thr Gly Leu Val Arg Asp Asn Met Ala Lys Leu Arg Glu Arg Leu Lys
545                 550                 555                 560
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Gln Arg Gln Gln Leu Phe Asp Ser Gln Gln Gly Trp Phe Glu Gly Trp
565 570 575

Phe Asn Arg Ser Pro Trp Phe Thr Thr Leu Ile Ser Ser Ile Met Gly
580 585 590

Pro Leu Leu Ile Leu Leu Leu Ile Leu Leu Phe Gly Pro Cys Ile Leu
595 600 605

Asn Arg Leu Val Gln Phe Val Lys Asp Arg Ile Ser Val Val Gln Ala
610 615 620

Leu Ile Leu Thr Gln Gln Tyr Gln Gln Ile Lys Gln Tyr Asp Pro Asp
625 630 635 640

Arg Pro

<210> 107

<211> 1464

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HTLV-1 ENV

<220>

<221> misc_feature

<222> (1165)..(1167)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 107
atgggtaagt ttctcgccac tttgatttta ttcttccagt tctgcccccc catcttcggt 60

gattacagcc ccagctgctg tactctcaca attggagtct cctcatacca ctctaaaccc 120

tgcaatcctg cccagccagt ttgttcgtgg accctcgacc tgctggccct ttcagcagat 180

caggccctac agccccctg ccctaaccta gtaagttact ccagctacca tgccacctat 240

tccctatatc tattccctca ttggactaag aagccaaacc gaaatggcgg aggctattat 300

tcagcctctt attcagaccc ttgttcctta aagtgcccat acctggggtg ccaatcatgg 360

acctgccccc atacaggagc cgtctccagc ccctactgga agtttcaaca cgatgtcaat 420

tttactcaag aagtttcacg cctcaatatt aatctccatt tttcaaaatg cggttttccc 480

ttctcccttc tagtcgacgc tccaggatat gaccccatct ggttccttaa taccgaaccc 540

agccaactgc ctcccaccgc ccctcctcta ctcccccact ctaacctaga ccacatcctc 600

gagccctcta taccatggaa atcaaaactc ctgacccttg tccagttaac cctacaaagc 660

actaattata cttgcattgt ctgtatcgat cgtgccagcc tctccacttg gcacgtccta 720

tactctccca acgtctctgt tccatcctct tcttctaccc ccctccttta cccatcgtta 780

gcgcttccag ccccccacct gacgttacca tttaactgga cccactgctt tgaccccag 840

attcaagcta tagtctcctc cccctgtcat aactccctca tcctgccccc cttttccttg 900

tcacctgttc ccaccctagg atcccgctcc cgccgagcgg taccggtggc ggtctggctt 960

gtctccgccc tggccatggg agccggagtg gctggcggga ttaccggctc catgtccctc 1020

gcctcaggaa agagcctcct acatgaggtg gacaaagata tttcccagtt aactcaagca 1080

atagtcaaaa accacaaaaa tctactcaaa attgcgcagt atgctgccca gaacagacga 1140

ggccttgatc tcctgttctg ggagnnnngga ggattatgca aagcattaca agaacagtgc 1200

cgttttccga atattaccaa ttcccatgtc ccaatactac aagaaagacc ccccttgag 1260

aatcgagtcc tgactggctg gggccttaac tgggaccttg gcctctcaca gtgggctcga 1320

gaggccttac aaactggaat caccttgtt gcgctactcc ttcttgttat ccttgcagga 1380

ccatgcatcc tccgtcagct acgacacctc ccctcgcgcg tcagataccc ccattactct 1440

cttataaacc ctgagtcatc cctg 1464

<210> 108

<211> 488

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HTLV-1 ENV

<400> 108

Met Gly Lys Phe Leu Ala Thr Leu Ile Leu Phe Phe Gln Phe Cys Pro
1 5 10 15

Leu Ile Phe Gly Asp Tyr Ser Pro Ser Cys Cys Thr Leu Thr Ile Gly
20 25 30

Val Ser Ser Tyr His Ser Lys Pro Cys Asn Pro Ala Gln Pro Val Cys
35 40 45

Ser Trp Thr Leu Asp Leu Leu Ala Leu Ser Ala Asp Gln Ala Leu Gln

50 55 60

Pro Pro Cys Pro Asn Leu Val Ser Tyr Ser Ser Tyr His Ala Thr Tyr
65 70 75 80

Ser Leu Tyr Leu Phe Pro His Trp Thr Lys Lys Pro Asn Arg Asn Gly
85 90 95

Gly Gly Tyr Tyr Ser Ala Ser Tyr Ser Asp Pro Cys Ser Leu Lys Cys
100 105 110

Pro Tyr Leu Gly Cys Gln Ser Trp Thr Cys Pro Tyr Thr Gly Ala Val
115 120 125

Ser Ser Pro Tyr Trp Lys Phe Gln His Asp Val Asn Phe Thr Gln Glu
130 135 140

Val Ser Arg Leu Asn Ile Asn Leu His Phe Ser Lys Cys Gly Phe Pro
145 150 155 160

Phe Ser Leu Leu Val Asp Ala Pro Gly Tyr Asp Pro Ile Trp Phe Leu
165 170 175

Asn Thr Glu Pro Ser Gln Leu Pro Pro Thr Ala Pro Pro Leu Leu Pro
180 185 190

His Ser Asn Leu Asp His Ile Leu Glu Pro Ser Ile Pro Trp Lys Ser
195 200 205

Lys Leu Leu Thr Leu Val Gln Leu Thr Leu Gln Ser Thr Asn Tyr Thr
210 215 220

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

Tyr Ser Pro Asn Val Ser Val Pro Ser Ser Ser Ser Thr Pro Leu Leu
245 250 255

Tyr Pro Ser Leu Ala Leu Pro Ala Pro His Leu Thr Leu Pro Phe Asn
260 265 270

Trp Thr His Cys Phe Asp Pro Gln Ile Gln Ala Ile Val Ser Ser Pro
275 280 285

Cys His Asn Ser Leu Ile Leu Pro Pro Phe Ser Leu Ser Pro Val Pro
290 295 300

Thr Leu Gly Ser Arg Ser Arg Arg Ala Val Pro Val Ala Val Trp Leu
305 310 315 320

Val Ser Ala Leu Ala Met Gly Ala Gly Val Ala Gly Gly Ile Thr Gly
325 330 335

Ser Met Ser Leu Ala Ser Gly Lys Ser Leu Leu His Glu Val Asp Lys
340 345 350

Asp Ile Ser Gln Leu Thr Gln Ala Ile Val Lys Asn His Lys Asn Leu
355 360 365

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

Leu Phe Trp Glu Arg Gly Gly Leu Cys Lys Ala Leu Gln Glu Gln Cys
385 390 395 400

Arg Phe Pro Asn Ile Thr Asn Ser His Val Pro Ile Leu Gln Glu Arg
405 410 415

Pro Pro Leu Glu Asn Arg Val Leu Thr Gly Trp Gly Leu Asn Trp Asp
420 425 430

Leu Gly Leu Ser Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr
435 440 445

Leu Val Ala Leu Leu Leu Leu Leu Val Ile Leu Ala Gly Pro Cys Ile Leu
450 455 460

Arg Gln Leu Arg His Leu Pro Ser Arg Val Arg Tyr Pro His Tyr Ser
465 470 475 480

Leu Ile Asn Pro Glu Ser Ser Leu
485

<210> 109

<211> 1464

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HTLV-1 ENV

<220>

<221> misc_feature

<222> (1165)..(1167)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1183)..(1185)

<223> TTT or TTC

<400> 109

atgggtaagt ttctcgccac tttgatttta ttcttccagt tctgcccccc catcttcggt 60

gattacagcc ccagctgctg tactctcaca attggagtct cctcatacca ctctaaaccc 120

tgcaatcctg cccagccagt ttgttcgtgg accctcgacc tgctggccct ttcagcagat 180

caggccctac agccccccctg ccctaaccta gtaagttact ccagctacca tgccacctat 240

tccctatatc tattccctca ttggactaag aagccaaacc gaaatggcgg aggctattat 300

tcagcctctt attcagaccc ttgttcctta aagtgcccat acctggggtg ccaatcatgg 360

acctgccccc atacaggagc cgtctccagc ccctactgga agtttcaaca cgatgtcaat 420

tttactcaag aagtttcacg cctcaatatt aatctccatt tttcaaaatg cggttttccc 480

ttctcccttc tagtcgacgc tccaggatat gaccccatct ggttccttaa taccgaaccc 540

agccaactgc ctcccaccgc ccctcctcta ctccccccact ctaacctaga ccacatcctc 600

gagccctcta taccatggaa atcaaaactc ctgacccttg tccagttaac cctacaaagc 660

actaattata cttgcattgt ctgtatcgat cgtgccagcc tctccacttg gcacgtccta 720

tactctccca acgtctctgt tccatcctct tcttctaccc ccctccttta cccatcgtta 780

gcgcttccag ccccccacct gacgttacca tttaactgga cccactgctt tgacccccag 840

attcaagcta tagtctcctc cccctgtcat aactccctca tcctgccccc cttttccttg 900

tcacctgttc ccaccctagg atcccgctcc cgccgagcgg taccggtggc ggtctggctt 960

gtctccgccc tggccatggg agccggagtg gctggcggga ttaccggctc catgtccctc 1020

gcctcaggaa agagcctcct acatgaggtg gacaaagata tttcccagtt aactcaagca 1080

atagtcaaaa accacaaaaa tctactcaaa attgcgcagt atgctgccca gaacagacga 1140

ggccttgatc tcctgttctg ggagnnnngga ggattatgca aannnttaca agaacagtgc 1200

cgttttccga atattaccaa ttcccatgtc ccaatactac aagaaagacc ccccttgag 1260

aatcgagtcc tgactggctg gggccttaac tgggaccttg gcctctcaca gtgggctcga 1320

gaggccttac aaactggaat cacccttgtt gcgctactcc ttcttgttat ccttgcagga 1380

ccatgcatcc tccgtcagct acgacacctc ccctcgcgcg tcagataccc ccattactct 1440

cttataaacc ctgagtcatc cctg 1464

<210> 110

<211> 488

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HTLV-1 ENV

<400> 110

Met Gly Lys Phe Leu Ala Thr Leu Ile Leu Phe Phe Gln Phe Cys Pro
1 5 10 15

Leu Ile Phe Gly Asp Tyr Ser Pro Ser Cys Cys Thr Leu Thr Ile Gly
20 25 30

Val Ser Ser Tyr His Ser Lys Pro Cys Asn Pro Ala Gln Pro Val Cys
35 40 45

Ser Trp Thr Leu Asp Leu Leu Ala Leu Ser Ala Asp Gln Ala Leu Gln
50 55 60

Pro Pro Cys Pro Asn Leu Val Ser Tyr Ser Ser Tyr His Ala Thr Tyr
65 70 75 80

Ser Leu Tyr Leu Phe Pro His Trp Thr Lys Lys Pro Asn Arg Asn Gly
85 90 95

Gly Gly Tyr Tyr Ser Ala Ser Tyr Ser Asp Pro Cys Ser Leu Lys Cys
100 105 110

Pro Tyr Leu Gly Cys Gln Ser Trp Thr Cys Pro Tyr Thr Gly Ala Val
115 120 125

Ser Ser Pro Tyr Trp Lys Phe Gln His Asp Val Asn Phe Thr Gln Glu
130 135 140

Val Ser Arg Leu Asn Ile Asn Leu His Phe Ser Lys Cys Gly Phe Pro
145 150 155 160

Phe Ser Leu Leu Val Asp Ala Pro Gly Tyr Asp Pro Ile Trp Phe Leu
165 170 175

Asn Thr Glu Pro Ser Gln Leu Pro Pro Thr Ala Pro Pro Leu Leu Pro
180 185 190

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His Ser Asn Leu Asp His Ile Leu Glu Pro Ser Ile Pro Trp Lys Ser
        195                 200                 205

Lys Leu Leu Thr Leu Val Gln Leu Thr Leu Gln Ser Thr Asn Tyr Thr
    210                 215                 220

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

Tyr Ser Pro Asn Val Ser Val Pro Ser Ser Ser Ser Thr Pro Leu Leu
                245                 250                 255

Tyr Pro Ser Leu Ala Leu Pro Ala Pro His Leu Thr Leu Pro Phe Asn
            260                 265                 270

Trp Thr His Cys Phe Asp Pro Gln Ile Gln Ala Ile Val Ser Ser Pro
        275                 280                 285

Cys His Asn Ser Leu Ile Leu Pro Pro Phe Ser Leu Ser Pro Val Pro
    290                 295                 300

Thr Leu Gly Ser Arg Ser Arg Arg Ala Val Pro Val Ala Val Trp Leu
305                 310                 315                 320

Val Ser Ala Leu Ala Met Gly Ala Gly Val Ala Gly Gly Ile Thr Gly
                325                 330                 335

Ser Met Ser Leu Ala Ser Gly Lys Ser Leu Leu His Glu Val Asp Lys
            340                 345                 350

Asp Ile Ser Gln Leu Thr Gln Ala Ile Val Lys Asn His Lys Asn Leu
        355                 360                 365

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

Leu Phe Trp Glu Arg Gly Gly Leu Cys Lys Phe Leu Gln Glu Gln Cys
385                 390                 395                 400

Arg Phe Pro Asn Ile Thr Asn Ser His Val Pro Ile Leu Gln Glu Arg
                405                 410                 415

Pro Pro Leu Glu Asn Arg Val Leu Thr Gly Trp Gly Leu Asn Trp Asp
            420                 425                 430

Leu Gly Leu Ser Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr
        435                 440                 445
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Leu Val Ala Leu Leu Leu Leu Val Ile Leu Ala Gly Pro Cys Ile Leu
450 455 460

