sites of initial HIV exposure (mucosa) offers the potential for reducing mucosal $CD4^+$ T-cell depletion and local control of HIV infection. Given their demonstrated capacity to recognise target cells expressing very low levels of viral antigen (e.g. early after infection of a cell), and their more rapid initiation of target cell lysis at low concentrations of target antigen, vaccine strategies that elicit high-avidity CTL are potentially likely to offer greater protection against infection.

A need exists for antiviral vaccines capable of eliciting high-avidity CTL. In particular, there is a need for antiviral vaccines capable of eliciting high-avidity CTL at mucosal surfaces which are the initial point of infection for many viruses.

Summary of the Invention

The present inventors have discovered that both the magnitude and avidity of antigen-specific T lymphocytes induced by antiviral vaccines can be increased by transiently reducing the availability of interleukin-4 (IL-4) and/or transiently inhibiting IL-4 function.

In one embodiment the present invention refers to use of an antigen in combination with an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for inducing an antigen-specific immune response in a subject, wherein the antigen is to be administered to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist, and wherein:

said administration comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

In another embodiment, the present invention refers to use of an antigen in combination with an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for increasing the avidity of immune cells for the antigen in a subject, wherein the antigen is to be administered to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist, and wherein:

said administration comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

In another embodiment, the present invention refers to use of an antigen in combination with an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for increasing the number of immune cells specific for the antigen in a subject, wherein the antigen is to be administered to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist, and wherein:

said administration comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

In another embodiment, the present invention referes to a composition comprising:

(i) a polynucleotide encoding an antigen; and

(ii) a polynucleotide encoding an IL-4R antagonist,

wherein:

the composition is formulated for administration to a subject in a priming dose and a booster dose,

each said polynucleotide is a component of a recombinant virus, and

the recombinant virus of each said dose transiently expresses the interleukin-4 receptor antagonist in a subject to which the composition is to be administered.

In another embodiment, the present invention refers to use of the composition according to any one of claims 16 to 22 in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for preventing or treating an infection in a subject, wherein the pharmaceutical composition or the combination of pharmaceutical compositions is or are to be administered to the subject as a primer dose and a booster dose.

In another embodiment, the present invention refers to use of the composition according to any one of claims 16 to 22 in the manufacture of a pharmaceutical

composition or a combination of pharmaceutical compositions for vaccinating a subject against an infection, wherein the pharmaceutical composition or the combination of pharmaceutical compositions is or are to be administered as a primer dose and a booster dose to the subject.

In a first aspect, the ~~present invention~~disclosure provides a method for inducing an antigen-specific immune response in a subject, the method comprising administering the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist.

In a second aspect, the ~~present invention~~disclosure provides a method for increasing the avidity of immune cells for an antigen in a subject, the method comprising administering the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist.

In a third aspect, the ~~present invention~~disclosure provides a method for increasing the number of immune cells specific for an antigen in a subject, the method comprising administering the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist.

In one ~~embodiment~~example of the above aspects, the method comprises administering a priming dose and a booster dose to the subject, each said dose comprising administering the antigen to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist.

In one ~~embodiment~~example of the above aspects, the method comprises administering a priming dose to the subject, wherein the priming dose comprises the antigen and an IL-4R antagonist.

In one ~~embodiment~~example of the above aspects, the method comprises administering a booster dose to the subject, wherein the booster dose comprises the antigen and an IL-4R antagonist.

In one ~~embodiment~~example of the above aspects, the antigen and IL-4R antagonist of the booster dose may be administered sequentially or simultaneously.

In one ~~embodiment~~example of the above aspects, administering the primer dose comprises administering a polynucleotide encoding the antigen, a polynucleotide encoding the IL-4R antagonist, or both.

In one ~~embodiment~~example of the above aspects, administering the booster dose comprises administering a polynucleotide encoding the antigen, a polynucleotide encoding the IL-4R antagonist, or both.

In one ~~embodiment~~example of the above aspects, any one or more of the polynucleotides in the primer dose may be a component of a recombinant virus.

In one ~~embodiment~~example of the above aspects, any one or more of the polynucleotides in the booster dose may be a component of a recombinant virus.

