can respond to one or more epitopes on an antigen. A responder can also respond to one or more polypeptides in an immunogenic composition of the invention and/or to one or more antigens in an immunogenic composition of the invention.

Immunological assays and serological tests that can be used to analyse the percentage of responders or the magnitude of an immune response are known in the art. Examples of such assays are known to a person skilled in the art and are described below in the Examples section.

Preferably, the level of cross-reactivity observed is up to 10%, up to 15%, up to 20%, up to 25%, up to 30%, up to 35%, up to 40%, up to 45%, up to 50%, up to 55%, up to 60%, up to 65% up to 70%, up to 80%, up to 90% or up to 100% of subjects in a sample are responders.

No matter which method of measurement is used, complete cross-reactivity, for example 100% cross-reactivity, against a strain of HIV-1 from a clade not represented in the immunogenic composition is not required in the present invention.

The immunogenic composition of the invention comprises an adjuvant that is a preferential inducer of a Th1 immune response.

Adjuvants are described in general in Vaccine Design – the Subunit and Adjuvant Approach, edited by Powell and Newman, Plenum Press, New York, 1995~~, incorporated herein by reference~~.

An adjuvant, an example of an immunostimulant, refers to the components in an immunogenic composition that enhance or potentiate a specific immune response (antibody and/or cell-mediated) to an antigen.

Adjuvants can induce immune responses of the Th1-type and Th-2 type response. Th1-type cytokines (e.g., IFN-γ, IL-2, and IL-12) tend to favour the induction of cell-mediated immune response to a given antigen, while Th-2 type cytokines (e.g., IL-4, IL-5, Il-6, IL-10) tend to favour the induction of humoral immune responses to the antigen.

In the present invention, the adjuvant is a preferential inducer of a Th1 immune response.

The distinction of Th1 and Th2-type immune response is not absolute. In reality an individual will support an immune response which is described as being predominantly Th1 or

predominantly Th2. However, it is often convenient to consider the families of cytokines in terms of that described in murine CD4 + T cell clones by Mosmann and Coffman (Mosmann, T.R. and Coffman, R.L. (1989) TH1 and TH2 cells: different patterns of lymphokine secretion lead to different functional properties. Annual Review of Immunology, 7, p145-173~~, incorporated herein by reference~~). Traditionally, Th1-type responses are associated with the production of the INF-γ and IL-2 cytokines by T-lymphocytes. Other cytokines often directly associated with the induction of Th1-type immune responses are not produced by T-cells, such as IL-12. In contrast, Th2-type responses are associated with the secretion of Il-4, IL-5, IL-6, IL-10. Suitable adjuvant systems which promote a predominantly Th1 response include: Monophosphoryl lipid A or a derivative thereof (or detoxified lipid A in general – see for instance WO2005107798), particularly 3-de-O-acylated monophosphoryl lipid A (3D-MPL) (for its preparation see GB 2220211 A); and a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with either an aluminum salt (for instance aluminum phosphate or aluminum hydroxide) or an oil-in-water emulsion. In such combinations, antigen and 3D-MPL are contained in the same particulate structures, allowing for more efficient delivery of antigenic and immunostimulatory signals. Studies have shown that 3D-MPL is able to further enhance the immunogenicity of an alum-adsorbed antigen [Thoelen *et al.* Vaccine (1998) 16:708-14; EP 689454-B1~~, each incorporated herein by reference~~].

An enhanced system involves the combination of a monophosphoryl lipid A and a saponin derivative, particularly the combination of QS21 and 3D-MPL as disclosed in WO 94/00153 ~~incorporated herein by reference,~~ or a less reactogenic composition where the QS21 is quenched with cholesterol as disclosed in WO 96/33739~~, incorporated herein by reference~~. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil in water emulsion is described in WO 95/17210~~, incorporated herein by reference~~. In one embodiment the immunogenic composition additionally comprises a saponin, which can be QS21. The formulation can also comprise an oil in water emulsion and tocopherol (WO 95/17210~~, incorporated herein by reference~~).

In an embodiment of the invention, the adjuvant comprises one or more components selected from an immunologically active saponin fraction and/or a lipopolysaccharide and/or an immunostimulatory oligonucleotides.

In an embodiment, the adjuvant comprises an immunologically active saponin fraction and a lipopolysaccharide.