Arg Gln Leu Arg His Leu Pro Ser Arg Val Arg Tyr Pro His Tyr Ser
465 470 475 480

Leu Ile Asn Pro Glu Ser Ser Leu
485

<210> 111

<211> 1458

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HTLV-2 ENV

<220>

<221> misc_feature

<222> (1153)..(1155)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 111
atgggtaatg ttttcttcct acttttattc agtctcacac attttccact agcccagcag 60

agccgatgca cactcacgat tggtatctcc tcctaccact ccagcccctg tagcccaacc 120

caacccgtct gcacgtggaa cctcgacctt aattccctaa caacggacca acgactacac 180

ccccccctgcc ctaacctaat tacttactct ggcttccata agacttattc cttatactta 240

ttcccacatt ggataaaaaa gccaaacaga cagggcctag ggtactactc gccttcctac 300

aatgaccctt gctcgctaca atgcccctac ttgggctgcc aagcatggac atccgcatac 360

acgggccccg tctccagtcc atcctggaag tttcattcag atgtaaattt cacccaggaa 420

gtcagccaag tgtcccttcg actacacttc tctaagtgcg gctcctccat gaccctccta 480

gtagatgccc ctggatatga tcctttatgg ttcatcacct cagaacccac tcagcctcca 540

ccaacttctc ccccattggt ccatgactcc gaccttgaac atgtcctaac cccctccacg 600

tcctggacga ccaaaatact caaatttatc cagctgacct tacagagcac caattactcc 660

tgcatggttt gcgtggatag atccagcctc tcatcctggc atgtactcta caccccaac 720

atctccattc cccaacaaac ctcctcccga accatcctct ttccttccct tgccctgccc 780

gctcctccat cccaaccctt cccttggacc cattgctacc aacctcgcct acaggcgata 840

acaacagata actgcaacaa ctccattatc ctccccctt tttccctcgc tcccgtacct 900

cctccggcga caagacgccg ccgtgccgtt ccaatagcag tgtggcttgt ctccgcccta 960

gcggccggaa caggtatcgc tggtggagta acaggctccc tatctctggc ttccagtaaa 1020

agccttctcc tcgaggttga caaagacatc tcccacctta cccaggccat agtcaaaaat 1080

catcaaaaca tcctccgggt tgcacagtat gcagcccaaa atagacgagg attagacctc 1140

ctattctggg aannnggggg tttgtgcaag gccatacagg agcaatgttg cttcctcaac 1200

atcagtaaca ctcatgtatc cgtcctccag gaacggcccc ctcttgaaaa acgtgtcatc 1260

accggctggg gactaaactg ggatcttgga ctgtcccaat gggcacgaga agccctccag 1320

acaggcataa ccattctcgc tctactcctc ctcgtcatat tgtttggccc ctgtatcctc 1380

cgccaaatcc aggcccttcc acagcggtta caaaaccgac ataaccagta ttcccttatc 1440

aacccagaaa ccatgcta 1458

<210> 112

<211> 486

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HTLV-2 ENV

<400> 112

Met Gly Asn Val Phe Phe Leu Leu Leu Phe Ser Leu Thr His Phe Pro
1 5 10 15

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

His Ser Ser Pro Cys Ser Pro Thr Gln Pro Val Cys Thr Trp Asn Leu
35 40 45

Asp Leu Asn Ser Leu Thr Thr Asp Gln Arg Leu His Pro Pro Cys Pro
50 55 60

Asn Leu Ile Thr Tyr Ser Gly Phe His Lys Thr Tyr Ser Leu Tyr Leu
65 70 75 80

Phe Pro His Trp Ile Lys Lys Pro Asn Arg Gln Gly Leu Gly Tyr Tyr
85 90 95

Ser Pro Ser Tyr Asn Asp Pro Cys Ser Leu Gln Cys Pro Tyr Leu Gly
100 105 110

Cys Gln Ala Trp Thr Ser Ala Tyr Thr Gly Pro Val Ser Ser Pro Ser
115 120 125

Trp Lys Phe His Ser Asp Val Asn Phe Thr Gln Glu Val Ser Gln Val
130 135 140

Ser Leu Arg Leu His Phe Ser Lys Cys Gly Ser Ser Met Thr Leu Leu
145 150 155 160

Val Asp Ala Pro Gly Tyr Asp Pro Leu Trp Phe Ile Thr Ser Glu Pro
165 170 175

Thr Gln Pro Pro Pro Thr Ser Pro Pro Leu Val His Asp Ser Asp Leu
180 185 190

Glu His Val Leu Thr Pro Ser Thr Ser Trp Thr Thr Lys Ile Leu Lys
195 200 205

Phe Ile Gln Leu Thr Leu Gln Ser Thr Asn Tyr Ser Cys Met Val Cys
210 215 220

Val Asp Arg Ser Ser Leu Ser Ser Trp His Val Leu Tyr Thr Pro Asn
225 230 235 240

Ile Ser Ile Pro Gln Gln Thr Ser Ser Arg Thr Ile Leu Phe Pro Ser
245 250 255

Leu Ala Leu Pro Ala Pro Pro Ser Gln Pro Phe Pro Trp Thr His Cys
260 265 270

Tyr Gln Pro Arg Leu Gln Ala Ile Thr Thr Asp Asn Cys Asn Asn Ser
275 280 285

Ile Ile Leu Pro Pro Phe Ser Leu Ala Pro Val Pro Pro Pro Ala Thr
290 295 300

Arg Arg Arg Arg Ala Val Pro Ile Ala Val Trp Leu Val Ser Ala Leu
305 310 315 320

Ala Ala Gly Thr Gly Ile Ala Gly Gly Val Thr Gly Ser Leu Ser Leu
325 330 335

Ala Ser Ser Lys Ser Leu Leu Leu Glu Val Asp Lys Asp Ile Ser His
340 345 350

Leu Thr Gln Ala Ile Val Lys Asn His Gln Asn Ile Leu Arg Val Ala
355 360 365

Gln Tyr Ala Ala Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Trp Glu
370 375 380

Arg Gly Gly Leu Cys Lys Ala Ile Gln Glu Gln Cys Cys Phe Leu Asn
385 390 395 400

Ile Ser Asn Thr His Val Ser Val Leu Gln Glu Arg Pro Pro Leu Glu
405 410 415

Lys Arg Val Ile Thr Gly Trp Gly Leu Asn Trp Asp Leu Gly Leu Ser
420 425 430

Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr Ile Leu Ala Leu
435 440 445

Leu Leu Leu Val Ile Leu Phe Gly Pro Cys Ile Leu Arg Gln Ile Gln
450 455 460

Ala Leu Pro Gln Arg Leu Gln Asn Arg His Asn Gln Tyr Ser Leu Ile
465 470 475 480

Asn Pro Glu Thr Met Leu
485

<210> 113

<211> 1458

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HTLV-2 ENV

<220>

<221> misc_feature

<222> (1153)..(1155)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1171)..(1173)

<223> TTT or TTC

<400> 113

atgggtaatg ttttcttcct acttttattc agtctcacac attttccact agcccagcag 60

agccgatgca cactcacgat tggtatctcc tcctaccact ccagcccctg tagcccaacc 120

caacccgtct gcacgtggaa cctcgacctt aattccctaa caacggacca acgactacac 180

ccccccctgcc ctaacctaat tacttactct ggcttccata agacttattc cttatactta 240

ttcccacatt ggataaaaaa gccaaacaga cagggcctag ggtactactc gccttcctac 300

aatgaccctt gctcgctaca atgcccctac ttgggctgcc aagcatggac atccgcatac 360

acgggccccg tctccagtcc atcctggaag tttcattcag atgtaaattt cacccaggaa 420

gtcagccaag tgtcccttcg actacacttc tctaagtgcg gctcctccat gaccctccta 480

gtagatgccc ctggatatga tcctttatgg ttcatcacct cagaacccac tcagcctcca 540

ccaacttctc ccccattggt ccatgactcc gaccttgaac atgtcctaac cccctccacg 600

tcctggacga ccaaaatact caaatttatc cagctgacct tacagagcac caattactcc 660

tgcatggttt gcgtggatag atccagcctc tcatcctggc atgtactcta caccccaac 720

atctccattc cccaacaaac ctcctcccga accatcctct ttccttccct tgccctgccc 780

gctcctccat cccaaccctt cccttggacc cattgctacc aacctcgcct acaggcgata 840

acaacagata actgcaacaa ctccattatc ctccccccctt tttccctcgc tcccgtacct 900

cctccggcga caagacgccg ccgtgccgtt ccaatagcag tgtggcttgt ctccgcccta 960

gcggccggaa caggtatcgc tggtggagta acaggctccc tatctctggc ttccagtaaa 1020

agccttctcc tcgaggttga caaagacatc tcccacctta cccaggccat agtcaaaaat 1080

catcaaaaca tcctccgggt tgcacagtat gcagcccaaa atagacgagg attagacctc 1140

ctattctggg aannnggggg tttgtgcaag nnnatacagg agcaatgttg cttcctcaac 1200

atcagtaaca ctcatgtatc cgtcctccag gaacggcccc ctcttgaaaa acgtgtcatc 1260

accggctggg gactaaactg ggatcttgga ctgtcccaat gggcacgaga agccctccag 1320

acaggcataa ccattctcgc tctactcctc ctcgtcatat tgtttggccc ctgtatcctc 1380

cgccaaatcc aggcccttcc acagcggtta caaaaccgac ataaccagta ttcccttatc 1440

aacccagaaa ccatgcta 1458

<210> 114

<211> 486

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HTLV-2 ENV

<400> 114

Met Gly Asn Val Phe Phe Leu Leu Leu Phe Ser Leu Thr His Phe Pro
1 5 10 15

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

His Ser Ser Pro Cys Ser Pro Thr Gln Pro Val Cys Thr Trp Asn Leu
35 40 45

Asp Leu Asn Ser Leu Thr Thr Asp Gln Arg Leu His Pro Pro Cys Pro
50 55 60

Asn Leu Ile Thr Tyr Ser Gly Phe His Lys Thr Tyr Ser Leu Tyr Leu
65 70 75 80

Phe Pro His Trp Ile Lys Lys Pro Asn Arg Gln Gly Leu Gly Tyr Tyr
85 90 95

Ser Pro Ser Tyr Asn Asp Pro Cys Ser Leu Gln Cys Pro Tyr Leu Gly
100 105 110

Cys Gln Ala Trp Thr Ser Ala Tyr Thr Gly Pro Val Ser Ser Pro Ser
115 120 125

Trp Lys Phe His Ser Asp Val Asn Phe Thr Gln Glu Val Ser Gln Val
130 135 140

Ser Leu Arg Leu His Phe Ser Lys Cys Gly Ser Ser Met Thr Leu Leu
145 150 155 160

Val Asp Ala Pro Gly Tyr Asp Pro Leu Trp Phe Ile Thr Ser Glu Pro
165 170 175

Thr Gln Pro Pro Pro Thr Ser Pro Pro Leu Val His Asp Ser Asp Leu
180 185 190

Glu His Val Leu Thr Pro Ser Thr Ser Trp Thr Thr Lys Ile Leu Lys
195 200 205

Phe Ile Gln Leu Thr Leu Gln Ser Thr Asn Tyr Ser Cys Met Val Cys
210 215 220

Val Asp Arg Ser Ser Leu Ser Ser Trp His Val Leu Tyr Thr Pro Asn
225 230 235 240

```
Ile Ser Ile Pro Gln Gln Thr Ser Ser Arg Thr Ile Leu Phe Pro Ser
                245                 250                 255

Leu Ala Leu Pro Ala Pro Pro Ser Gln Pro Phe Pro Trp Thr His Cys
            260                 265                 270

Tyr Gln Pro Arg Leu Gln Ala Ile Thr Thr Asp Asn Cys Asn Asn Ser
        275                 280                 285

Ile Ile Leu Pro Pro Phe Ser Leu Ala Pro Val Pro Pro Pro Ala Thr
    290                 295                 300

Arg Arg Arg Arg Ala Val Pro Ile Ala Val Trp Leu Val Ser Ala Leu
305                 310                 315                 320

Ala Ala Gly Thr Gly Ile Ala Gly Gly Val Thr Gly Ser Leu Ser Leu
                325                 330                 335

Ala Ser Ser Lys Ser Leu Leu Leu Glu Val Asp Lys Asp Ile Ser His
            340                 345                 350

Leu Thr Gln Ala Ile Val Lys Asn His Gln Asn Ile Leu Arg Val Ala
        355                 360                 365

Gln Tyr Ala Ala Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Trp Glu
    370                 375                 380

Arg Gly Gly Leu Cys Lys Phe Ile Gln Glu Gln Cys Cys Phe Leu Asn
385                 390                 395                 400

Ile Ser Asn Thr His Val Ser Val Leu Gln Glu Arg Pro Pro Leu Glu
                405                 410                 415

Lys Arg Val Ile Thr Gly Trp Gly Leu Asn Trp Asp Leu Gly Leu Ser
            420                 425                 430

Gln Trp Ala Arg Glu Ala Leu Gln Thr Gly Ile Thr Ile Leu Ala Leu
        435                 440                 445

Leu Leu Leu Val Ile Leu Phe Gly Pro Cys Ile Leu Arg Gln Ile Gln
    450                 455                 460

Ala Leu Pro Gln Arg Leu Gln Asn Arg His Asn Gln Tyr Ser Leu Ile
465                 470                 475                 480

Asn Pro Glu Thr Met Leu
                485
```

<210> 115

<211> 1614

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-W ENV

<220>

<221> misc_feature

<222> (1177)..(1179)

<223> GAA or GAG or CAA or CAG

<400> 115

atggccctcc cttatcatat ttttctcttt actgttcttt taccctcttt cactctcact 60

gcacccccctc catgccgctg tatgaccagt agctcccctt accaagagtt tctatggaga 120

atgcagcgtc ccggaaatat tgatgcccca tcgtatagga gtctttctaa gggaaccccc 180

accttcactg cccacaccca tatgccccgc aactgctatc actctgccac tctttgcatg 240

catgcaaata ctcattattg gacaggaaaa atgattaatc ctagttgtcc tggaggactt 300

ggagtcactg tctgttggac ttacttcacc caaactggta tgtctgatgg gggtggagtt 360

caagatcagg caagagaaaa acatgtaaaa gaagtaatct cccaactcac ccgggtacat 420

ggcacctcta gcccctacaa aggactagat ctctcaaaac tacatgaaac cctccgtacc 480

catactcgcc tggtaagcct atttaatacc accctcactg ggctccatga ggtctcggcc 540

caaaacccta ctaactgttg gatatgcctc cccctgaact tcaggccata tgtttcaatc 600

cctgtacctg aacaatggaa caacttcagc acagaaataa acaccacttc cgttttagta 660

ggacctcttg tttccaatct ggaaataacc catacctcaa acctcacctg tgtaaaattt 720

agcaatacta catacacaac caactcccaa tgcatcaggt gggtaactcc tcccacacaa 780

atagtctgcc taccctcagg aatatttttt gtctgtggta cctcagccta tcgttgtttg 840

aatggctctt cagaatctat gtgcttcctc tcattcttag tgccccctat gaccatctac 900

actgaacaag atttatacag ttatgtcata tctaagcccc gcaacaaaag agtacccatt 960

cttccttttg ttataggagc aggagtgcta ggtgcactag gtactggcat tggcggtatc 1020

acaacctcta ctcagttcta ctacaaacta tctcaagaac taaatgggga catggaacgg 1080

gtcgccgact ccctggtcac cttgcaagat caacttaact ccctagcagc agtagtcctt 1140

caaaatcgaa gagctttaga cttgctaacc gctgaannng ggggaacctg tttatttta 1200

ggggaagaat gctgttatta tgttaatcaa tccggaatcg tcactgagaa agttaaagaa 1260

attcgagatc gaatacaacg tagagcagag gagcttcgaa acactggacc ctggggcctc 1320

ctcagccaat ggatgccctg gattctcccc ttcttaggac ctctagcagc tataatattg 1380

ctactcctct ttggaccctg tatctttaac ctccttgtta actttgtctc ttccagaatc 1440

gaagctgtaa aactacaaat ggagcccaag atgcagtcca agactaagat ctaccgcaga 1500

cccctggacc ggcctgctag cccacgatct gatgttaatg acatcaaagg caccctcct 1560

gaggaaatct cagctgcaca acctctacta cgccccaatt cagcaggaag cagt 1614

<210> 116

<211> 538

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-W ENV

<220>

<221> MISC_FEATURE

<222> (393)..(393)

<223> E or Q

<400> 116

Met Ala Leu Pro Tyr His Ile Phe Leu Phe Thr Val Leu Leu Pro Ser
1 5 10 15

Phe Thr Leu Thr Ala Pro Pro Pro Cys Arg Cys Met Thr Ser Ser Ser
20 25 30

Pro Tyr Gln Glu Phe Leu Trp Arg Met Gln Arg Pro Gly Asn Ile Asp
35 40 45

Ala Pro Ser Tyr Arg Ser Leu Ser Lys Gly Thr Pro Thr Phe Thr Ala
50 55 60

His Thr His Met Pro Arg Asn Cys Tyr His Ser Ala Thr Leu Cys Met
65 70 75 80

His Ala Asn Thr His Tyr Trp Thr Gly Lys Met Ile Asn Pro Ser Cys
85 90 95

Pro Gly Gly Leu Gly Val Thr Val Cys Trp Thr Tyr Phe Thr Gln Thr

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            100                 105                 110

Gly Met Ser Asp Gly Gly Gly Val Gln Asp Gln Ala Arg Glu Lys His
        115                 120                 125

Val Lys Glu Val Ile Ser Gln Leu Thr Arg Val His Gly Thr Ser Ser
    130                 135                 140

Pro Tyr Lys Gly Leu Asp Leu Ser Lys Leu His Glu Thr Leu Arg Thr
145                 150                 155                 160

His Thr Arg Leu Val Ser Leu Phe Asn Thr Thr Leu Thr Gly Leu His
                165                 170                 175