In one ~~embodiment~~example of the above aspects, the recombinant virus of the primer dose is a poxvirus.

In one ~~embodiment~~example of the above aspects, the recombinant virus of the booster dose is a poxvirus.

In one ~~embodiment~~example of the above aspects, the recombinant virus of the primer dose is a poxvirus selected from the group consisting of a vaccinia virus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, and a modified vaccinia ankara (MVA) virus.

In one ~~embodiment~~example of the above aspects, the recombinant virus of the booster dose is a poxvirus selected from the group consisting of a vaccinia virus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, and a modified vaccinia ankara (MVA) virus.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist of the primer dose is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

In one embodiment of the above aspects, the IL-4R antagonist of the booster dose is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist of the primer dose is a human interleukin-4 molecule lacking a signal peptide and comprising one or more

mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist of the booster dose is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist of the primer dose is a human interleukin-4 molecule comprising a mutation selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist of the booster dose is a human interleukin-4 molecule comprising a mutation selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In one ~~embodiment~~example of the above aspects, the administering comprises administering a polynucleotide encoding the antigen, a polynucleotide encoding the interleukin-4 receptor antagonist, or both.

In one ~~embodiment~~example of the above aspects, any one or more of said polynucleotides is a component of a recombinant virus.

In one ~~embodiment~~example of the above aspects, the recombinant virus is a poxvirus.

In one ~~embodiment~~example of the above aspects, the recombinant virus is a poxvirus selected from the group consisting of a vaccinia virus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, and a modified vaccinia ankara virus.

In one ~~embodiment~~example of the above aspects, the recombinant virus transiently expresses the interleukin-4 receptor (IL-4R) antagonist in the subject.

In one ~~embodiment~~example of the above aspects, the administering of the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist decreases the number of CD103+, b220+, CD8α+ cells in the subject and/or increases CD11b+, CD103-,b220-, CD8α - cells in the subject. The CD103+, b220+, CD8α+ cells and/or CD11b+, CD103-, b220-, CD8α - cells may be specific for the antigen. The antigen may be an HIV antigen (e.g. HIV gag, pol and/or env antigen).

In a fourth aspect, the ~~present invention~~disclosure provides the use of an antigen and an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a medicament for inducing a specific immune response against the antigen in a subject.

In a fifth aspect, the ~~present invention~~disclosure provides the use of an antigen and an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a medicament for increasing the avidity of immune cells specific for the antigen in a subject.

In a sixth aspect, the ~~present invention~~disclosure provides the use of an antigen and an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a medicament for increasing the number of immune cells specific for the antigen in a subject.

In a seventh aspect, the ~~present invention~~disclosure provides an antigen and an interleukin-4 receptor (IL-4R) antagonist for use in inducing a specific immune response against the antigen in a subject.

In an eighth aspect, the ~~present invention~~disclosure provides an antigen and an interleukin-4 receptor (IL-4R) antagonist for use in increasing the avidity of immune cells specific for the antigen in a subject.

In a ninth aspect, the ~~present invention~~disclosure provides an antigen and an interleukin-4 receptor (IL-4R) antagonist for use in increasing the number of immune cells specific for the antigen in a subject.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth, and ninth aspects, the antigen is provided as a polynucleotide encoding the antigen.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth, and ninth aspects, the interleukin-4 receptor antagonist is provided a polynucleotide encoding the interleukin-4 receptor antagonist.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth, and ninth aspects, any one or more of said polynucleotides is a component of a recombinant virus.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth, and ninth aspects, the recombinant virus is a poxvirus.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth, and ninth aspects, the recombinant virus is a poxvirus selected from the group consisting of a vaccinia virus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, and a modified vaccinia ankara virus.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth, and ninth aspects, the recombinant virus transiently expresses the interleukin-4 receptor (IL-4R) antagonist in the subject.

In one ~~embodiment~~example of the fourth, fifth, and sixth aspects, the medicament is a vaccine.

In one ~~embodiment~~example of the fourth, fifth, and sixth aspects, the medicament is a vaccine comprising first and second components, wherein the first component comprises the interleukin-4 receptor (IL-4R) antagonist and the second component comprises the antigen, and wherein the first and second components are for, or are formulated for, simultaneous or sequential administration to the subject.