Conveniently, the immunologically active saponin fraction is QS21 and/or the lipopolysaccharide is a lipid A derivative. Suitably, the lipid A derivative is 3D-MPL.

Suitable adjuvants are combinations of 3D-MPL and QS21 (EP 0 671 948 B1~~, incorporated herein by reference~~), oil in water emulsions comprising 3D-MPL and QS21 (WO 95/17210, WO 98/56414~~, each incorporated herein by reference~~), or 3D-MPL formulated with other carriers (EP 0 689 454 B1~~, incorporated herein by reference~~).

3D–MPL is available from GlaxoSmithKline Biologicals North America and primarily promotes CD4+ T cell responses with an IFN-γ (Th1) phenotype . It can be produced according to the methods disclosed in GB 2 220 211 A. Chemically it is a mixture of 3-deacylated monophosphoryl lipid A with 3, 4, 5 or 6 acylated chains. Preferably in the compositions of the present invention small particle 3D-MPL is used. Small particle 3D-MPL has a particle size such that it can be sterile-filtered through a 0.22µm filter. Such preparations are described in WO 94/21292~~, incorporated herein by reference~~.

Another suitable adjuvant for use in the present invention is Quil A and its derivatives. Quil A is a saponin preparation isolated from the South American tree Quilaja Saponaria Molina and was first described as having adjuvant activity by Dalsgaard et al. in 1974 ("Saponin adjuvants", Archiv. für die gesamte Virusforschung, Vol. 44, Springer Verlag, Berlin, p243-254~~, incorporated herein by reference~~). Purified fragments of Quil A have been isolated by HPLC which retain adjuvant activity without the toxicity associated with Quil A (EP 0 362 278~~, incorporated herein by reference~~), for example QS7 and QS21 (also known as QA7 and QA21). QS21 is a natural saponin derived from the bark of Quillaja saponaria Molina which induces CD8+ cytotoxic T cells (CTLs), Th1 cells and a predominant IgG2a antibody response and is a preferred saponin in the context of the present invention.

Particular formulations of QS21 have been described which are particularly suitable, these formulations further comprise a sterol (WO96/33739~~, incorporated herein by reference~~). The saponins forming part of the present invention can be separate in the form of micelles, mixed micelles (preferentially, but not exclusively with bile salts) or can be in the form of ISCOM matrices (EP 0 109 942 B1~~, incorporated herein by reference~~), liposomes or related colloidal

structures such as worm-like or ring-like multimeric complexes or lipidic/layered structures and lamellae when formulated with cholesterol and lipid, or in the form of an oil in water emulsion (for example as in WO 95/17210~~, incorporated herein by reference~~). The saponins can be associated with a metallic salt, such as aluminium hydroxide or aluminium phosphate (WO 98/15287~~, incorporated herein by reference~~).

An enhanced system involves the combination of a monophosphoryl lipid A (or detoxified lipid A) and a saponin derivative, particularly the combination of QS21 and 3D-MPL as disclosed in WO 94/00153~~, incorporated herein by reference,~~ or a less reactogenic composition where the QS21 is quenched with cholesterol as disclosed in WO 96/33739~~, incorporated herein by reference~~. A particularly potent adjuvant formulation involving tocopherol with or without QS21 and/or 3D-MPL in an oil in water emulsion is described in WO 95/17210~~, incorporated herein by reference~~.

In an embodiment, the adjuvant comprises a sterol, which can suitably be cholesterol. Suitable sterols, for instance cholesterol, act to reduce the reactogenicity of the composition while maintaining the adjuvant effect of the saponin.

In an embodiment of the invention, the adjuvant comprises a liposome carrier.

In an embodiment, the adjuvant comprises a saponin and a sterol with a ratio of saponin : sterol from 1:1 to 1:100 (w/w). Conveniently, the ratio of saponin : sterol is from 1:1 to 1:10 (w/w) or the ratio of saponin : sterol is from 1:1 to 1:5 (w/w).

In an embodiment, the adjuvant comprises a saponin and a lipopolysaccharide with a ratio of saponin : lipopolysaccharide of 1 : 1.

Conveniently, the adjuvant comprises a lipopolysaccharide and said lipopolysaccharide is present at an amount of 1 – 60 µg per dose. Suitably, the lipopolysaccharide is present at an amount of 50 µg per dose, 25 µg per dose, 10 µg per dose or 5 µg per dose.