Glu Val Ser Ala Gln Asn Pro Thr Asn Cys Trp Ile Cys Leu Pro Leu
            180                 185                 190

Asn Phe Arg Pro Tyr Val Ser Ile Pro Val Pro Glu Gln Trp Asn Asn
        195                 200                 205

Phe Ser Thr Glu Ile Asn Thr Thr Ser Val Leu Val Gly Pro Leu Val
    210                 215                 220

Ser Asn Leu Glu Ile Thr His Thr Ser Asn Leu Thr Cys Val Lys Phe
225                 230                 235                 240

Ser Asn Thr Thr Tyr Thr Thr Asn Ser Gln Cys Ile Arg Trp Val Thr
                245                 250                 255

Pro Pro Thr Gln Ile Val Cys Leu Pro Ser Gly Ile Phe Phe Val Cys
            260                 265                 270

Gly Thr Ser Ala Tyr Arg Cys Leu Asn Gly Ser Ser Glu Ser Met Cys
        275                 280                 285

Phe Leu Ser Phe Leu Val Pro Pro Met Thr Ile Tyr Thr Glu Gln Asp
    290                 295                 300

Leu Tyr Ser Tyr Val Ile Ser Lys Pro Arg Asn Lys Arg Val Pro Ile
305                 310                 315                 320

Leu Pro Phe Val Ile Gly Ala Gly Val Leu Gly Ala Leu Gly Thr Gly
                325                 330                 335

Ile Gly Gly Ile Thr Thr Ser Thr Gln Phe Tyr Tyr Lys Leu Ser Gln
            340                 345                 350

Glu Leu Asn Gly Asp Met Glu Arg Val Ala Asp Ser Leu Val Thr Leu
        355                 360                 365
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Gln Asp Gln Leu Asn Ser Leu Ala Ala Val Val Leu Gln Asn Arg Arg
    370                 375                 380

Ala Leu Asp Leu Leu Thr Ala Glu Xaa Gly Gly Thr Cys Leu Phe Leu
385                 390                 395                 400

Gly Glu Glu Cys Cys Tyr Tyr Val Asn Gln Ser Gly Ile Val Thr Glu
                405                 410                 415

Lys Val Lys Glu Ile Arg Asp Arg Ile Gln Arg Arg Ala Glu Glu Leu
            420                 425                 430

Arg Asn Thr Gly Pro Trp Gly Leu Leu Ser Gln Trp Met Pro Trp Ile
        435                 440                 445

Leu Pro Phe Leu Gly Pro Leu Ala Ala Ile Ile Leu Leu Leu Leu Phe
    450                 455                 460

Gly Pro Cys Ile Phe Asn Leu Leu Val Asn Phe Val Ser Ser Arg Ile
465                 470                 475                 480

Glu Ala Val Lys Leu Gln Met Glu Pro Lys Met Gln Ser Lys Thr Lys
                485                 490                 495

Ile Tyr Arg Arg Pro Leu Asp Arg Pro Ala Ser Pro Arg Ser Asp Val
            500                 505                 510

Asn Asp Ile Lys Gly Thr Pro Pro Glu Glu Ile Ser Ala Ala Gln Pro
        515                 520                 525

Leu Leu Arg Pro Asn Ser Ala Gly Ser Ser
    530                 535
```

<210> 117

<211> 1614

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-W ENV

<220>

<221> misc_feature

<222> (1177)..(1179)

<223> GAA or GAG or CAA or CAG

<220>

<221> misc_feature

<222> (1195)..(1197)

<223> GCT or GCC or GCA or GCG

<400> 117

atggccctcc cttatcatat ttttctcttt actgttcttt taccctcttt cactctcact 60

gcacccccctc catgccgctg tatgaccagt agctcccctt accaagagtt tctatggaga 120

atgcagcgtc ccggaaatat tgatgcccca tcgtatagga gtctttctaa gggaaccccc 180

accttcactg cccacaccca tatgccccgc aactgctatc actctgccac tctttgcatg 240

catgcaaata ctcattattg gacaggaaaa atgattaatc ctagttgtcc tggaggactt 300

ggagtcactg tctgttggac ttacttcacc caaactggta tgtctgatgg gggtggagtt 360

caagatcagg caagagaaaa acatgtaaaa gaagtaatct cccaactcac ccgggtacat 420

ggcacctcta gcccctacaa aggactagat ctctcaaaac tacatgaaac cctccgtacc 480

catactcgcc tggtaagcct atttaatacc accctcactg ggctccatga ggtctcggcc 540

caaaacccta ctaactgttg gatatgcctc cccctgaact tcaggccata tgtttcaatc 600

cctgtacctg aacaatggaa caacttcagc acagaaataa acaccacttc cgttttagta 660

ggacctcttg tttccaatct ggaaataacc catacctcaa acctcacctg tgtaaaattt 720

agcaatacta catacacaac caactcccaa tgcatcaggt gggtaactcc tcccacacaa 780

atagtctgcc taccctcagg aatatttttt gtctgtggta cctcagccta tcgttgtttg 840

aatggctctt cagaatctat gtgcttcctc tcattcttag tgccccctat gaccatctac 900

actgaacaag atttatacag ttatgtcata tctaagcccc gcaacaaaag agtacccatt 960

cttccttttg ttataggagc aggagtgcta ggtgcactag gtactggcat tggcggtatc 1020

acaacctcta ctcagttcta ctacaaacta tctcaagaac taaatgggga catggaacgg 1080

gtcgccgact ccctggtcac cttgcaagat caacttaact ccctagcagc agtagtcctt 1140

caaaatcgaa gagctttaga cttgctaacc gctgaannng ggggaacctg tttannntta 1200

ggggaagaat gctgttatta tgttaatcaa tccggaatcg tcactgagaa agttaaagaa 1260

attcgagatc gaatacaacg tagagcagag gagcttcgaa acactggacc ctggggcctc 1320

ctcagccaat ggatgccctg gattctcccc ttcttaggac ctctagcagc tataatattg 1380

ctactcctct ttggaccctg tatctttaac ctccttgtta actttgtctc ttccagaatc 1440

gaagctgtaa aactacaaat ggagcccaag atgcagtcca agactaagat ctaccgcaga 1500

cccctggacc ggcctgctag cccacgatct gatgttaatg acatcaaagg cacccctcct 1560

gaggaaatct cagctgcaca acctctacta cgccccaatt cagcaggaag cagt 1614

<210> 118

<211> 538

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-W ENV

<220>

<221> MISC_FEATURE

<222> (393)..(393)

<223> E or Q

<400> 118

Met Ala Leu Pro Tyr His Ile Phe Leu Phe Thr Val Leu Leu Pro Ser
1 5 10 15

Phe Thr Leu Thr Ala Pro Pro Pro Cys Arg Cys Met Thr Ser Ser Ser
20 25 30

Pro Tyr Gln Glu Phe Leu Trp Arg Met Gln Arg Pro Gly Asn Ile Asp
35 40 45

Ala Pro Ser Tyr Arg Ser Leu Ser Lys Gly Thr Pro Thr Phe Thr Ala
50 55 60

His Thr His Met Pro Arg Asn Cys Tyr His Ser Ala Thr Leu Cys Met
65 70 75 80

His Ala Asn Thr His Tyr Trp Thr Gly Lys Met Ile Asn Pro Ser Cys
85 90 95

Pro Gly Gly Leu Gly Val Thr Val Cys Trp Thr Tyr Phe Thr Gln Thr
100 105 110

Gly Met Ser Asp Gly Gly Gly Val Gln Asp Gln Ala Arg Glu Lys His
115 120 125

Val Lys Glu Val Ile Ser Gln Leu Thr Arg Val His Gly Thr Ser Ser

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    130                 135                 140

Pro Tyr Lys Gly Leu Asp Leu Ser Lys Leu His Glu Thr Leu Arg Thr
145                 150                 155                 160

His Thr Arg Leu Val Ser Leu Phe Asn Thr Thr Leu Thr Gly Leu His
                165                 170                 175

Glu Val Ser Ala Gln Asn Pro Thr Asn Cys Trp Ile Cys Leu Pro Leu
            180                 185                 190

Asn Phe Arg Pro Tyr Val Ser Ile Pro Val Pro Glu Gln Trp Asn Asn
        195                 200                 205

Phe Ser Thr Glu Ile Asn Thr Thr Ser Val Leu Val Gly Pro Leu Val
    210                 215                 220

Ser Asn Leu Glu Ile Thr His Thr Ser Asn Leu Thr Cys Val Lys Phe
225                 230                 235                 240

Ser Asn Thr Thr Tyr Thr Thr Asn Ser Gln Cys Ile Arg Trp Val Thr
                245                 250                 255

Pro Pro Thr Gln Ile Val Cys Leu Pro Ser Gly Ile Phe Phe Val Cys
            260                 265                 270

Gly Thr Ser Ala Tyr Arg Cys Leu Asn Gly Ser Ser Glu Ser Met Cys
        275                 280                 285

Phe Leu Ser Phe Leu Val Pro Pro Met Thr Ile Tyr Thr Glu Gln Asp
    290                 295                 300

Leu Tyr Ser Tyr Val Ile Ser Lys Pro Arg Asn Lys Arg Val Pro Ile
305                 310                 315                 320

Leu Pro Phe Val Ile Gly Ala Gly Val Leu Gly Ala Leu Gly Thr Gly
                325                 330                 335

Ile Gly Gly Ile Thr Thr Ser Thr Gln Phe Tyr Tyr Lys Leu Ser Gln
            340                 345                 350

Glu Leu Asn Gly Asp Met Glu Arg Val Ala Asp Ser Leu Val Thr Leu
        355                 360                 365

Gln Asp Gln Leu Asn Ser Leu Ala Ala Val Val Leu Gln Asn Arg Arg
    370                 375                 380

Ala Leu Asp Leu Leu Thr Ala Glu Xaa Gly Gly Thr Cys Leu Ala Leu
385                 390                 395                 400
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Gly Glu Glu Cys Cys Tyr Tyr Val Asn Gln Ser Gly Ile Val Thr Glu
405 410 415

Lys Val Lys Glu Ile Arg Asp Arg Ile Gln Arg Arg Ala Glu Glu Leu
420 425 430

Arg Asn Thr Gly Pro Trp Gly Leu Leu Ser Gln Trp Met Pro Trp Ile
435 440 445

Leu Pro Phe Leu Gly Pro Leu Ala Ala Ile Ile Leu Leu Leu Leu Phe
450 455 460

Gly Pro Cys Ile Phe Asn Leu Leu Val Asn Phe Val Ser Ser Arg Ile
465 470 475 480

Glu Ala Val Lys Leu Gln Met Glu Pro Lys Met Gln Ser Lys Thr Lys
485 490 495

Ile Tyr Arg Arg Pro Leu Asp Arg Pro Ala Ser Pro Arg Ser Asp Val
500 505 510

Asn Asp Ile Lys Gly Thr Pro Pro Glu Glu Ile Ser Ala Ala Gln Pro
515 520 525

Leu Leu Arg Pro Asn Ser Ala Gly Ser Ser
530 535

<210> 119

<211> 1615

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-FRD ENV

<220>

<221> misc_feature

<222> (1279)..(1281)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 119
atgggcctgc tcctgctggt tctcattctc acgccttcac tagcagccta ccgccatcct 60

gatttcccgt tattggaaaa agctcagcaa ctgctccaaa gtacaggatc cccttactcc 120

accaattgct ggttatgtac tagctcttcc actgaaacac cagggacagc ttatccagcc 180

tcgcccagag aatggacaag catagaggcg gaattacata tttcctatcg atgggaccct 240

aatctgaaag gactgatgag gcctgcaaat agtcttcttt caacagtaaa gcaagatttc 300

cctgatatcc gccagaaacc tcccattttc ggacccatct ttactaatat caacctaatg 360

ggaatagccc ctatttgtgt tatggccaaa aggaaaaatg gaacaaatgt aggcactctt 420

ccaagtacag tctgtaatgt tactttcact gtagattcta accaacagac ttaccaaaca 480

tacacccaca accaattccg ccatcaacca agattcccca aacctccaaa tattactttt 540

cctcagggaa ctttgctaga taaatccagc cggttttgcc agggacgccc aagctcatgc 600

agtactcgaa acttctggtt ccggcctgct gattataacc aatgtctgca aatttccaac 660

ctcagctcta cagcggaatg ggttctattg gaccaaactc gaaattctct tttttgggaa 720

aataaaacca agggagctaa ccagagccaa acaccctgcg tccaagtctt agcaggcatg 780

actatagcca ccagctacct gggcatatca gcagtctcag aatttttgg aacctccctc 840

acccccttat ttcatttcca tatctctaca tgccttaaaa ctcaaggagc cttttatatt 900

tgtggccagt cgattcacca atgcctcccc agtaactgga ctggaacttg taccataggc 960

tatgtaaccc cagacatctt catagcccct ggcaatctct ctcttccaat accaatctat 1020

gggaattccc cgttgcccag ggtgaggagg gcaatccatt tcattccccc tctcgcggga 1080

ctcggcattc tagctggtac gggaaccgga attgctggaa tcacaaaagc ttccctcacc 1140

tatagccagc tctcaaagga aatagccaac aacattgaca ccatggctaa agccttaacg 1200

accatgcaag aacaaatcga ctctttagca gccgtagtcc ttcaaaatcg tcgaggacta 1260

gacatgttaa cggcagcann nggaggaatt tgtttggcct tagatgaaaa atgttgcttt 1320

tgggtaaatc aatcaggaaa agtacaagac aacatcagac aactcctaaa tcaagcctcc 1380

agtttacggg aacgagccac tcagggttgg ttaaattggg aaggaacttg gaaatggttc 1440

tcttgggttc ttcccccttac aggcccactt gttagtctcc tacttttgct ccttttttggt 1500

ccatgtctcc taaatctaat aacccaattt gtctcctctc gccttcaggc cataaagctc 1560

cagacgaatc tcagtgcagg acgccatcct cgcaatattc aagagtcacc cttct 1615

<210> 120

<211> 538

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-FRD ENV

<400> 120

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Met Gly Leu Leu Leu Leu Val Leu Ile Leu Thr Pro Ser Leu Ala Ala
1               5                  10                  15

Tyr Arg His Pro Asp Phe Pro Leu Leu Glu Lys Ala Gln Gln Leu Leu
            20                  25                  30

Gln Ser Thr Gly Ser Pro Tyr Ser Thr Asn Cys Trp Leu Cys Thr Ser
        35                  40                  45

Ser Ser Thr Glu Thr Pro Gly Thr Ala Tyr Pro Ala Ser Pro Arg Glu
    50                  55                  60

Trp Thr Ser Ile Glu Ala Glu Leu His Ile Ser Tyr Arg Trp Asp Pro
65                  70                  75                  80

Asn Leu Lys Gly Leu Met Arg Pro Ala Asn Ser Leu Leu Ser Thr Val
                85                  90                  95

Lys Gln Asp Phe Pro Asp Ile Arg Gln Lys Pro Pro Ile Phe Gly Pro
            100                 105                 110

Ile Phe Thr Asn Ile Asn Leu Met Gly Ile Ala Pro Ile Cys Val Met
        115                 120                 125

Ala Lys Arg Lys Asn Gly Thr Asn Val Gly Thr Leu Pro Ser Thr Val
    130                 135                 140

Cys Asn Val Thr Phe Thr Val Asp Ser Asn Gln Gln Thr Tyr Gln Thr
145                 150                 155                 160

Tyr Thr His Asn Gln Phe Arg His Gln Pro Arg Phe Pro Lys Pro Pro
                165                 170                 175

Asn Ile Thr Phe Pro Gln Gly Thr Leu Leu Asp Lys Ser Ser Arg Phe
            180                 185                 190

Cys Gln Gly Arg Pro Ser Ser Cys Ser Thr Arg Asn Phe Trp Phe Arg
        195                 200                 205

Pro Ala Asp Tyr Asn Gln Cys Leu Gln Ile Ser Asn Leu Ser Ser Thr
    210                 215                 220

Ala Glu Trp Val Leu Leu Asp Gln Thr Arg Asn Ser Leu Phe Trp Glu
225                 230                 235                 240

Asn Lys Thr Lys Gly Ala Asn Gln Ser Gln Thr Pro Cys Val Gln Val
```