In one ~~embodiment~~example of the seventh, eighth, and ninth aspects aspects, the antigen and interleukin-4 receptor (IL-4R) antagonist are components of a vaccine.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eighth and ninth aspects, the vaccine is for administration to the subject, or formulated for administration to the subject, as a primer dose, a booster dose, or both.

In one ~~embodiment~~example of the fourth, fifth, sixth, seventh, eight and ninth aspects, the vaccine is capable of decreasing the number of CD103+, b220+, CD8α+ cells in the subject and/or increasing CD11b+, CD103-,b220-, CD8α - cells in the subject, upon administration to the subject. The CD103+, b220+, CD8α+ cells and/or CD11b+, CD103-, b220-, CD8α - cells may be specific for the antigen. The antigen may be an HIV antigen (e.g. HIV gag, pol and/or env antigen).

In one ~~embodiment~~example of the first, second, third, fifth, sixth, eighth and ninth aspects, the immune cell is a T-lymphocyte.

In one ~~embodiment~~example the first, second, third, fifth, sixth, eighth and ninth aspects, the immune cell is a $CD8^+$ T-lymphocyte.

In one ~~embodiment~~example the first, second, third, fifth, sixth, eighth and ninth aspects, the immune cell is a cytotoxic $CD8^+$ T-lymphocyte.

In one ~~embodiment~~example of the above aspects, the antigen is a viral antigen.

In one ~~embodiment~~example of the above aspects, the antigen is a human immunodeficiency virus antigen.

In one ~~embodiment~~example of the above aspects, the antigen is a human immunodeficiency virus antigen selected from a gp120 env, gp140 env, gp160 env, p18, gag, pol, vif, vpr, vpu, tat, rev, and nef gene product, and combinations thereof.

In one ~~embodiment~~example of the above aspects, the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

In one ~~embodiment~~example of the above aspects, the antigen is a human immunodeficiency virus antigen selected from a combined gag/pol, or a combined gag/pol/env gene product.

In one ~~embodiment~~example of the above aspects, the antigen and interleukin-4 receptor antagonist are administered to the subject sequentially.

In one ~~embodiment~~example of the above aspects, the antigen and interleukin-4 receptor antagonist are administered to the subject simultaneously.

In one ~~embodiment~~example of the above aspects, the antigen and interleukin-4 receptor antagonist are administered to the subject as a priming dose.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

In one ~~embodiment~~example of the above aspects, the IL-4R antagonist is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In a tenth aspect, the ~~present invention~~disclosure provides a composition comprising:

(i) an antigen and/or a polynucleotide encoding the antigen; and

(ii) an interleukin-4 receptor (IL-4R) antagonist and/or a polynucleotide encoding the IL-4R antagonist.

In an eleventh aspect, the ~~present invention~~disclosure provides the use of an antigen and an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a medicament for preventing or treating an infection in a subject.

In a twelfth aspect, the present invention provides the use of an antigen and an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a medicament for vaccinating a subject against an infection.

In a thirteenth aspect, the ~~present invention~~disclosure provides an antigen and an interleukin-4 receptor (IL-4R) antagonist for use in preventing or treating an infection in a subject.

In a fourteenth aspect, the ~~present invention~~disclosure provides the use of an antigen and an interleukin-4 receptor (IL-4R) antagonist for use in vaccinating a subject against an infection.

In one ~~embodiment~~example of the eleventh aspect the medicament is a vaccine.

In one ~~embodiment~~example of the thirteenth aspect the antigen and interleukin-4 receptor (IL-4R) antagonist are components of a vaccine.

In one ~~embodiment~~example of the eleventh and thirteenth aspects, the vaccine comprises first and second components, wherein the first component comprises the interleukin-4 receptor (IL-4R) antagonist and the second component comprises the antigen, and

wherein the first and second components are for, or are formulated for, simultaneous or sequential administration to the subject.

In one ~~embodiment~~example of the eleventh and thirteenth aspects, the vaccine is for administration to a subject, or formulated for administration to a subject, as a primer dose, a booster dose, or both.

In one ~~embodiment~~example of the twelfth aspect, the medicament is for administration to the subject, or formulated for administration to the subject, as a primer dose, a booster dose, or both.