Conveniently, the adjuvant comprises a saponin and said saponin is present at an amount of 1 – 60 µg per dose. Suitably, the saponin is present at an amount of 50 µg per dose, 25 µg per dose, 10 µg per dose or 5 µg per dose.

mixed internucleotide linkages. Methods for producing phosphorothioate oligonucleotides or phosphorodithioate are described in US5,666,153, US5,278,302 and WO95/26204~~, each incorporated herein by reference~~.

Examples of preferred oligonucleotides have the following sequences. The sequences preferably contain phosphorothioate modified internucleotide linkages.
OLIGO 1(SEQ ID NO:1): TCC ATG ACG TTC CTG ACG TT
OLIGO 2 (SEQ ID NO:2): TCT CCC AGC GTG CGC CAT
OLIGO 3(SEQ ID NO:3): ACC GAT GAC GTC GCC GGT GAC GGC ACC ACG
OLIGO 4 (SEQ ID NO:4): TCG TCG TTT TGT CGT TTT GTC GTT
OLIGO 5 (SEQ ID NO:5): TCC ATG ACG TTC CTG ATG CT
OLIGO 6 (SEQ ID NO:6): TCG ACG TTT TCG GCG CGC GCC G

Alternative CpG oligonucleotides can comprise the preferred sequences above in that they have inconsequential deletions or additions thereto.

The CpG oligonucleotides utilised in the present invention can be synthesized by any method known in the art (for example see EP 468520~~, incorporated herein by reference~~). Conveniently, such oligonucleotides can be synthesized utilising an automated synthesizer.

According to an aspect of the invention, the immunogenic composition of the invention is for use in the treatment or prevention of disease or infection by HIV-1 strains from one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

Additionally, in an embodiment of the invention, the immunogenic composition of the invention is for use in the treatment or prevention of disease or infection by HIV-1 strains from one or more clades that are in the immunogenic composition.

Accordingly, the immunogenic composition is capable of inducing homologous immune responses to the clades represented therein as well as inducing cross-reactive immune responses to clades that are not covered by the strains of antigen present in the composition. The immunogenic compositions are thus capable of broadly treating or preventing disease or infection by multiple HIV-1 strains from multiple clades.

Accordingly, the present invention also provides for methods for the treatment or prophylaxis of HIV infection comprising administering the immunogenic composition to a subject and inducing an immune response in the subject against an HIV-1 strain from one or more clades different from the one or more HIV-1 clades in the immunogenic composition. In other embodiments, the present invention provides methods for the use of the composition as described herein.

Fusion proteins comprising one or more of the antigens which can be present in the immunogenic composition of the invention have been disclosed in WO2006/013106~~, incorporated herein by reference~~. The antigens Pol, Nef, Gag and variants and fragments thereof have previously been selected for inclusion in a fusion protein for use in an immunogenic composition because they are considered to be relatively well conserved across different strains of HIV, and thus is more likely to cross-react with antigens from different strains of HIV, than less well conserved antigens. However, the incorporation of these antigens into fusion proteins may introduce unpredictable complications because the antigens therein do not correspond to native proteins. Accordingly, fusion proteins are not straightforward to produce and cannot be presumed to behave as the native protein would.

In an embodiment of the invention, two, three, four or more of the antigens in the immunogenic composition are fused to form a fusion protein.

Conveniently, Gag is fused to Pol or Pol is fused to Gag, Pol is fused to Nef or Nef is fused to Pol, and/or Nef is fused to Gag or Gag is fused to Nef.

Suitably, in a fusion protein of the invention, Gag is p17 and/or p24, and/or Pol is RT

In particular, it is convenient that the antigens in the immunogenic composition are fused to form a fusion protein comprising Nef, RT, p17 and p24 in any order. Suitably, the antigens are fused to form a fusion protein comprising p24-RT-Nef-p17. Such a fusion protein is known as F4 and is described in the Examples.

The antigens in a fusion protein can be fused directly to each other or by means of a linker. Such linker can comprise a heterologous amino acid sequence comprising one or more amino acids.

In an embodiment, the immunogenic composition of the invention is used as part of a prime-boost regimen for use in the treatment or prevention of disease or infection by HIV-1 strains from one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

Conveniently, the composition is the priming dose. Alternatively, the composition is the boosting dose.

Suitably, two or more priming and/or boosting doses are administered.