245 250 255

Leu Ala Gly Met Thr Ile Ala Thr Ser Tyr Leu Gly Ile Ser Ala Val
260 265 270

Ser Glu Phe Phe Gly Thr Ser Leu Thr Pro Leu Phe His Phe His Ile
275 280 285

Ser Thr Cys Leu Lys Thr Gln Gly Ala Phe Tyr Ile Cys Gly Gln Ser
290 295 300

Ile His Gln Cys Leu Pro Ser Asn Trp Thr Gly Thr Cys Thr Ile Gly
305 310 315 320

Tyr Val Thr Pro Asp Ile Phe Ile Ala Pro Gly Asn Leu Ser Leu Pro
325 330 335

Ile Pro Ile Tyr Gly Asn Ser Pro Leu Pro Arg Val Arg Arg Ala Ile
340 345 350

His Phe Ile Pro Leu Leu Ala Gly Leu Gly Ile Leu Ala Gly Thr Gly
355 360 365

Thr Gly Ile Ala Gly Ile Thr Lys Ala Ser Leu Thr Tyr Ser Gln Leu
370 375 380

Ser Lys Glu Ile Ala Asn Asn Ile Asp Thr Met Ala Lys Ala Leu Thr
385 390 395 400

Thr Met Gln Glu Gln Ile Asp Ser Leu Ala Ala Val Val Leu Gln Asn
405 410 415

Arg Arg Gly Leu Asp Met Leu Thr Ala Ala Arg Gly Gly Ile Cys Leu
420 425 430

Ala Leu Asp Glu Lys Cys Cys Phe Trp Val Asn Gln Ser Gly Lys Val
435 440 445

Gln Asp Asn Ile Arg Gln Leu Leu Asn Gln Ala Ser Ser Leu Arg Glu
450 455 460

Arg Ala Thr Gln Gly Trp Leu Asn Trp Glu Gly Thr Trp Lys Trp Phe
465 470 475 480

Ser Trp Val Leu Pro Leu Thr Gly Pro Leu Val Ser Leu Leu Leu Leu
485 490 495

Leu Leu Phe Gly Pro Cys Leu Leu Asn Leu Ile Thr Gln Phe Val Ser
500 505 510

Ser Arg Leu Gln Ala Ile Lys Leu Gln Thr Asn Leu Ser Ala Gly Arg
515 520 525

His Pro Arg Asn Ile Gln Glu Ser Pro Phe
530 535

<210> 121

<211> 1615

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-FRD ENV

<220>

<221> misc_feature

<222> (1279)..(1281)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1297)..(1299)

<223> TTT or TTC

<400> 121
atgggcctgc tcctgctggt tctcattctc acgccttcac tagcagccta ccgccatcct 60

gatttcccgt tattggaaaa agctcagcaa ctgctccaaa gtacaggatc cccttactcc 120

accaattgct ggttatgtac tagctcttcc actgaaacac cagggacagc ttatccagcc 180

tcgcccagag aatggacaag catagaggcg gaattacata tttcctatcg atgggaccct 240

aatctgaaag gactgatgag gcctgcaaat agtcttcttt caacagtaaa gcaagatttc 300

cctgatatcc gccagaaacc tcccattttc ggacccatct ttactaatat caacctaatg 360

ggaatagccc ctatttgtgt tatggccaaa aggaaaaatg gaacaaatgt aggcactctt 420

ccaagtacag tctgtaatgt tactttcact gtagattcta accaacagac ttaccaaaca 480

tacacccaca accaattccg ccatcaacca agattcccca aacctccaaa tattactttt 540

cctcagggaa ctttgctaga taaatccagc cggttttgcc agggacgccc aagctcatgc 600

agtactcgaa acttctggtt ccggcctgct gattataacc aatgtctgca aatttccaac 660

ctcagctcta cagcggaatg ggttctattg gaccaaactc gaaattctct tttttgggaa 720

aataaaacca agggagctaa ccagagccaa acaccctgcg tccaagtctt agcaggcatg 780

actatagcca ccagctacct gggcatatca gcagtctcag aatttttttgg aacctccctc 840

acccccttat ttcatttcca tatctctaca tgccttaaaa ctcaaggagc cttttatatt 900

tgtggccagt cgattcacca atgcctcccc agtaactgga ctggaacttg taccataggc 960

tatgtaaccc cagacatctt catagcccct ggcaatctct ctcttccaat accaatctat 1020

gggaattccc cgttgcccag ggtgaggagg gcaatccatt tcattcccct tctcgcggga 1080

ctcggcattc tagctggtac gggaaccgga attgctggaa tcacaaaagc ttccctcacc 1140

tatagccagc tctcaaagga aatagccaac aacattgaca ccatggctaa agccttaacg 1200

accatgcaag aacaaatcga ctctttagca gccgtagtcc ttcaaaatcg tcgaggacta 1260

gacatgttaa cggcagcann nggaggaatt tgtttgnnnt tagatgaaaa atgttgcttt 1320

tgggtaaatc aatcaggaaa agtacaagac aacatcagac aactcctaaa tcaagcctcc 1380

agtttacggg aacgagccac tcagggttgg ttaaattggg aaggaacttg gaaatggttc 1440

tcttgggttc ttcccttac aggcccactt gttagtctcc tacttttgct ccttttttggt 1500

ccatgtctcc taaatctaat aacccaattt gtctcctctc gccttcaggc cataaagctc 1560

cagacgaatc tcagtgcagg acgccatcct cgcaatattc aagagtcacc cttct 1615

<210> 122

<211> 538

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-FRD ENV

<400> 122

Met Gly Leu Leu Leu Leu Val Leu Ile Leu Thr Pro Ser Leu Ala Ala
1 5 10 15

Tyr Arg His Pro Asp Phe Pro Leu Leu Glu Lys Ala Gln Gln Leu Leu
20 25 30

Gln Ser Thr Gly Ser Pro Tyr Ser Thr Asn Cys Trp Leu Cys Thr Ser
35 40 45

Ser Ser Thr Glu Thr Pro Gly Thr Ala Tyr Pro Ala Ser Pro Arg Glu
50 55 60

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Trp Thr Ser Ile Glu Ala Glu Leu His Ile Ser Tyr Arg Trp Asp Pro
65                  70                  75                  80

Asn Leu Lys Gly Leu Met Arg Pro Ala Asn Ser Leu Leu Ser Thr Val
                85                  90                  95

Lys Gln Asp Phe Pro Asp Ile Arg Gln Lys Pro Pro Ile Phe Gly Pro
            100                 105                 110

Ile Phe Thr Asn Ile Asn Leu Met Gly Ile Ala Pro Ile Cys Val Met
        115                 120                 125

Ala Lys Arg Lys Asn Gly Thr Asn Val Gly Thr Leu Pro Ser Thr Val
    130                 135                 140

Cys Asn Val Thr Phe Thr Val Asp Ser Asn Gln Gln Thr Tyr Gln Thr
145                 150                 155                 160

Tyr Thr His Asn Gln Phe Arg His Gln Pro Arg Phe Pro Lys Pro Pro
                165                 170                 175

Asn Ile Thr Phe Pro Gln Gly Thr Leu Leu Asp Lys Ser Ser Arg Phe
            180                 185                 190

Cys Gln Gly Arg Pro Ser Ser Cys Ser Thr Arg Asn Phe Trp Phe Arg
        195                 200                 205

Pro Ala Asp Tyr Asn Gln Cys Leu Gln Ile Ser Asn Leu Ser Ser Thr
    210                 215                 220

Ala Glu Trp Val Leu Leu Asp Gln Thr Arg Asn Ser Leu Phe Trp Glu
225                 230                 235                 240

Asn Lys Thr Lys Gly Ala Asn Gln Ser Gln Thr Pro Cys Val Gln Val
                245                 250                 255

Leu Ala Gly Met Thr Ile Ala Thr Ser Tyr Leu Gly Ile Ser Ala Val
            260                 265                 270

Ser Glu Phe Phe Gly Thr Ser Leu Thr Pro Leu Phe His Phe His Ile
        275                 280                 285

Ser Thr Cys Leu Lys Thr Gln Gly Ala Phe Tyr Ile Cys Gly Gln Ser
    290                 295                 300

Ile His Gln Cys Leu Pro Ser Asn Trp Thr Gly Thr Cys Thr Ile Gly
305                 310                 315                 320
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Tyr Val Thr Pro Asp Ile Phe Ile Ala Pro Gly Asn Leu Ser Leu Pro
325 330 335

Ile Pro Ile Tyr Gly Asn Ser Pro Leu Pro Arg Val Arg Arg Ala Ile
340 345 350

His Phe Ile Pro Leu Leu Ala Gly Leu Gly Ile Leu Ala Gly Thr Gly
355 360 365

Thr Gly Ile Ala Gly Ile Thr Lys Ala Ser Leu Thr Tyr Ser Gln Leu
370 375 380

Ser Lys Glu Ile Ala Asn Asn Ile Asp Thr Met Ala Lys Ala Leu Thr
385 390 395 400

Thr Met Gln Glu Gln Ile Asp Ser Leu Ala Ala Val Val Leu Gln Asn
405 410 415

Arg Arg Gly Leu Asp Met Leu Thr Ala Ala Arg Gly Gly Ile Cys Leu
420 425 430

Phe Leu Asp Glu Lys Cys Cys Phe Trp Val Asn Gln Ser Gly Lys Val
435 440 445

Gln Asp Asn Ile Arg Gln Leu Leu Asn Gln Ala Ser Ser Leu Arg Glu
450 455 460

Arg Ala Thr Gln Gly Trp Leu Asn Trp Glu Gly Thr Trp Lys Trp Phe
465 470 475 480

Ser Trp Val Leu Pro Leu Thr Gly Pro Leu Val Ser Leu Leu Leu Leu
485 490 495

Leu Leu Phe Gly Pro Cys Leu Leu Asn Leu Ile Thr Gln Phe Val Ser
500 505 510

Ser Arg Leu Gln Ala Ile Lys Leu Gln Thr Asn Leu Ser Ala Gly Arg
515 520 525

His Pro Arg Asn Ile Gln Glu Ser Pro Phe
530 535

<210> 123

<211> 1563

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-V ENV

<220>

<221> misc_feature

<222> (1141)..(1143)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 123
atgcccctac tctcacaggc acagtggaat gaaaattccc ttgtcagttt ttccaaaata 60

attgcttcgg gaaaccatct aagcaactgt tggatctgcc acaacttcat caccaggtcc 120

tcatcttacc aatatatttt ggtaagaaat ttttctttaa acctaacatt tggttcagga 180

atccctgaag gccaacataa atctgttccg ctccaggttt cgcttgctaa ctcagcgcac 240

caagtcccct gcctggatct cactccacct ttcaatcaaa gctctaaaac ttctttctat 300

ttctacaact gctcttctct aaaccaaacc tgttgtccat gccctgaagg acactgtgac 360

aggaagaaca cctctgagga gggattcccc agtcccacca tccatcccat gagcttctcc 420

ccagcaggct gccaccctaa cttgactcac tggtgtccag ctaaacaaat gaacgattat 480

cgagacaagt caccccaaaa ccgctgtgca gcttgggaag gaaaagagct aatcacatgg 540

agggttctat attcgcttcc caaggcacac actgtcccca catggccaaa atctactgtt 600

cccctgggag ggcctctatc ccctgcatgc aatcaaacta ttccagcagg gtggaaatcg 660

cagttacaca agtggttcga cagccacatc ccccggtggg cctgtacccc tcctggctat 720

gtatttttat gtgggccaca aaaaaataaa ctgccctttg atggaagtcc taagataacc 780

tattcaaccc cccctgtggc aaacctctac acttgcatta ataacatcca acatacggga 840

gaatgtgctg tgggactttt gggaccacgg gggataggtg tgaccattta taacaccacc 900

caacccagac agaaaagagc tctgggtcta atactggcag ggatgggtgc ggccatagga 960

atgatcgccc catggggagg gttcacttat catgatgtca ccctcagaaa tctctccaga 1020

caaatagaca acatagctaa gagtaccaga gatagcatct ctaaactcaa ggcctccata 1080

gattctctag caaatgtagt catggacaac agattggcct tagattacct cttagcagag 1140

nnnggtggag tctgtgcagt gatcaataaa tcctgttgcg tttatgtcaa taacagtggg 1200

gcgatagagg aggatataaa aaagatctat gatgaggcta cgtggctcca tgactttgga 1260

aaaggaggtg cttcagcaag ggccatctgg gaggctgtga agtctgccct cccctccctc 1320

aactggtttg tcccttttact gggaccagca acagttatac tcttactttt cctctttggc 1380

ccttgtttct ttaatttact gattaagtgt gtctcttcta ggataaagca atttcacatg 1440

aagtcccccc aaatggaaag atatcagcta tctgtcattg gaggccccag cacctataag 1500

cacatctccc ccttggatgc cagtgggcaa agattccggg aaactatgga ggaattttct 1560

ctc 1563

<210> 124

<211> 521

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-V ENV

<400> 124

Met Pro Leu Leu Ser Gln Ala Gln Trp Asn Glu Asn Ser Leu Val Ser
1 5 10 15

Phe Ser Lys Ile Ile Ala Ser Gly Asn His Leu Ser Asn Cys Trp Ile
20 25 30

Cys His Asn Phe Ile Thr Arg Ser Ser Ser Tyr Gln Tyr Ile Leu Val
35 40 45

Arg Asn Phe Ser Leu Asn Leu Thr Phe Gly Ser Gly Ile Pro Glu Gly
50 55 60

Gln His Lys Ser Val Pro Leu Gln Val Ser Leu Ala Asn Ser Ala His
65 70 75 80

Gln Val Pro Cys Leu Asp Leu Thr Pro Pro Phe Asn Gln Ser Ser Lys
85 90 95

Thr Ser Phe Tyr Phe Tyr Asn Cys Ser Ser Leu Asn Gln Thr Cys Cys
100 105 110

Pro Cys Pro Glu Gly His Cys Asp Arg Lys Asn Thr Ser Glu Glu Gly
115 120 125

Phe Pro Ser Pro Thr Ile His Pro Met Ser Phe Ser Pro Ala Gly Cys
130 135 140

His Pro Asn Leu Thr His Trp Cys Pro Ala Lys Gln Met Asn Asp Tyr
145 150 155 160

Arg Asp Lys Ser Pro Gln Asn Arg Cys Ala Ala Trp Glu Gly Lys Glu
165 170 175

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Leu Ile Thr Trp Arg Val Leu Tyr Ser Leu Pro Lys Ala His Thr Val
            180                 185                 190

Pro Thr Trp Pro Lys Ser Thr Val Pro Leu Gly Gly Pro Leu Ser Pro
        195                 200                 205

Ala Cys Asn Gln Thr Ile Pro Ala Gly Trp Lys Ser Gln Leu His Lys
    210                 215                 220

Trp Phe Asp Ser His Ile Pro Arg Trp Ala Cys Thr Pro Pro Gly Tyr
225                 230                 235                 240

Val Phe Leu Cys Gly Pro Gln Lys Asn Lys Leu Pro Phe Asp Gly Ser
                245                 250                 255

Pro Lys Ile Thr Tyr Ser Thr Pro Pro Val Ala Asn Leu Tyr Thr Cys
            260                 265                 270

Ile Asn Asn Ile Gln His Thr Gly Glu Cys Ala Val Gly Leu Leu Gly
        275                 280                 285

Pro Arg Gly Ile Gly Val Thr Ile Tyr Asn Thr Thr Gln Pro Arg Gln
    290                 295                 300

Lys Arg Ala Leu Gly Leu Ile Leu Ala Gly Met Gly Ala Ala Ile Gly
305                 310                 315                 320