In one ~~embodiment~~example of the fourteenth aspect, the antigen and interleukin-4 receptor (IL-4R) antagonist is for administration to the subject, or formulated for administration to the subject, as a primer dose, a booster dose, or both.

In one ~~embodiment~~example of the eleventh and thirteenth aspects, the vaccine is capable of decreasing the number of CD103+, b220+, CD8α+ cells in the subject and/or increasing CD11b+, CD103-,b220-, CD8α - cells in the subject, upon administration to the subject. The CD103+, b220+, CD8α+ cells and/or CD11b+, CD103-, b220-, CD8α - cells may be specific for the antigen. The antigen may be an HIV antigen (e.g. HIV gag, pol and/or env antigen).

In one ~~embodiment~~example of the twelfth and fourteenth aspects, said vaccinating is capable of decreasing the number of CD103+, b220+, CD8α+ cells in the subject and/or increasing CD11b+, CD103-, b220-, CD8α - cells in the subject. The CD103+, b220+, CD8α+ cells and/or CD11b+, CD103-, b220-, CD8α - cells may be specific for the antigen. The antigen may be an HIV antigen (e.g. HIV gag, pol and/or env antigen).

In one ~~embodiment~~example of the eleventh, twelfth, thirteenth and fourteenth aspects, the antigen is provided as a polynucleotide encoding the antigen.

In one ~~embodiment~~example of the eleventh, twelfth, thirteenth and fourteenth aspects, the interleukin-4 receptor is provided as a polynucleotide encoding the interleukin-4 receptor antagonist.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, any one or more of said polynucleotides is a component of a recombinant virus.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the recombinant virus is a poxvirus.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the recombinant virus is a poxvirus selected from the group consisting of a vaccinia virus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, and a modified vaccinia ankara virus.

In one ~~embodiment~~example of the eleventh, twelfth, thirteenth and fourteenth aspects, the recombinant virus transiently expresses the interleukin-4 receptor (IL-4R) antagonist in the subject.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the antigen is a viral antigen.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the antigen is a human immunodeficiency virus antigen selected from a gp120 env, gp140 env, gp160 env, p18, gag, pol, vif, vpr, vpu, tat, rev, and nef gene product, and combinations thereof.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the antigen is a human immunodeficiency virus antigen selected from a combined gag/pol, or a combined gag/pol/env gene product.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the IL-4R antagonist is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-Rα and preventing IL-4R signalling.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the IL-4R antagonist is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In one ~~embodiment~~example of the tenth, eleventh, twelfth, thirteenth and fourteenth aspects, the mutation is selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

In a fifteenth aspect, the ~~present invention~~disclosure provides a method for preventing or treating an infection in a subject, the method comprising administering to the subject the composition according to the tenth aspect.

In a sixteenth aspect, the ~~present invention~~disclosure provides a method of vaccinating a subject against an infection, the method comprising administering a primer dose and a booster dose of the composition according to the tenth aspect.

In one ~~embodiment~~example of the fifteenth and sixteenth aspects, the infection is human immunodeficiency virus infection and the composition comprises a human

immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

In one ~~embodiment~~example of the eleventh, twelfth, thirteenth, and fourteenth aspects, the infection is human immunodeficiency virus infection and the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

Brief Description of the Figures

Preferred embodiments of the present invention will now be described, by way of example only, with reference to the accompanying figures wherein:

Figure 1 shows the MVA del-III synthetic vector sequence comprising an intergenic insertion site created between MVA164 and MVA165 including sequences from FseI to HindIII sites, and incorporating a fowlpox virus early/late promoter.

Figure 2 shows the MVA "HindIII F" insertion site, wherein a multiple cloning site containing FseI to HindIII (including an upstream T5NT early transcription termination signal) has been inserted between ORFs F8L and F7L.

Figure 3 shows a synthetic SIV mac239 gag/pol sequence optimised for expression in macaque monkeys. The sequence contains a synthetic poxvirus early/late promoter upstream of the genes and an early transcription terminator sequence (T5NT) downstream flanked by restriction endonuclease site to facilitate cloning. The genes are expressed as a fusion protein resulting from a frame-shift during translation in the overlapping region.