A heterologous prime-boost regime uses administration of different forms of immunogenic composition or vaccine in the prime and the boost, each of which can itself include two or more administrations. The priming composition and the boosting composition will have at least one antigen in common, although it is not necessarily an identical form of the antigen, it can be a different form of the same antigen.

Prime boost immunisations according to the invention can be homologous prime-boost regimes or heterologous prime-boost regimes. Homologous prime-boost regimes utilize the same composition for prime and boost, for instance the immunogenic composition of the invention.

Heterologous prime-boost regimes can be performed with a combination of protein and DNA-based formulations. Such a strategy is considered to be effective in inducing broad immune responses. Adjuvanted protein vaccines induce mainly antibodies and CD4+ T cell immune responses, while delivery of DNA as a plasmid or a recombinant vector induces strong CD8+ T cell responses. Thus, the combination of protein and DNA vaccination can provide for a wide variety of immune responses. This is particularly relevant in the context of HIV, since neutralizing antibodies, CD4+ T cells and CD8+ T cells are thought to be important for the immune defense against HIV-1.

In one embodiment the DNA is delivered in a viral vector. For example, the viral vector may be derived from an adenovirus. In a further embodiment, the viral vector may be as described in US20100055166~~, which is hereby incorporated by reference~~ for its disclosure of viral vectors and prime-boost methods. In another embodiment, the viral vector may be derived from a measles virus. In a further embodiment, the viral vector may be a recombinant measles vector as described

in WO2010/023260~~, which is hereby incorporated by reference~~ for its disclosure of viral vectors and prime-boost methods.

Accordingly, the present invention also provides for methods for the treatment or prophylaxis of HIV infection comprising administering a first composition to a subject and subsequently administering a second composition to the subject, wherein after administration, the subject has a detectable immune response in the subject against an HIV-1 strain from one or more clades different from the one or more HIV-1 clades in the immunogenic composition. In alternative embodiments, the method can be a homologous prime-boost regime or a heterologous prime-boost regime.

In a further aspect of the invention, the immunogenic composition of the invention is a vaccine composition.

Vaccine preparation is generally described in New Trends and Developments in Vaccines, edited by Voller et al., University Park Press, Baltimore, Maryland, U.S.A. 1978~~, incorporated herein by reference~~.

In a further aspect of the invention, there is provided use of the immunogenic composition or the vaccine of the invention in the manufacture of a medicament for the treatment or prevention of disease or infection by HIV-1 strains as described in all instances above.

In a further aspect of the invention, there is provided a method of treating or preventing HIV-1 disease or infection according to in all instances described above comprising the step of administering to a subject the immunogenic composition or the vaccine of the invention.

The terms "comprising", "comprise" and "comprises" herein are intended by the inventors to be optionally substitutable with the terms "consisting of", "consist of" and "consists of", respectively, in every instance.

Embodiments herein relating to "immunogenic compositions" of the invention are also applicable to embodiments relating to "vaccines" of the invention, and vice versa.

dilution: 1/10.000

- Rabbit polyclonal anti Nef-Tat (rabbit 388)

dilution 1/10.000

- Alkaline phosphatase-conjugate anti- rabbit antibody

dilution: 1/7500

After induction at 22°C over 19 hours, recombinant BLR(DE3) cells expressed the F4 fusion at a very high level ranging from 10-15% of total protein.

In comparison with F4 from the native gene, the F4 recombinant product profile from the codon-optimised gene is slightly simplified. The major F4-related band at 60 kDa, as well as minor bands below, disappeared (see Figure 10).

2.2 Preparation of F4co GMP lots

A pre-culture was prepared using a frozen seed culture of *Escherichia coli* strain B1977. This strain is a BLR(DE3) strain transformed with a pET28b derivative containing a codon-optimized sequence coding for F4 (F4co). The seed culturability was determined as approximately 1E+10 colony forming units per ml.

The seed culture was thawed to room temperature and 500 µl were used to inoculate a 2 litre Erlenmeyer flask (without baffles) containing 400 ml of preculture medium supplemented with 50 µg/ml kanamycin (adapted from Zabriskie *et al.* (J. Ind. Microbiol. 2:87-95 (1987)~~, incorporated herein by reference~~).