Met Ile Ala Pro Trp Gly Gly Phe Thr Tyr His Asp Val Thr Leu Arg
                325                 330                 335

Asn Leu Ser Arg Gln Ile Asp Asn Ile Ala Lys Ser Thr Arg Asp Ser
            340                 345                 350

Ile Ser Lys Leu Lys Ala Ser Ile Asp Ser Leu Ala Asn Val Val Met
        355                 360                 365

Asp Asn Arg Leu Ala Leu Asp Tyr Leu Leu Ala Glu Arg Gly Gly Val
    370                 375                 380

Cys Ala Val Ile Asn Lys Ser Cys Cys Val Tyr Val Asn Asn Ser Gly
385                 390                 395                 400

Ala Ile Glu Glu Asp Ile Lys Lys Ile Tyr Asp Glu Ala Thr Trp Leu
                405                 410                 415

His Asp Phe Gly Lys Gly Gly Ala Ser Ala Arg Ala Ile Trp Glu Ala
            420                 425                 430
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Val Lys Ser Ala Leu Pro Ser Leu Asn Trp Phe Val Pro Leu Leu Gly
435 440 445

Pro Ala Thr Val Ile Leu Leu Leu Phe Leu Phe Gly Pro Cys Phe Phe
450 455 460

Asn Leu Leu Ile Lys Cys Val Ser Ser Arg Ile Lys Gln Phe His Met
465 470 475 480

Lys Ser Pro Gln Met Glu Arg Tyr Gln Leu Ser Val Ile Gly Gly Pro
485 490 495

Ser Thr Tyr Lys His Ile Ser Pro Leu Asp Ala Ser Gly Gln Arg Phe
500 505 510

Arg Glu Thr Met Glu Glu Phe Ser Leu
515 520

<210> 125

<211> 1563

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-V ENV

<220>

<221> misc_feature

<222> (1141)..(1143)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1159)..(1161)

<223> TTT or TTC

<400> 125
atgcccctac tctcacaggc acagtggaat gaaaattccc ttgtcagttt ttccaaaata 60

attgcttcgg gaaaccatct aagcaactgt tggatctgcc acaacttcat caccaggtcc 120

tcatcttacc aatatatttt ggtaagaaat ttttctttaa acctaacatt tggttcagga 180

atccctgaag gccaacataa atctgttccg ctccaggttt cgcttgctaa ctcagcgcac 240

caagtcccct gcctggatct cactccacct ttcaatcaaa gctctaaaac ttctttctat 300

ttctacaact gctcttctct aaaccaaacc tgttgtccat gccctgaagg acactgtgac 360

aggaagaaca cctctgagga gggattcccc agtcccacca tccatcccat gagcttctcc 420

ccagcaggct gccaccctaa cttgactcac tggtgtccag ctaaacaaat gaacgattat 480

cgagacaagt caccccaaaa ccgctgtgca gcttgggaag gaaaagagct aatcacatgg 540

agggttctat attcgcttcc caaggcacac actgtcccca catggccaaa atctactgtt 600

cccctgggag ggcctctatc ccctgcatgc aatcaaacta ttccagcagg gtggaaatcg 660

cagttacaca agtggttcga cagccacatc ccccggtggg cctgtacccc tcctggctat 720

gtatttttat gtgggccaca aaaaaataaa ctgccctttg atggaagtcc taagataacc 780

tattcaaccc cccctgtggc aaacctctac acttgcatta ataacatcca acatacggga 840

gaatgtgctg tgggactttt gggaccacgg gggataggtg tgaccattta taacaccacc 900

caacccagac agaaaagagc tctgggtcta atactggcag ggatgggtgc ggccatagga 960

atgatcgccc catggggagg gttcacttat catgatgtca ccctcagaaa tctctccaga 1020

caaatagaca acatagctaa gagtaccaga gatagcatct ctaaactcaa ggcctccata 1080

gattctctag caaatgtagt catggacaac agattggcct tagattacct cttagcagag 1140

nnnggtggag tctgtgcann natcaataaa tcctgttgcg tttatgtcaa taacagtggg 1200

gcgatagagg aggatataaa aaagatctat gatgaggcta cgtggctcca tgactttgga 1260

aaaggaggtg cttcagcaag ggccatctgg gaggctgtga agtctgccct cccctccctc 1320

aactggtttg tccctttact gggaccagca acagttatac tcttactttt cctctttggc 1380

ccttgtttct ttaatttact gattaagtgt gtctcttcta ggataaagca atttcacatg 1440

aagtcccccc aaatggaaag atatcagcta tctgtcattg gaggccccag cacctataag 1500

cacatctccc ccttggatgc cagtgggcaa agattccggg aaactatgga ggaattttct 1560

ctc 1563

<210> 126

<211> 521

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-V ENV

<400> 126

Met Pro Leu Leu Ser Gln Ala Gln Trp Asn Glu Asn Ser Leu Val Ser
1 5 10 15

Phe Ser Lys Ile Ile Ala Ser Gly Asn His Leu Ser Asn Cys Trp Ile
20 25 30

Cys His Asn Phe Ile Thr Arg Ser Ser Ser Tyr Gln Tyr Ile Leu Val
35 40 45

Arg Asn Phe Ser Leu Asn Leu Thr Phe Gly Ser Gly Ile Pro Glu Gly
50 55 60

Gln His Lys Ser Val Pro Leu Gln Val Ser Leu Ala Asn Ser Ala His
65 70 75 80

Gln Val Pro Cys Leu Asp Leu Thr Pro Pro Phe Asn Gln Ser Ser Lys
85 90 95

Thr Ser Phe Tyr Phe Tyr Asn Cys Ser Ser Leu Asn Gln Thr Cys Cys
100 105 110

Pro Cys Pro Glu Gly His Cys Asp Arg Lys Asn Thr Ser Glu Glu Gly
115 120 125

Phe Pro Ser Pro Thr Ile His Pro Met Ser Phe Ser Pro Ala Gly Cys
130 135 140

His Pro Asn Leu Thr His Trp Cys Pro Ala Lys Gln Met Asn Asp Tyr
145 150 155 160

Arg Asp Lys Ser Pro Gln Asn Arg Cys Ala Ala Trp Glu Gly Lys Glu
165 170 175

Leu Ile Thr Trp Arg Val Leu Tyr Ser Leu Pro Lys Ala His Thr Val
180 185 190

Pro Thr Trp Pro Lys Ser Thr Val Pro Leu Gly Gly Pro Leu Ser Pro
195 200 205

Ala Cys Asn Gln Thr Ile Pro Ala Gly Trp Lys Ser Gln Leu His Lys
210 215 220

Trp Phe Asp Ser His Ile Pro Arg Trp Ala Cys Thr Pro Pro Gly Tyr
225 230 235 240

Val Phe Leu Cys Gly Pro Gln Lys Asn Lys Leu Pro Phe Asp Gly Ser
245 250 255

```
Pro Lys Ile Thr Tyr Ser Thr Pro Pro Val Ala Asn Leu Tyr Thr Cys
            260                 265                 270

Ile Asn Asn Ile Gln His Thr Gly Glu Cys Ala Val Gly Leu Leu Gly
        275                 280                 285

Pro Arg Gly Ile Gly Val Thr Ile Tyr Asn Thr Thr Gln Pro Arg Gln
    290                 295                 300

Lys Arg Ala Leu Gly Leu Ile Leu Ala Gly Met Gly Ala Ala Ile Gly
305                 310                 315                 320

Met Ile Ala Pro Trp Gly Gly Phe Thr Tyr His Asp Val Thr Leu Arg
                325                 330                 335

Asn Leu Ser Arg Gln Ile Asp Asn Ile Ala Lys Ser Thr Arg Asp Ser
            340                 345                 350

Ile Ser Lys Leu Lys Ala Ser Ile Asp Ser Leu Ala Asn Val Val Met
        355                 360                 365

Asp Asn Arg Leu Ala Leu Asp Tyr Leu Leu Ala Glu Arg Gly Gly Val
    370                 375                 380

Cys Ala Phe Ile Asn Lys Ser Cys Cys Val Tyr Val Asn Asn Ser Gly
385                 390                 395                 400

Ala Ile Glu Glu Asp Ile Lys Lys Ile Tyr Asp Glu Ala Thr Trp Leu
                405                 410                 415

His Asp Phe Gly Lys Gly Gly Ala Ser Ala Arg Ala Ile Trp Glu Ala
            420                 425                 430

Val Lys Ser Ala Leu Pro Ser Leu Asn Trp Phe Val Pro Leu Leu Gly
        435                 440                 445

Pro Ala Thr Val Ile Leu Leu Leu Phe Leu Phe Gly Pro Cys Phe Phe
    450                 455                 460

Asn Leu Leu Ile Lys Cys Val Ser Ser Arg Ile Lys Gln Phe His Met
465                 470                 475                 480

Lys Ser Pro Gln Met Glu Arg Tyr Gln Leu Ser Val Ile Gly Gly Pro
                485                 490                 495

Ser Thr Tyr Lys His Ile Ser Pro Leu Asp Ala Ser Gly Gln Arg Phe
            500                 505                 510

Arg Glu Thr Met Glu Glu Phe Ser Leu
```

515 520

<210> 127

<211> 1878

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-T ENV

<220>

<221> misc_feature

<222> (1546)..(1548)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 127

atgggtcccg aagcctgggt caggcccctt aaaactgcgc ctaagccggg tgaagccatt 60

agattaattc tttttattta cctctcttgt ttctttttgc ctgttatgtc ctctgagcct 120

tcctactcct ttctcctcac ctctttcaca acaggacgtg tattcgcaaa cactacttgg 180

agggccggta cctccaagga agtctccttt gcagttgatt tatgtgtact gttcccagag 240

ccagctcgta cccatgaaga gcaacataat ttgccggtca taggagcagg aagtgtcgac 300

cttgcagcag gatttggaca ctctgggagc caaactggat gtggaagctc caaaggtgca 360

gaaaaagggc tccaaaatgt tgacttttac ctctgtcctg gaaatcaccc tgacgctagc 420

tgtagagata cttaccagtt tttctgccct gattggacat gtgtaacttt agccacctac 480

tctgggggat caactagatc ttcaactctt tccataagtc gtgttcctca tcctaaatta 540

tgtactagaa aaaattgtaa tcctcttact ataactgtcc atgaccctaa tgcagctcaa 600

tggtattatg gcatgtcatg gggattaaga ctttatatcc caggatttga tgttgggact 660

atgttcacca tccaaaagaa aatcttggtc tcatggagct cccccaagcc aatcgggcct 720

ttaactgatc taggtgaccc tatattccag aaacaccctg acaaagttga tttaactgtt 780

cctctgccat tcttagttcc tagaccccag ctacaacaac aacatcttca acccagccta 840

atgtctatac taggtggagt acaccatctc cttaacctca cccagcctaa actagcccaa 900

gattgttggc tatgtttaaa agcaaaaccc ccttattatg taggattagg agtagaagcc 960

acacttaaac gtggccctct atcttgtcat acacgacccc gtgctctcac aataggagat 1020

gtgtctggaa atgcttcctg tctgattagt accgggtata acttatctgc ttctcctttt 1080

caggctactt gtaatcagtc cctgcttact tccataagca cctcagtctc ttaccaagca 1140

cccaacaata cctggttggc ctgcacctca ggtctcactc gctgcattaa tggaactgaa 1200

ccaggacctc tcctgtgcgt gttagttcat gtacttcccc aggtatatgt gtacagtgga 1260

ccagaaggac gacaactcat cgctcccccc gagttacatc ccaggttgca ccaagctgtc 1320

ccacttctgg ttcccctatt ggctggtctt agcatagctg gatcagcagc cattggtacg 1380

gctgccctgg ttcaaggaga aactggacta atatccctgt ctcaacaggt ggatgctgat 1440

tttagtaacc tccagtctgc catagatata ctacattccc aggtagagtc tctggctgaa 1500

gtagttcttc aaaactgccg atgcttagat ctgctattcc tctctnnngg aggtttatgt 1560

gcagctctag gagaaagttg ttgcttctat gccaatcaat ctggagtcat aaaaggtaca 1620

gtaaaaaaag ttcgagaaaa tctagatagg caccaacaag aacgagaaaa taacatcccc 1680

tggtatcaaa gcatgtttaa ctggaaccca tggctaacta ctttaatcac tgggttagct 1740

ggacctctcc tcatcctact attaagttta atttttgggc cttgtatatt aaattcgttt 1800

cttaatttta taaaacaacg catagcttct gtcaaactta cgtatcttaa gactcaatat 1860

gacacccttg ttaataac 1878

<210> 128

<211> 626

<212> PRT

<213> Mutated HERV-T ENV

<400> 128

Met Gly Pro Glu Ala Trp Val Arg Pro Leu Lys Thr Ala Pro Lys Pro
1 5 10 15

Gly Glu Ala Ile Arg Leu Ile Leu Phe Ile Tyr Leu Ser Cys Phe Phe
20 25 30

Leu Pro Val Met Ser Ser Glu Pro Ser Tyr Ser Phe Leu Leu Thr Ser
35 40 45

Phe Thr Thr Gly Arg Val Phe Ala Asn Thr Thr Trp Arg Ala Gly Thr
50 55 60

Ser Lys Glu Val Ser Phe Ala Val Asp Leu Cys Val Leu Phe Pro Glu
65 70 75 80

Pro Ala Arg Thr His Glu Glu Gln His Asn Leu Pro Val Ile Gly Ala
85 90 95

Gly Ser Val Asp Leu Ala Ala Gly Phe Gly His Ser Gly Ser Gln Thr

100 105 110

Gly Cys Gly Ser Ser Lys Gly Ala Glu Lys Gly Leu Gln Asn Val Asp
115 120 125

Phe Tyr Leu Cys Pro Gly Asn His Pro Asp Ala Ser Cys Arg Asp Thr
130 135 140

Tyr Gln Phe Phe Cys Pro Asp Trp Thr Cys Val Thr Leu Ala Thr Tyr
145 150 155 160

Ser Gly Gly Ser Thr Arg Ser Ser Thr Leu Ser Ile Ser Arg Val Pro
165 170 175

His Pro Lys Leu Cys Thr Arg Lys Asn Cys Asn Pro Leu Thr Ile Thr
180 185 190

Val His Asp Pro Asn Ala Ala Gln Trp Tyr Tyr Gly Met Ser Trp Gly
195 200 205

Leu Arg Leu Tyr Ile Pro Gly Phe Asp Val Gly Thr Met Phe Thr Ile
210 215 220

Gln Lys Lys Ile Leu Val Ser Trp Ser Ser Pro Lys Pro Ile Gly Pro
225 230 235 240

Leu Thr Asp Leu Gly Asp Pro Ile Phe Gln Lys His Pro Asp Lys Val
245 250 255

Asp Leu Thr Val Pro Leu Pro Phe Leu Val Pro Arg Pro Gln Leu Gln
260 265 270

Gln Gln His Leu Gln Pro Ser Leu Met Ser Ile Leu Gly Gly Val His
275 280 285

His Leu Leu Asn Leu Thr Gln Pro Lys Leu Ala Gln Asp Cys Trp Leu
290 295 300

Cys Leu Lys Ala Lys Pro Pro Tyr Tyr Val Gly Leu Gly Val Glu Ala
305 310 315 320

Thr Leu Lys Arg Gly Pro Leu Ser Cys His Thr Arg Pro Arg Ala Leu
325 330 335

Thr Ile Gly Asp Val Ser Gly Asn Ala Ser Cys Leu Ile Ser Thr Gly
340 345 350

Tyr Asn Leu Ser Ala Ser Pro Phe Gln Ala Thr Cys Asn Gln Ser Leu
355 360 365

Leu Thr Ser Ile Ser Thr Ser Val Ser Tyr Gln Ala Pro Asn Asn Thr
370 375 380

Trp Leu Ala Cys Thr Ser Gly Leu Thr Arg Cys Ile Asn Gly Thr Glu
385 390 395 400

Pro Gly Pro Leu Leu Cys Val Leu Val His Val Leu Pro Gln Val Tyr
405 410 415

Val Tyr Ser Gly Pro Glu Gly Arg Gln Leu Ile Ala Pro Pro Glu Leu
420 425 430

His Pro Arg Leu His Gln Ala Val Pro Leu Leu Val Pro Leu Leu Ala
435 440 445

Gly Leu Ser Ile Ala Gly Ser Ala Ala Ile Gly Thr Ala Ala Leu Val
450 455 460

Gln Gly Glu Thr Gly Leu Ile Ser Leu Ser Gln Gln Val Asp Ala Asp
465 470 475 480

Phe Ser Asn Leu Gln Ser Ala Ile Asp Ile Leu His Ser Gln Val Glu
485 490 495

Ser Leu Ala Glu Val Val Leu Gln Asn Cys Arg Cys Leu Asp Leu Leu
500 505 510

Phe Leu Ser Arg Gly Gly Leu Cys Ala Ala Leu Gly Glu Ser Cys Cys
515 520 525

Phe Tyr Ala Asn Gln Ser Gly Val Ile Lys Gly Thr Val Lys Lys Val
530 535 540

Arg Glu Asn Leu Asp Arg His Gln Gln Glu Arg Glu Asn Asn Ile Pro
545 550 555 560

Trp Tyr Gln Ser Met Phe Asn Trp Asn Pro Trp Leu Thr Thr Leu Ile
565 570 575

Thr Gly Leu Ala Gly Pro Leu Leu Ile Leu Leu Leu Ser Leu Ile Phe
580 585 590

Gly Pro Cys Ile Leu Asn Ser Phe Leu Asn Phe Ile Lys Gln Arg Ile
595 600 605

Ala Ser Val Lys Leu Thr Tyr Leu Lys Thr Gln Tyr Asp Thr Leu Val
610 615 620

Asn Asn
625

<210> 129

<211> 1878

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-T ENV

<220>

<221> misc_feature

<222> (1546)..(1548)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1564)..(1566)