Figure 4 is a timecourse graph showing HIV KdGag-specific $CD8^+$ T-cell avidity following co-vaccination with IL-4 receptor (IL-4R) antagonist (IL-4C118). FPV HIV IL-4C118/VV HIV IL-4C118 = priming vaccination with recombinant fowlpox virus encoding HIV gag/pol antigen and mutant IL-4C118 followed by booster vaccine with recombinant vaccinia virus encoding HIV gag/pol antigen and mutant IL-4C118. FPV HIV/VV HIV = primer vaccination with recombinant fowlpox encoding HIV gag/pol (no IL-4 receptor antagonist) followed by booster vaccination with recombinant vaccinia virus encoding HIV gag/pol (no IL-4 receptor antagonist).

Figure 5 is a column graph showing HIV KdGag-specific $CD8^+$ T-cell avidity and magnitude of HIV KdGag-specific $CD8^+$ T-cell responses following co-vaccination with IL-4 receptor antagonist. FPV HIV/VV HIV = priming vaccination with recombinant fowlpox encoding HIV gag/pol (no IL-4 receptor antagonist) followed by booster vaccination with recombinant vaccinia virus encoding HIV gag/pol (no IL-4 receptor

PCT/AU2013/000589
Received 17/07/2014

CLAIMS:

1. A method for inducing an antigen-specific immune response in a subject, the method comprising administering the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist, wherein:

said administering comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

2. A method for increasing the avidity of immune cells for an antigen in a subject, the method comprising administering the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist, wherein:

said administering comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

3. A method for increasing the number of immune cells specific for an antigen in a subject, the method comprising administering the antigen to the subject in combination with an interleukin-4 receptor (IL-4R) antagonist, wherein:

said administering comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

4. The method according to claim 2 or claim 3, wherein the immune cells are T-lymphocytes, CD8+ T lymphocytes, and/or B lymphocytes.

5. The method according to claim 1, wherein the antigen-specific immune response comprises T-lymphocytes and/or B-lymphocytes specific for said antigen.

6. The method according to any one of claims 1 to 5, wherein the antigen is a viral antigen.

7. The method according to any one of claims 1 to 6, wherein the antigen is a human immunodeficiency virus antigen.

8. The method according to any one of claims 1 to 7, wherein the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

9. The method according to any one of claims 1 to 8, wherein the antigen and interleukin-4 receptor antagonist of the primer dose are administered to the subject sequentially.

10. The method according to any one of claims 1 to 8, wherein the antigen and interleukin-4 receptor antagonist of the primer dose are administered to the subject simultaneously.

11. The method according to any one of claims 1 to 10, wherein the IL-4R antagonist of the primer and/or booster dose is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

12. The method according to any one of claims 1 to 11, wherein the IL-4R antagonist of the primer and/or booster dose is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

13. The method according to any one of claims 1 to 12, wherein the antigen and IL-4R antagonist of the booster dose are administered simultaneously.

14. The method according to any one of claims 1 to 12, wherein the antigen and IL-4R antagonist of the booster dose are administered sequentially.

15. The method according to claim 12, wherein the mutation is selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

16. A composition comprising:

(i) a polynucleotide encoding an antigen; and

(ii) a polynucleotide encoding an IL-4R antagonist,

wherein:

the composition is formulated for administration to a subject in a priming dose and a booster dose,

each said polynucleotide is a component of a recombinant virus, and

the recombinant virus of each said dose transiently expresses the interleukin-4 receptor antagonist in a subject to which the composition is administered.

17. The composition according to claim 16, wherein the antigen is a viral antigen.

18. The composition according to claim 16 or claim 17, wherein the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

19. The composition according to any one of claims 16 to 18, wherein the IL-4R antagonist is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

20. The composition according to any one of claims 16 to 19, wherein the IL-4R antagonist is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

21. The composition according to claim 20, wherein the mutation is selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

22. The composition according to claim 16, wherein the recombinant virus is selected from the group consisting of a poxvirus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, an adenovirus, a live-attenuated virus, and a modified vaccinia Ankara (MVA) virus.

23. A method for preventing or treating an infection in a subject, the method comprising administering to the subject a primer dose and a booster dose of the composition according to any one of claims 16 to 22.