The inoculated flask was then incubated at 37°C (± 1°C) and 200 rpm (New Brunswick Scientific, Innova 4430 with a stroke of 1 inch). The pre-culture was stopped when the optical density at 650nm (OD_{650nm}) reached 2, which corresponds to around 5h30 of incubation. Pre-culture was used for inoculation immediately after it was stopped.

Where inoculation of a large scale fermenter is necessary, multiple batches of pre-culture can be combined.

2.3 Purification of F4co (p24-RT-Nef-p17) - E. coli strain B1977

During the 30-day post-vaccination period, 50.0–70.0% of subjects in the F4/WFI groups reported unsolicited symptoms, compared to 60.0–84.0% of subjects in the F4/ $AS01_B$ groups. Symptoms were considered causally related to vaccination in 30.0–44.0% of subjects in the F4/ $AS01_B$ groups (most frequently chills and injection site reactions) and only few were of grade 3 severity. Symptoms were, on the whole, transient and resolved without sequelae, generally within two to three days. Throughout the study period, six SAEs were reported in the F4/ $AS01_B$ groups. All were considered unrelated to vaccination and resolved without sequelae. No deaths occurred during the study period and no subject withdrew from the study due to adverse events.

3.3 T-cell responses

The CD4+ T-cell responses were evaluated by intracellular cytokine staining (ICS) following stimulation with p17, p24, RT and Nef peptide pools to assess the expression of interleukin 2 (IL-2), interferon gamma (IFN-γ), tumor necrosis factor alpha (TNF-α) and CD40-ligand (CD40L). The ICS carried out was an adaptation of previously described methodology [see Maecker HT, Maino VC, Picker LJ (2000) Immunofluorescence analysis of T-cell responses in health and disease. J Clin Immunol 20: 391-399 and Maecker HT, Dunn HS, Suni MA, Khatamzas E, Pitcher CJ, et al. (2001) Use of overlapping peptide mixtures as antigens for cytokine flow cytometry. J Immunol Methods 255: 27-40~~, each incorporated herein by reference~~] using peripheral blood mononuclear cells (PBMC) that were isolated from whole blood cells by standard Ficoll-Isopaque density gradient centrifugation within six hours following blood sampling, and cryopreserved in liquid nitrogen until further analysis.

In brief, the thawed PBMC were stimulated in vitro with pools of 15 mer peptides overlapping by 11 amino acids (Eurogentec, Belgium) covering the sequences of clade B p17, p24, RT or Nef matched antigens, in the presence of anti-CD28 and anti-CD49d antibodies (BD Biosciences, Belgium). After two hours of incubation at 37°C, the intracellular blocking agent Brefeldin A (BD Biosciences, Belgium) was added to inhibit cytokine secretion during an additional overnight incubation. Cells were subsequently harvested, stained for surface markers CD4+ and CD8+ (BD Biosciences), and then fixed (Cytofix/Cytoperm kit, BD Biosciences). The fixed cells were then permeabilized and stained with labeled antibodies to IL-2, IFN-γ, TNF-α and CD40L (BD Biosciences), washed, resuspended in foetal-calf-serum-containing phosphate buffered saline and analysed by flow cytometry using a FACSCanto flow cytometer and FACSDiva software (BD Biosciences) or FlowJo software (Tree Star).

CLAIMS

1. An immunogenic composition comprising
   a. one or more polypeptides comprising HIV-1 antigens Nef, Pol and Gag; wherein Nef, Pol and Gag are from an HIV-1 strain of clade A, B, C, D, E, F, G, H, J, K, or a circulating recombinant form of HIV-1 (CRF); and
   b. an adjuvant that is a preferential inducer of a Th1 immune response,

for use in the treatment or prevention of disease or infection by an HIV-1 strain from one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

2. The immunogenic composition of claim 1, wherein Nef, Pol and Gag are from an HIV-1 strain of clade B.

3. The immunogenic composition of claims 1-2, wherein the antigens form a fusion protein comprising p24-RT-Nef-p17.

4. The immunogenic composition of any preceding claim further comprising Env.

5. The immunogenic composition of claims 1-4, wherein the adjuvant comprises an immunologically active saponin fraction, a lipopolysaccharide and optionally an immunostimulatory oligonucleotide.

6. The immunogenic composition of claim 5, wherein said immunologically active saponin fraction is QS21; said lipopolysaccharide is a lipid A derivative, preferably 3D- MPL; and said immunostimulatory oligonucleotide comprises a CpG motif.