<223> TTT or TTC

<400> 129
atgggtcccg aagcctgggt caggcccctt aaaactgcgc ctaagccggg tgaagccatt 60

agattaattc tttttattta cctctcttgt ttctttttgc ctgttatgtc ctctgagcct 120

tcctactcct ttctcctcac ctctttcaca acaggacgtg tattcgcaaa cactacttgg 180

agggccggta cctccaagga agtctccttt gcagttgatt tatgtgtact gttcccagag 240

ccagctcgta cccatgaaga gcaacataat ttgccggtca taggagcagg aagtgtcgac 300

cttgcagcag gatttggaca ctctgggagc caaactggat gtggaagctc caaaggtgca 360

gaaaaagggc tccaaaatgt tgacttttac ctctgtcctg gaaatcaccc tgacgctagc 420

tgtagagata cttaccagtt tttctgccct gattggacat gtgtaacttt agccacctac 480

tctgggggat caactagatc ttcaactctt tccataagtc gtgttcctca tcctaaatta 540

tgtactagaa aaaattgtaa tcctcttact ataactgtcc atgaccctaa tgcagctcaa 600

tggtattatg gcatgtcatg gggattaaga ctttatatcc caggatttga tgttgggact 660

atgttcacca tccaaaagaa aatcttggtc tcatggagct cccccaagcc aatcgggcct 720

ttaactgatc taggtgaccc tatattccag aaacaccctg acaaagttga tttaactgtt 780

cctctgccat tcttagttcc tagaccccag ctacaacaac aacatcttca acccagccta 840

atgtctatac taggtggagt acaccatctc cttaacctca cccagcctaa actagcccaa 900

gattgttggc tatgtttaaa agcaaaaccc ccttattatg taggattagg agtagaagcc 960

acacttaaac gtggccctct atcttgtcat acacgacccc gtgctctcac aataggagat 1020

gtgtctggaa atgcttcctg tctgattagt accgggtata acttatctgc ttctcctttt 1080

caggctactt gtaatcagtc cctgcttact tccataagca cctcagtctc ttaccaagca 1140

cccaacaata cctggttggc ctgcacctca ggtctcactc gctgcattaa tggaactgaa 1200

ccaggacctc tcctgtgcgt gttagttcat gtacttcccc aggtatatgt gtacagtgga 1260

ccagaaggac gacaactcat cgctcccccc gagttacatc ccaggttgca ccaagctgtc 1320

ccacttctgg ttcccctatt ggctggtctt agcatagctg gatcagcagc cattggtacg 1380

gctgccctgg ttcaaggaga aactggacta atatccctgt ctcaacaggt ggatgctgat 1440

tttagtaacc tccagtctgc catagatata ctacattccc aggtagagtc tctggctgaa 1500

gtagttcttc aaaactgccg atgcttagat ctgctattcc tctctnnngg aggtttatgt 1560

gcannnctag gagaaagttg ttgcttctat gccaatcaat ctggagtcat aaaaggtaca 1620

gtaaaaaaag ttcgagaaaa tctagatagg caccaacaag aacgagaaaa taacatcccc 1680

tggtatcaaa gcatgtttaa ctggaaccca tggctaacta ctttaatcac tgggttagct 1740

ggacctctcc tcatcctact attaagttta atttttgggc cttgtatatt aaattcgttt 1800

cttaatttta taaaacaacg catagcttct gtcaaactta cgtatcttaa gactcaatat 1860

gacacccttg ttaataac 1878

<210> 130

<211> 626

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-T ENV

<400> 130

Met Gly Pro Glu Ala Trp Val Arg Pro Leu Lys Thr Ala Pro Lys Pro
1 5 10 15

Gly Glu Ala Ile Arg Leu Ile Leu Phe Ile Tyr Leu Ser Cys Phe Phe
20 25 30

Leu Pro Val Met Ser Ser Glu Pro Ser Tyr Ser Phe Leu Leu Thr Ser

35 40 45

Phe Thr Thr Gly Arg Val Phe Ala Asn Thr Thr Trp Arg Ala Gly Thr
50 55 60

Ser Lys Glu Val Ser Phe Ala Val Asp Leu Cys Val Leu Phe Pro Glu
65 70 75 80

Pro Ala Arg Thr His Glu Glu Gln His Asn Leu Pro Val Ile Gly Ala
85 90 95

Gly Ser Val Asp Leu Ala Ala Gly Phe Gly His Ser Gly Ser Gln Thr
100 105 110

Gly Cys Gly Ser Ser Lys Gly Ala Glu Lys Gly Leu Gln Asn Val Asp
115 120 125

Phe Tyr Leu Cys Pro Gly Asn His Pro Asp Ala Ser Cys Arg Asp Thr
130 135 140

Tyr Gln Phe Phe Cys Pro Asp Trp Thr Cys Val Thr Leu Ala Thr Tyr
145 150 155 160

Ser Gly Gly Ser Thr Arg Ser Ser Thr Leu Ser Ile Ser Arg Val Pro
165 170 175

His Pro Lys Leu Cys Thr Arg Lys Asn Cys Asn Pro Leu Thr Ile Thr
180 185 190

Val His Asp Pro Asn Ala Ala Gln Trp Tyr Tyr Gly Met Ser Trp Gly
195 200 205

Leu Arg Leu Tyr Ile Pro Gly Phe Asp Val Gly Thr Met Phe Thr Ile
210 215 220

Gln Lys Lys Ile Leu Val Ser Trp Ser Ser Pro Lys Pro Ile Gly Pro
225 230 235 240

Leu Thr Asp Leu Gly Asp Pro Ile Phe Gln Lys His Pro Asp Lys Val
245 250 255

Asp Leu Thr Val Pro Leu Pro Phe Leu Val Pro Arg Pro Gln Leu Gln
260 265 270

Gln Gln His Leu Gln Pro Ser Leu Met Ser Ile Leu Gly Gly Val His
275 280 285

His Leu Leu Asn Leu Thr Gln Pro Lys Leu Ala Gln Asp Cys Trp Leu
290 295 300

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Cys Leu Lys Ala Lys Pro Pro Tyr Tyr Val Gly Leu Gly Val Glu Ala
305                 310                 315                 320

Thr Leu Lys Arg Gly Pro Leu Ser Cys His Thr Arg Pro Arg Ala Leu
                325                 330                 335

Thr Ile Gly Asp Val Ser Gly Asn Ala Ser Cys Leu Ile Ser Thr Gly
            340                 345                 350

Tyr Asn Leu Ser Ala Ser Pro Phe Gln Ala Thr Cys Asn Gln Ser Leu
        355                 360                 365

Leu Thr Ser Ile Ser Thr Ser Val Ser Tyr Gln Ala Pro Asn Asn Thr
    370                 375                 380

Trp Leu Ala Cys Thr Ser Gly Leu Thr Arg Cys Ile Asn Gly Thr Glu
385                 390                 395                 400

Pro Gly Pro Leu Leu Cys Val Leu Val His Val Leu Pro Gln Val Tyr
                405                 410                 415

Val Tyr Ser Gly Pro Glu Gly Arg Gln Leu Ile Ala Pro Pro Glu Leu
            420                 425                 430

His Pro Arg Leu His Gln Ala Val Pro Leu Leu Val Pro Leu Leu Ala
        435                 440                 445

Gly Leu Ser Ile Ala Gly Ser Ala Ala Ile Gly Thr Ala Ala Leu Val
    450                 455                 460

Gln Gly Glu Thr Gly Leu Ile Ser Leu Ser Gln Gln Val Asp Ala Asp
465                 470                 475                 480

Phe Ser Asn Leu Gln Ser Ala Ile Asp Ile Leu His Ser Gln Val Glu
                485                 490                 495

Ser Leu Ala Glu Val Val Leu Gln Asn Cys Arg Cys Leu Asp Leu Leu
            500                 505                 510

Phe Leu Ser Arg Gly Gly Leu Cys Ala Phe Leu Gly Glu Ser Cys Cys
        515                 520                 525

Phe Tyr Ala Asn Gln Ser Gly Val Ile Lys Gly Thr Val Lys Lys Val
    530                 535                 540

Arg Glu Asn Leu Asp Arg His Gln Gln Glu Arg Glu Asn Asn Ile Pro
545                 550                 555                 560
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Trp Tyr Gln Ser Met Phe Asn Trp Asn Pro Trp Leu Thr Thr Leu Ile
565 570 575

Thr Gly Leu Ala Gly Pro Leu Leu Ile Leu Leu Leu Ser Leu Ile Phe
580 585 590

Gly Pro Cys Ile Leu Asn Ser Phe Leu Asn Phe Ile Lys Gln Arg Ile
595 600 605

Ala Ser Val Lys Leu Thr Tyr Leu Lys Thr Gln Tyr Asp Thr Leu Val
610 615 620

Asn Asn
625

<210> 131

<211> 30

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 131
caaccttacc aaccctgata aaactcaaga 30

<210> 132

<211> 35

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 132
cagtcctcct ctttttagga acaacaggtc taggc 35

<210> 133

<211> 28

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 133
tgtgctgccc taaaagaaga atgttgtt 28

<210> 134

<211> 29

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 134
ggactaaagc ctggactact gagatcctg 29

<210> 135

<211> 29

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 135
cagtcctcct tcttttagga acaacaggt 29

<210> 136

<211> 33

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 136
tgtgctttcc taaaagaaga atgttgtttc tat 33

<210> 137

<211> 39

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 137
atacatccat ggcgtgttca acgctcccaa aatccccta 39

<210> 138

<211> 43

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 138
atacatctcg agttctcttt tatgtctata ggatttttca aac 43

<210> 139

<211> 33

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 139
atacatccat ggctgccgta caagatgatc tca 33

<210> 140

<211> 33

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 140
atacatccat ggctgccgta caagatgatc tca 33

<210> 141

<211> 39

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 141
atacatctcg agatctctta ctaggcctgt atggtcagc 39

<210> 142

<211> 17

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 142
ctcagggagc agcggga 17

<210> 143

<211> 25

<212> DNA

<213> Artificial sequence

<220>

<223> PCR primer

<400> 143
tagcttaagt ctgttccagg cagtg 25

<210> 144

<211> 20

<212> DNA

<213> Artificial sequence

<220>

<223> Control oligonucleotide

<400> 144
tccatgacgt tcctgacgtt 20

<210> 145

<211> 1812

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-R ENV

<220>

<221> misc_feature

<222> (1681)..(1683)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 145
atgctgggta tgaacatgct actcatcact ttgttcttgc tactcccctt atccatgtta 60

aaaggagaac cctgggaggg atgcctccac tgcacccaca ctacgtggtc ggggaacatc 120

atgactaaaa ccctgttgta tcacacttat tatgagtgtg ctgggacctg cctaggaact 180

tgtactcaca accagacaac ctactcagtc tgtgacccag gaaggggcca gccttatgtg 240

tgttatgacc ctaagtcttc acctgggatc tggtttgaaa ttcatgtcgg gtcaaaggaa 300

ggggatcttc taaaccaaac caaggtattt ccctctggca aggatgtcgt atccttatac 360

tttgatgttt gccagatagt atccatgggc tcactctttc ccgtaatctt cagttccatg 420

gagtactata gtagctgcca taaaaatagg tatgcacacc ctgcttgttc caccgattcc 480

ccagtaacaa cttgctggga ctgcacaacg tggtccacta accaacaatc actagggcca 540

attatgctta ccaaaatacc attagaacca gattgtaaaa caagcacttg caattctgta 600

aatcttacca tcttagagcc agatcagccc atatggacaa caggtttaaa agcaccgcta 660

ggggcacgag tcagcggtga agaaattggc ccaggagcct atgtctatct atatatcata 720

aagaaaactc ggacccgctc aacccaacag ttccgagttt ttgagtcatt ctatgagcat 780

gttaaccaga aattgcctga gccccctccc ttggccagta atttattcgc ccaactggct 840

gaaaacatag ccagcagcct gcacgttgct tcatgttatg tctgtggggg aatgaacatg 900

ggagaccaat ggccatggga agcaagggaa ctaatgcccc aagataattt cacactaacc 960

gcctcttccc tcgaacctgc accatcaagt cagagcatct ggttcttaaa aacctccatt 1020

attggaaaat tctgtattgc tcgctgggga aaggccttta cagacccagt aggagagtta 1080

acttgcctag gacaacaata ttacaacgag acactaggaa agactttatg gaggggcaaa 1140

agcaataatt ctgaatcacc acacccaagc ccattctctc gtttcccatc tttaaaccat 1200

tcttggtacc aacttgaagc tccaaatacc tggcaggcac cctctggcct ctactggatc 1260

tgtgggccac aagcatatcg acaactgcca gctaaatggt caggggcctg tgtactgggg 1320

acaattaggc cgtccttctt cctaatgccc ctaaaacagg gagaagcctt aggatacccc 1380

atctatgatg aaactaaaag gaaaagcaaa agaggcataa ctataggaga ttggaaggac 1440

agtgaatggc ctcctgaaag aataattcaa tattatggcc cagccacctg ggcagaagat 1500

ggaatgtggg gataccgcac cccagtttac atgcttaacc gcattataag attgcaggca 1560

gtactagaaa tcattaccaa tgaaactgca ggggccttga atctgcttgc ccagcaagcc 1620

acaaaaatga gaaatgtcat ttatcaaaat agactggcct tagactacct cctagcccag 1680

nnngagggag tatgcggaaa gttcagcctt actaactgct gcctggaact tgatgacgaa 1740

ggaaaggtta tcaaagaaat aactgctaaa atccaaaagt tagctcacat cccagttcag 1800

acttggaaag ga 1812

<210> 146

<211> 604

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-R ENV

<400> 146

Met Leu Gly Met Asn Met Leu Leu Ile Thr Leu Phe Leu Leu Leu Pro
1 5 10 15

Leu Ser Met Leu Lys Gly Glu Pro Trp Glu Gly Cys Leu His Cys Thr
20 25 30

His Thr Thr Trp Ser Gly Asn Ile Met Thr Lys Thr Leu Leu Tyr His
35 40 45

Thr Tyr Tyr Glu Cys Ala Gly Thr Cys Leu Gly Thr Cys Thr His Asn

50 55 60

Gln Thr Thr Tyr Ser Val Cys Asp Pro Gly Arg Gly Gln Pro Tyr Val
65 70 75 80

Cys Tyr Asp Pro Lys Ser Ser Pro Gly Ile Trp Phe Glu Ile His Val
85 90 95

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

Gly Lys Asp Val Val Ser Leu Tyr Phe Asp Val Cys Gln Ile Val Ser
115 120 125

Met Gly Ser Leu Phe Pro Val Ile Phe Ser Ser Met Glu Tyr Tyr Ser
130 135 140

Ser Cys His Lys Asn Arg Tyr Ala His Pro Ala Cys Ser Thr Asp Ser
145 150 155 160

Pro Val Thr Thr Cys Trp Asp Cys Thr Thr Trp Ser Thr Asn Gln Gln
165 170 175

Ser Leu Gly Pro Ile Met Leu Thr Lys Ile Pro Leu Glu Pro Asp Cys
180 185 190

Lys Thr Ser Thr Cys Asn Ser Val Asn Leu Thr Ile Leu Glu Pro Asp
195 200 205

Gln Pro Ile Trp Thr Thr Gly Leu Lys Ala Pro Leu Gly Ala Arg Val
210 215 220

Ser Gly Glu Glu Ile Gly Pro Gly Ala Tyr Val Tyr Leu Tyr Ile Ile
225 230 235 240

Lys Lys Thr Arg Thr Arg Ser Thr Gln Gln Phe Arg Val Phe Glu Ser
245 250 255

Phe Tyr Glu His Val Asn Gln Lys Leu Pro Glu Pro Pro Pro Leu Ala
260 265 270

Ser Asn Leu Phe Ala Gln Leu Ala Glu Asn Ile Ala Ser Ser Leu His
275 280 285

Val Ala Ser Cys Tyr Val Cys Gly Gly Met Asn Met Gly Asp Gln Trp
290 295 300

Pro Trp Glu Ala Arg Glu Leu Met Pro Gln Asp Asn Phe Thr Leu Thr
305 310 315 320

Ala Ser Ser Leu Glu Pro Ala Pro Ser Ser Gln Ser Ile Trp Phe Leu
325 330 335

Lys Thr Ser Ile Ile Gly Lys Phe Cys Ile Ala Arg Trp Gly Lys Ala
340 345 350

Phe Thr Asp Pro Val Gly Glu Leu Thr Cys Leu Gly Gln Gln Tyr Tyr
355 360 365

Asn Glu Thr Leu Gly Lys Thr Leu Trp Arg Gly Lys Ser Asn Asn Ser
370 375 380

Glu Ser Pro His Pro Ser Pro Phe Ser Arg Phe Pro Ser Leu Asn His
385 390 395 400

Ser Trp Tyr Gln Leu Glu Ala Pro Asn Thr Trp Gln Ala Pro Ser Gly
405 410 415

Leu Tyr Trp Ile Cys Gly Pro Gln Ala Tyr Arg Gln Leu Pro Ala Lys
420 425 430

Trp Ser Gly Ala Cys Val Leu Gly Thr Ile Arg Pro Ser Phe Phe Leu
435 440 445

Met Pro Leu Lys Gln Gly Glu Ala Leu Gly Tyr Pro Ile Tyr Asp Glu
450 455 460

Thr Lys Arg Lys Ser Lys Arg Gly Ile Thr Ile Gly Asp Trp Lys Asp
465 470 475 480

Ser Glu Trp Pro Pro Glu Arg Ile Ile Gln Tyr Tyr Gly Pro Ala Thr
485 490 495

Trp Ala Glu Asp Gly Met Trp Gly Tyr Arg Thr Pro Val Tyr Met Leu
500 505 510

Asn Arg Ile Ile Arg Leu Gln Ala Val Leu Glu Ile Ile Thr Asn Glu
515 520 525

Thr Ala Gly Ala Leu Asn Leu Leu Ala Gln Gln Ala Thr Lys Met Arg
530 535 540

Asn Val Ile Tyr Gln Asn Arg Leu Ala Leu Asp Tyr Leu Leu Ala Gln
545 550 555 560

Arg Glu Gly Val Cys Gly Lys Phe Ser Leu Thr Asn Cys Cys Leu Glu
565 570 575

Leu Asp Asp Glu Gly Lys Val Ile Lys Glu Ile Thr Ala Lys Ile Gln
580 585 590

Lys Leu Ala His Ile Pro Val Gln Thr Trp Lys Gly
595 600

<210> 147

<211> 1812

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated HERV-R ENV

<220>

<221> misc_feature

<222> (1681)..(1693)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<220>

<221> misc_feature

<222> (1699)..(1701)

<223> TTT or TTC

<400> 147
atgctgggta tgaacatgct actcatcact ttgttcttgc tactcccctt atccatgtta 60

aaaggagaac cctgggaggg atgcctccac tgcacccaca ctacgtggtc ggggaacatc 120

atgactaaaa ccctgttgta tcacacttat tatgagtgtg ctgggacctg cctaggaact 180

tgtactcaca accagacaac ctactcagtc tgtgacccag gaaggggcca gccttatgtg 240

tgttatgacc ctaagtcttc acctgggatc tggtttgaaa ttcatgtcgg gtcaaaggaa 300

ggggatcttc taaaccaaac caaggtattt ccctctggca aggatgtcgt atccttatac 360

tttgatgttt gccagatagt atccatgggc tcactctttc ccgtaatctt cagttccatg 420

gagtactata gtagctgcca taaaaatagg tatgcacacc ctgcttgttc caccgattcc 480

ccagtaacaa cttgctggga ctgcacaacg tggtccacta accaacaatc actagggcca 540

attatgctta ccaaaatacc attagaacca gattgtaaaa caagcacttg caattctgta 600

aatcttacca tcttagagcc agatcagccc atatggacaa caggtttaaa agcaccgcta 660

ggggcacgag tcagcggtga agaaattggc ccaggagcct atgtctatct atatatcata 720

aagaaaactc ggacccgctc aacccaacag ttccgagttt ttgagtcatt ctatgagcat 780

gttaaccaga aattgcctga gccccctccc ttggccagta atttattcgc ccaactggct 840

gaaaacatag ccagcagcct gcacgttgct tcatgttatg tctgtggggg aatgaacatg 900

ggagaccaat ggccatggga agcaagggaa ctaatgcccc aagataattt cacactaacc 960

gcctcttccc tcgaacctgc accatcaagt cagagcatct ggttcttaaa aacctccatt 1020

attggaaaat tctgtattgc tcgctgggga aaggccttta cagacccagt aggagagtta 1080

acttgcctag gacaacaata ttacaacgag acactaggaa agactttatg gaggggcaaa 1140

agcaataatt ctgaatcacc acacccaagc ccattctctc gtttcccatc tttaaaccat 1200

tcttggtacc aacttgaagc tccaaatacc tggcaggcac cctctggcct ctactggatc 1260

tgtgggccac aagcatatcg acaactgcca gctaaatggt caggggcctg tgtactgggg 1320

acaattaggc cgtccttctt cctaatgccc ctaaaacagg gagaagcctt aggatacccc 1380

atctatgatg aaactaaaag gaaaagcaaa agaggcataa ctataggaga ttggaaggac 1440

agtgaatggc ctcctgaaag aataattcaa tattatggcc cagccacctg ggcagaagat 1500

ggaatgtggg gataccgcac cccagtttac atgcttaacc gcattataag attgcaggca 1560

gtactagaaa tcattaccaa tgaaactgca ggggccttga atctgcttgc ccagcaagcc 1620

acaaaaatga gaaatgtcat ttatcaaaat agactggcct tagactacct cctagcccag 1680

nnngagggag tatgcggann nttcagcctt actaactgct gcctggaact tgatgacgaa 1740

ggaaaggtta tcaaagaaat aactgctaaa atccaaaagt tagctcacat cccagttcag 1800

acttggaaag ga 1812

<210> 148

<211> 604

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated HERV-R ENV

<400> 148

Met Leu Gly Met Asn Met Leu Leu Ile Thr Leu Phe Leu Leu Leu Pro
1 5 10 15

Leu Ser Met Leu Lys Gly Glu Pro Trp Glu Gly Cys Leu His Cys Thr
20 25 30

```
His Thr Thr Trp Ser Gly Asn Ile Met Thr Lys Thr Leu Leu Tyr His
        35                  40                  45

Thr Tyr Tyr Glu Cys Ala Gly Thr Cys Leu Gly Thr Cys Thr His Asn
    50                  55                  60

Gln Thr Thr Tyr Ser Val Cys Asp Pro Gly Arg Gly Gln Pro Tyr Val
65                  70                  75                  80

Cys Tyr Asp Pro Lys Ser Ser Pro Gly Ile Trp Phe Glu Ile His Val
                85                  90                  95

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

Gly Lys Asp Val Val Ser Leu Tyr Phe Asp Val Cys Gln Ile Val Ser
        115                 120                 125

Met Gly Ser Leu Phe Pro Val Ile Phe Ser Ser Met Glu Tyr Tyr Ser
    130                 135                 140

Ser Cys His Lys Asn Arg Tyr Ala His Pro Ala Cys Ser Thr Asp Ser
145                 150                 155                 160

Pro Val Thr Thr Cys Trp Asp Cys Thr Thr Trp Ser Thr Asn Gln Gln
                165                 170                 175

Ser Leu Gly Pro Ile Met Leu Thr Lys Ile Pro Leu Glu Pro Asp Cys
            180                 185                 190

Lys Thr Ser Thr Cys Asn Ser Val Asn Leu Thr Ile Leu Glu Pro Asp
        195                 200                 205

Gln Pro Ile Trp Thr Thr Gly Leu Lys Ala Pro Leu Gly Ala Arg Val
    210                 215                 220

Ser Gly Glu Glu Ile Gly Pro Gly Ala Tyr Val Tyr Leu Tyr Ile Ile
225                 230                 235                 240

Lys Lys Thr Arg Thr Arg Ser Thr Gln Gln Phe Arg Val Phe Glu Ser
                245                 250                 255

Phe Tyr Glu His Val Asn Gln Lys Leu Pro Glu Pro Pro Pro Leu Ala
            260                 265                 270

Ser Asn Leu Phe Ala Gln Leu Ala Glu Asn Ile Ala Ser Ser Leu His
        275                 280                 285
```

Val Ala Ser Cys Tyr Val Cys Gly Gly Met Asn Met Gly Asp Gln Trp
290 295 300

Pro Trp Glu Ala Arg Glu Leu Met Pro Gln Asp Asn Phe Thr Leu Thr
305 310 315 320

Ala Ser Ser Leu Glu Pro Ala Pro Ser Ser Gln Ser Ile Trp Phe Leu
325 330 335

Lys Thr Ser Ile Ile Gly Lys Phe Cys Ile Ala Arg Trp Gly Lys Ala
340 345 350

Phe Thr Asp Pro Val Gly Glu Leu Thr Cys Leu Gly Gln Gln Tyr Tyr
355 360 365

Asn Glu Thr Leu Gly Lys Thr Leu Trp Arg Gly Lys Ser Asn Asn Ser
370 375 380

Glu Ser Pro His Pro Ser Pro Phe Ser Arg Phe Pro Ser Leu Asn His
385 390 395 400

Ser Trp Tyr Gln Leu Glu Ala Pro Asn Thr Trp Gln Ala Pro Ser Gly
405 410 415

Leu Tyr Trp Ile Cys Gly Pro Gln Ala Tyr Arg Gln Leu Pro Ala Lys
420 425 430

Trp Ser Gly Ala Cys Val Leu Gly Thr Ile Arg Pro Ser Phe Phe Leu
435 440 445

Met Pro Leu Lys Gln Gly Glu Ala Leu Gly Tyr Pro Ile Tyr Asp Glu
450 455 460

Thr Lys Arg Lys Ser Lys Arg Gly Ile Thr Ile Gly Asp Trp Lys Asp
465 470 475 480

Ser Glu Trp Pro Pro Glu Arg Ile Ile Gln Tyr Tyr Gly Pro Ala Thr
485 490 495

Trp Ala Glu Asp Gly Met Trp Gly Tyr Arg Thr Pro Val Tyr Met Leu
500 505 510

Asn Arg Ile Ile Arg Leu Gln Ala Val Leu Glu Ile Ile Thr Asn Glu
515 520 525

Thr Ala Gly Ala Leu Asn Leu Leu Ala Gln Gln Ala Thr Lys Met Arg
530 535 540

Asn Val Ile Tyr Gln Asn Arg Leu Ala Leu Asp Tyr Leu Leu Ala Gln

545 550 555 560

Arg Glu Gly Val Cys Gly Phe Phe Ser Leu Thr Asn Cys Cys Leu Glu
565 570 575

Leu Asp Asp Glu Gly Lys Val Ile Lys Glu Ile Thr Ala Lys Ile Gln
580 585 590

Lys Leu Ala His Ile Pro Val Gln Thr Trp Lys Gly
595 600

<210> 149

<211> 1977

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated PERV ENV

<220>

<221> misc_feature

<222> (1633)..(1635)