7. The immunogenic composition of claims 5-6, wherein the adjuvant comprises a liposome carrier or an oil-in-water emulsion.

8. The immunogenic composition of any preceding claim for use in inducing a humoral immune response against HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

9. The immunogenic composition of claims 1-7 for use in inducing multiple-cytokine-producing CD4+ T cells against HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the cytokines are selected from IL-2, IFNγ and/or TNFα.

10. The immunogenic composition of claims 1-7 for use in preventing progressive CD4+ T cell decline in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

11. The immunogenic composition of claims 1-7 for use in reducing or eliminating viral reservoirs in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

12. The immunogenic composition of claims 1-7 for use in eliciting HIV-1-specific polyfunctional CD4+ T-cells in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

13. The immunogenic composition of claims 1-7 for use in controlling or reducing viremia in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

14. The immunogenic composition of claims 1-7 for use in inducing a long term immune response against HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

15. The immunogenic composition of claims 1-7 for use in the treatment or prevention of disease or infection by HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the composition is administered to a subject as two or three doses, wherein the doses are separated by a period of two weeks to three months, preferably one month.

16. The immunogenic composition of claims 1-7 for use in the treatment or prevention of disease or infection by HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the composition is administered to a subject every 6-24 months or preferably 9-18 months, or preferably annually.

17. The immunogenic composition of claims 1-7 for use in the treatment or prevention of disease or infection by HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the composition is used as part of a prime-boost regimen.

18. Use of the immunogenic composition of claims 1-7 in the manufacture of a medicament for the treatment or prevention of disease or infection by HIV-1 strains one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

CLAIMS

1. Use of an immunogenic composition comprising

   a. one or more polypeptides comprising HIV-1 antigens Nef, Pol and Gag; wherein Nef, Pol and Gag are from an HIV-1 strain of clade A, B, C, D, E, F, G, H, J, K, or a circulating recombinant form of HIV-1 (CRF); and

   b. an adjuvant that is a preferential inducer of a Th1 immune response,

for the manufacture of a medicament for the treatment or prevention of disease or infection by an HIV-1 strain from one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the medicament induces multiple-cytokine-producing CD4+ T cells against HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the cytokines are selected from IL-2, IFNγ and/or TNFα

2. The use according to claim 1, wherein Nef, Pol and Gag are from an HIV-1 strain of clade B.

3. The use according to any one of claims 1-2, wherein the antigens form a fusion protein comprising p24-RT-Nef-p17.

4. The use according to any one of the preceding claims further comprising Env.

5. The use according to any one of claims 1-4, wherein the adjuvant comprises an immunologically active saponin fraction, a lipopolysaccharide and optionally an immunostimulatory oligonucleotide.

6. The use according to claim 5, wherein said immunologically active saponin fraction is QS21; said lipopolysaccharide is a lipid A derivative, preferably 3D-MPL; and said immunostimulatory oligonucleotide comprises a CpG motif.

7. The use according to any one of claims 5-6, wherein the adjuvant comprises a liposome carrier or an oil-in-water emulsion.

8. The use according to any one of the preceding claims for inducing a humoral immune response against HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

9. The use according to any one of claims 1-7 for preventing progressive CD4+ T cell decline in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

10. The use according to any one of claims 1-7 for reducing or eliminating viral reservoirs in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

11. The use according to any one of claims 1-7 for eliciting HIV-1-specific polyfunctional CD4+ T-cells in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

12. The use according to any one of claims 1-7 for controlling or reducing viremia in an individual infected with an HIV-1 strain from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

13. The use according to any one of claims 1-7 for inducing a long term immune response against HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition.

14. The use according to any one of claims 1-7 for the treatment or prevention of disease or infection by HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the medicament is for administration to a subject as two or three doses, wherein the doses are separated by a period of two weeks to three months, preferably one month.

15. The use according to any one of claims 1-7 for the treatment or prevention of disease or infection by HIV-1 strains from said one or more clades different from the

one or more HIV-1 clades in the immunogenic composition, wherein the medicament is for administration to a subject every 6-24 months or preferably 9-18 months, or preferably annually.

16. The use according to any one of claims 1-7 for the treatment or prevention of disease or infection by HIV-1 strains from said one or more clades different from the one or more HIV-1 clades in the immunogenic composition, wherein the composition is used as part of a prime-boost regimen.