<223> CGT or CGC or CGA or CGG or AGA or AGG

<400> 149
atgcatccca cgttaagccg gcgccacctc ccgattcggg gtggaaagcc gaaaagactg 60

aaaatcccct taagcttcgc ctccatcgcg tggttcctta ctctgtcaat aactcctcaa 120

gttaatggta aacgccttgt ggacagcccg aactcccata aacccttatc tctcacctgg 180

ttacttactg actccggtac aggtattaat attaacagca ctcaagggga ggctcccttg 240

gggacctggt ggcctgaatt atatgtctgc cttcgatcag taatccctgg tctcaatgac 300

caggccacac cccccgatgt actccgtgct tacgggtttt acgtttgccc agggccccca 360

aataatgaag aatattgtgg aaatcctcag gatttctttt gcaagcaatg gagctgcgta 420

acttctaatg atgggaattg gaaatggcca gtctctcagc aagacagagt aagttactct 480

tttgttaaca atcctaccag ttataatcaa tttaattatg gccatgggag atggaaagat 540

tggcaacagc gggtacaaaa agatgtacga aataagcaaa taagctgtca ttcgttagac 600

ctagattact taaaaataag tttcactgaa aaaggaaaac aagaaaatat tcaaaagtgg 660

gtaaatggta tgtcttgggg aatagtgtac tatagaggct ctgggagaaa gaaaggatct 720

gttctgacta ttcgcctcag aatagaaact cagatggaac ctccggttgc tataggacca 780

aataagggtt tggccgaaca aggacctcca atccaagaac agaggccatc tcctaacccc 840

tctgattaca atacaacctc tggatcagtc cccactgagc ctaacatcac tattaaaaca 900

ggggcgaaac tttttaacct catccaggga gcttttcaag ctcttaactc cacgactcca 960

gaggctacct cttcttgttg gctttgctta gcttcgggcc caccttacta tgagggaatg 1020

gctagaggag ggaaattcaa tgtgacaaag gaacatagag accaatgtac atggggatcc 1080

caaaataagc ttacccttac tgaggtttct ggaaaaggca cctgcatagg gatggttccc 1140

ccatcccacc aacacctttg taaccacact gaagccttta atcgaacctc tgagagtcag 1200

tatctggtac ctggttatga caggtggtgg gcatgtaata ctggattaac cccttgtgtt 1260

tccaccttgg ttttcaacca aactaaagac ttttgcgtta tggtccaaat tgtcccccgg 1320

gtgtactact atcccgaaaa agcagtcctt gatgaatatg actatagata taatcggcca 1380

aaaagagagc ccatatccct gacactagct gtaatgctcg gattgggagt ggctgcaggc 1440

gtgggaacag gaacggctgc cctaatcaca ggaccgcaac agctggagaa aggacttagt 1500

aacctacatc gaattgtaac ggaaaatctc caagccctag aaaaatctgt cagtaacctg 1560

gaggaatccc taacctcctt atctgaagtg gttctacaga acagaagggg gttagatctg 1620

ttatttctaa aannnggagg gttatgtgta gccttaaaag aggaatgctg cttctatgta 1680

gatcactcag gagccatcag agactccatg agcaagctta gagaaaggtt agagaggcgt 1740

cgaagggaaa gagaggctga ccaggggtgg tttgaaggat ggttcaacag gtctccttgg 1800

atggctaccc tactttctgc tttaacagga cccttaatag tcctcctcct gttactcaca 1860

gttgggccat gtattattaa caagttaatt gccttcatta gagaacgaat aagtgcagtc 1920

cagatcatgg tacttagaca acagtaccaa agcccgtcta gcagagaagc tggccgc 1977

<210> 150

<211> 659

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated PERV ENV

<400> 150

Met His Pro Thr Leu Ser Arg Arg His Leu Pro Ile Arg Gly Gly Lys
1 5 10 15

Pro Lys Arg Leu Lys Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe
20 25 30

```
Leu Thr Leu Ser Ile Thr Pro Gln Val Asn Gly Lys Arg Leu Val Asp
        35                  40                  45

Ser Pro Asn Ser His Lys Pro Leu Ser Leu Thr Trp Leu Leu Thr Asp
    50                  55                  60

Ser Gly Thr Gly Ile Asn Ile Asn Ser Thr Gln Gly Glu Ala Pro Leu
65                  70                  75                  80

Gly Thr Trp Trp Pro Glu Leu Tyr Val Cys Leu Arg Ser Val Ile Pro
                85                  90                  95

Gly Leu Asn Asp Gln Ala Thr Pro Pro Asp Val Leu Arg Ala Tyr Gly
            100                 105                 110

Phe Tyr Val Cys Pro Gly Pro Pro Asn Asn Glu Glu Tyr Cys Gly Asn
        115                 120                 125

Pro Gln Asp Phe Phe Cys Lys Gln Trp Ser Cys Val Thr Ser Asn Asp
    130                 135                 140

Gly Asn Trp Lys Trp Pro Val Ser Gln Gln Asp Arg Val Ser Tyr Ser
145                 150                 155                 160

Phe Val Asn Asn Pro Thr Ser Tyr Asn Gln Phe Asn Tyr Gly His Gly
                165                 170                 175

Arg Trp Lys Asp Trp Gln Gln Arg Val Gln Lys Asp Val Arg Asn Lys
            180                 185                 190

Gln Ile Ser Cys His Ser Leu Asp Leu Asp Tyr Leu Lys Ile Ser Phe
        195                 200                 205

Thr Glu Lys Gly Lys Gln Glu Asn Ile Gln Lys Trp Val Asn Gly Met
    210                 215                 220

Ser Trp Gly Ile Val Tyr Tyr Arg Gly Ser Gly Arg Lys Lys Gly Ser
225                 230                 235                 240

Val Leu Thr Ile Arg Leu Arg Ile Glu Thr Gln Met Glu Pro Pro Val
                245                 250                 255

Ala Ile Gly Pro Asn Lys Gly Leu Ala Glu Gln Gly Pro Pro Ile Gln
            260                 265                 270

Glu Gln Arg Pro Ser Pro Asn Pro Ser Asp Tyr Asn Thr Thr Ser Gly
        275                 280                 285
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Ser Val Pro Thr Glu Pro Asn Ile Thr Ile Lys Thr Gly Ala Lys Leu
    290                 295                 300

Phe Asn Leu Ile Gln Gly Ala Phe Gln Ala Leu Asn Ser Thr Thr Pro
305                 310                 315                 320

Glu Ala Thr Ser Ser Cys Trp Leu Cys Leu Ala Ser Gly Pro Pro Tyr
                325                 330                 335

Tyr Glu Gly Met Ala Arg Gly Gly Lys Phe Asn Val Thr Lys Glu His
            340                 345                 350

Arg Asp Gln Cys Thr Trp Gly Ser Gln Asn Lys Leu Thr Leu Thr Glu
        355                 360                 365

Val Ser Gly Lys Gly Thr Cys Ile Gly Met Val Pro Pro Ser His Gln
    370                 375                 380

His Leu Cys Asn His Thr Glu Ala Phe Asn Arg Thr Ser Glu Ser Gln
385                 390                 395                 400

Tyr Leu Val Pro Gly Tyr Asp Arg Trp Trp Ala Cys Asn Thr Gly Leu
                405                 410                 415

Thr Pro Cys Val Ser Thr Leu Val Phe Asn Gln Thr Lys Asp Phe Cys
            420                 425                 430

Val Met Val Gln Ile Val Pro Arg Val Tyr Tyr Tyr Pro Glu Lys Ala
        435                 440                 445

Val Leu Asp Glu Tyr Asp Tyr Arg Tyr Asn Arg Pro Lys Arg Glu Pro
    450                 455                 460

Ile Ser Leu Thr Leu Ala Val Met Leu Gly Leu Gly Val Ala Ala Gly
465                 470                 475                 480

Val Gly Thr Gly Thr Ala Ala Leu Ile Thr Gly Pro Gln Gln Leu Glu
                485                 490                 495

Lys Gly Leu Ser Asn Leu His Arg Ile Val Thr Glu Asn Leu Gln Ala
            500                 505                 510

Leu Glu Lys Ser Val Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser
        515                 520                 525

Glu Val Val Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys
    530                 535                 540

Arg Gly Gly Leu Cys Val Ala Leu Lys Glu Glu Cys Cys Phe Tyr Val
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545 550 555 560

Asp His Ser Gly Ala Ile Arg Asp Ser Met Ser Lys Leu Arg Glu Arg
565 570 575

Leu Glu Arg Arg Arg Arg Glu Arg Glu Ala Asp Gln Gly Trp Phe Glu
580 585 590

Gly Trp Phe Asn Arg Ser Pro Trp Met Ala Thr Leu Leu Ser Ala Leu
595 600 605

Thr Gly Pro Leu Ile Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys
610 615 620

Ile Ile Asn Lys Leu Ile Ala Phe Ile Arg Glu Arg Ile Ser Ala Val
625 630 635 640

Gln Ile Met Val Leu Arg Gln Gln Tyr Gln Ser Pro Ser Ser Arg Glu
645 650 655

Ala Gly Arg

<210> 151

<211> 1977

<212> DNA

<213> Artificial sequence

<220>

<223> Mutated PERV ENV

<220>

<221> misc_feature

<222> (1633)..(1635)

<223> CGT or CGC or CGA or CGT or AGA or AGG

<220>

<221> misc_feature

<222> (1651)..(1653)

<223> TTT or TTC

<400> 151

atgcatccca cgttaagccg gcgccacctc ccgattcggg gtggaaagcc gaaaagactg 60

aaaatcccct taagcttcgc ctccatcgcg tggttcctta ctctgtcaat aactcctcaa 120

gttaatggta aacgccttgt ggacagcccg aactcccata aacccttatc tctcacctgg 180

ttacttactg actccggtac aggtattaat attaacagca ctcaagggga ggctcccttg 240

gggacctggt ggcctgaatt atatgtctgc cttcgatcag taatccctgg tctcaatgac 300

caggccacac cccccgatgt actccgtgct tacgggtttt acgtttgccc agggccccca 360

aataatgaag aatattgtgg aaatcctcag gatttctttt gcaagcaatg gagctgcgta 420

acttctaatg atgggaattg gaaatggcca gtctctcagc aagacagagt aagttactct 480

tttgttaaca atcctaccag ttataatcaa tttaattatg gccatgggag atggaaagat 540

tggcaacagc gggtacaaaa agatgtacga aataagcaaa taagctgtca ttcgttagac 600

ctagattact taaaaataag tttcactgaa aaaggaaaac aagaaaatat tcaaaagtgg 660

gtaaatggta tgtcttgggg aatagtgtac tatagaggct ctgggagaaa gaaaggatct 720

gttctgacta ttcgcctcag aatagaaact cagatggaac ctccggttgc tataggacca 780

aataagggtt tggccgaaca aggacctcca atccaagaac agaggccatc tcctaacccc 840

tctgattaca atacaacctc tggatcagtc cccactgagc ctaacatcac tattaaaaca 900

ggggcgaaac tttttaacct catccaggga gcttttcaag ctcttaactc cacgactcca 960

gaggctacct cttcttgttg gctttgctta gcttcgggcc caccttacta tgagggaatg 1020

gctagaggag ggaaattcaa tgtgacaaag gaacatagag accaatgtac atggggatcc 1080

caaaataagc ttacccttac tgaggtttct ggaaaaggca cctgcatagg gatggttccc 1140

ccatcccacc aacacctttg taaccacact gaagccttta atcgaacctc tgagagtcag 1200

tatctggtac ctggttatga caggtggtgg gcatgtaata ctggattaac cccttgtgtt 1260

tccaccttgg ttttcaacca aactaaagac ttttgcgtta tggtccaaat tgtcccccgg 1320

gtgtactact atcccgaaaa agcagtcctt gatgaatatg actatagata taatcggcca 1380

aaaagagagc ccatatccct gacactagct gtaatgctcg gattgggagt ggctgcaggc 1440

gtgggaacag gaacggctgc cctaatcaca ggaccgcaac agctggagaa aggacttagt 1500

aacctacatc gaattgtaac ggaaaatctc caagccctag aaaaatctgt cagtaacctg 1560

gaggaatccc taacctcctt atctgaagtg gttctacaga acagaagggg gttagatctg 1620

ttatttctaa aannnggagg gttatgtgta nnnttaaaag aggaatgctg cttctatgta 1680

gatcactcag gagccatcag agactccatg agcaagctta gagaaaggtt agagaggcgt 1740

cgaagggaaa gagaggctga ccaggggtgg tttgaaggat ggttcaacag gtctccttgg 1800

atggctaccc tactttctgc tttaacagga cccttaatag tcctcctcct gttactcaca 1860

gttgggccat gtattattaa caagttaatt gccttcatta gagaacgaat aagtgcagtc 1920

cagatcatgg tacttagaca acagtaccaa agcccgtcta gcagagaagc tggccgc 1977

<210> 152

<211> 659

<212> PRT

<213> Artificial sequence

<220>

<223> Mutated PERV ENV

<400> 152

Met His Pro Thr Leu Ser Arg Arg His Leu Pro Ile Arg Gly Gly Lys
1 5 10 15

Pro Lys Arg Leu Lys Ile Pro Leu Ser Phe Ala Ser Ile Ala Trp Phe
20 25 30

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

Ser Pro Asn Ser His Lys Pro Leu Ser Leu Thr Trp Leu Leu Thr Asp
50 55 60

Ser Gly Thr Gly Ile Asn Ile Asn Ser Thr Gln Gly Glu Ala Pro Leu
65 70 75 80

Gly Thr Trp Trp Pro Glu Leu Tyr Val Cys Leu Arg Ser Val Ile Pro
85 90 95

Gly Leu Asn Asp Gln Ala Thr Pro Pro Asp Val Leu Arg Ala Tyr Gly
100 105 110

Phe Tyr Val Cys Pro Gly Pro Pro Asn Asn Glu Glu Tyr Cys Gly Asn
115 120 125

Pro Gln Asp Phe Phe Cys Lys Gln Trp Ser Cys Val Thr Ser Asn Asp
130 135 140

Gly Asn Trp Lys Trp Pro Val Ser Gln Gln Asp Arg Val Ser Tyr Ser
145 150 155 160

Phe Val Asn Asn Pro Thr Ser Tyr Asn Gln Phe Asn Tyr Gly His Gly
165 170 175

Arg Trp Lys Asp Trp Gln Gln Arg Val Gln Lys Asp Val Arg Asn Lys
180 185 190

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Gln Ile Ser Cys His Ser Leu Asp Leu Asp Tyr Leu Lys Ile Ser Phe
        195                 200                 205

Thr Glu Lys Gly Lys Gln Glu Asn Ile Gln Lys Trp Val Asn Gly Met
    210                 215                 220

Ser Trp Gly Ile Val Tyr Tyr Arg Gly Ser Gly Arg Lys Lys Gly Ser
225                 230                 235                 240

Val Leu Thr Ile Arg Leu Arg Ile Glu Thr Gln Met Glu Pro Pro Val
                245                 250                 255

Ala Ile Gly Pro Asn Lys Gly Leu Ala Glu Gln Gly Pro Pro Ile Gln
            260                 265                 270

Glu Gln Arg Pro Ser Pro Asn Pro Ser Asp Tyr Asn Thr Thr Ser Gly
        275                 280                 285

Ser Val Pro Thr Glu Pro Asn Ile Thr Ile Lys Thr Gly Ala Lys Leu
    290                 295                 300

Phe Asn Leu Ile Gln Gly Ala Phe Gln Ala Leu Asn Ser Thr Thr Pro
305                 310                 315                 320

Glu Ala Thr Ser Ser Cys Trp Leu Cys Leu Ala Ser Gly Pro Pro Tyr
                325                 330                 335

Tyr Glu Gly Met Ala Arg Gly Gly Lys Phe Asn Val Thr Lys Glu His
            340                 345                 350

Arg Asp Gln Cys Thr Trp Gly Ser Gln Asn Lys Leu Thr Leu Thr Glu
        355                 360                 365

Val Ser Gly Lys Gly Thr Cys Ile Gly Met Val Pro Pro Ser His Gln
    370                 375                 380

His Leu Cys Asn His Thr Glu Ala Phe Asn Arg Thr Ser Glu Ser Gln
385                 390                 395                 400

Tyr Leu Val Pro Gly Tyr Asp Arg Trp Trp Ala Cys Asn Thr Gly Leu
                405                 410                 415

Thr Pro Cys Val Ser Thr Leu Val Phe Asn Gln Thr Lys Asp Phe Cys
            420                 425                 430

Val Met Val Gln Ile Val Pro Arg Val Tyr Tyr Tyr Pro Glu Lys Ala
        435                 440                 445
```

Val Leu Asp Glu Tyr Asp Tyr Arg Tyr Asn Arg Pro Lys Arg Glu Pro
450 455 460

Ile Ser Leu Thr Leu Ala Val Met Leu Gly Leu Gly Val Ala Ala Gly
465 470 475 480

Val Gly Thr Gly Thr Ala Ala Leu Ile Thr Gly Pro Gln Gln Leu Glu
485 490 495

Lys Gly Leu Ser Asn Leu His Arg Ile Val Thr Glu Asn Leu Gln Ala
500 505 510

Leu Glu Lys Ser Val Ser Asn Leu Glu Glu Ser Leu Thr Ser Leu Ser
515 520 525

Glu Val Val Leu Gln Asn Arg Arg Gly Leu Asp Leu Leu Phe Leu Lys
530 535 540

Arg Gly Gly Leu Cys Val Phe Leu Lys Glu Glu Cys Cys Phe Tyr Val
545 550 555 560

Asp His Ser Gly Ala Ile Arg Asp Ser Met Ser Lys Leu Arg Glu Arg
565 570 575

Leu Glu Arg Arg Arg Arg Glu Arg Glu Ala Asp Gln Gly Trp Phe Glu
580 585 590

Gly Trp Phe Asn Arg Ser Pro Trp Met Ala Thr Leu Leu Ser Ala Leu
595 600 605

Thr Gly Pro Leu Ile Val Leu Leu Leu Leu Leu Thr Val Gly Pro Cys
610 615 620

Ile Ile Asn Lys Leu Ile Ala Phe Ile Arg Glu Arg Ile Ser Ala Val
625 630 635 640

Gln Ile Met Val Leu Arg Gln Gln Tyr Gln Ser Pro Ser Ser Arg Glu
645 650 655

Ala Gly Arg