24. A method of vaccinating a subject against an infection, the method comprising administering a primer dose and a booster dose of the composition according to any one of claims 16 to 22 to the subject.

25. The method according to claim 23 or claim 24, wherein the infection is human immunodeficiency virus infection and the composition comprises a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

26. The method according to any one of claims 1 to 10, wherein the recombinant virus is selected from the group consisting of a poxvirus, an attenuated vaccinia virus (e.g.

PCT/AU2013/000589
Received 17/07/2014

NYVAC), a fowlpox virus, a canarypox virus, an adenovirus, a live- attenuated virus, and a modified vaccinia Ankara (MVA) virus.

27. The method according to any one of claims 1 to 15, or 23 to 26, wherein the antigen and the interleukin-4 receptor are encoded by the same polynucleotide.

28. The method according to any one of claims 1 to 15, or 23 to 27, wherein the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject for a period of less than less than 1, 2, 3, 4, 5, 6, or 7 days.

29. The method according to any one of claims 1 to 15, 23 to 28, wherein the priming dose is administered to the subject mucosally and the booster dose is administered to the subject intramuscularly, subcutaneously or intravenously.

30. The composition according to any one of claims 16 to 22, wherein the antigen and the interleukin-4 receptor are encoded by the same polynucleotide.

31. The composition according to any one of claims 16 to 22, or 30, wherein the recombinant virus of each said dose transiently expresses the interleukin-4 receptor antagonist in a subject to which the composition is administered for a period of less than less than 1, 2, 3, 4, 5, 6, or 7 days.

32. The composition according to any one of claims 16 to 22, 30, or 31, wherein the priming dose is formulated for mucosal administration, and the booster dose is formulated for intramuscular, subcutaneous, or intravenous administration.

CLAIMS:

1. Use of an antigen in combination with an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for inducing an antigen-specific immune response in a subject, wherein the antigen is to be administered to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist, and wherein:

said administration comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

2. Use of an antigen in combination with an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for increasing the avidity of immune cells for the antigen in a subject, wherein the antigen is to be administered to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist, and wherein:

said administration comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

3. Use of an antigen in combination with an interleukin-4 receptor (IL-4R) antagonist in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for increasing the number of immune cells specific for the antigen in a subject, wherein the antigen is to be administered to the subject in combination with the interleukin-4 receptor (IL-4R) antagonist, and wherein:

said administration comprises expressing one or more polynucleotides encoding the antigen and the interleukin-4 receptor antagonist in the subject in a priming dose and a booster dose,

the one or more polynucleotides is or are a component of a recombinant virus, and

the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject.

4. The use according to claim 2 or claim 3, wherein the immune cells are T-lymphocytes, CD8+ T lymphocytes, and/or B lymphocytes.

5. The use according to claim 1, wherein the antigen-specific immune response comprises T-lymphocytes and/or B-lymphocytes specific for said antigen.

6. The use according to any one of claims 1 to 5, wherein the antigen is a viral antigen.

7. The use according to any one of claims 1 to 6, wherein the antigen is a human immunodeficiency virus antigen.

8. The use according to any one of claims 1 to 7, wherein the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

9. The use according to any one of claims 1 to 8, wherein the antigen and interleukin-4 receptor antagonist of the primer dose are to be administered to the subject sequentially.

10. The use according to any one of claims 1 to 8, wherein the antigen and interleukin-4 receptor antagonist of the primer dose are to be administered to the subject simultaneously.

11. The use according to any one of claims 1 to 10, wherein the IL-4R antagonist of the primer and/or booster dose is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

12. The use according to any one of claims 1 to 11, wherein the IL-4R antagonist of the primer and/or booster dose is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at

residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

13. The use according to any one of claims 1 to 12, wherein the antigen and IL-4R antagonist of the booster dose are to be administered simultaneously.

14. The use according to any one of claims 1 to 12, wherein the antigen and IL-4R antagonist of the booster dose are to be administered sequentially.

15. The use according to claim 12, wherein the mutation is selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

16. A composition comprising:

(i) a polynucleotide encoding an antigen; and

(ii) a polynucleotide encoding an IL-4R antagonist,

wherein:

the composition is formulated for administration to a subject in a priming dose and a booster dose,

each said polynucleotide is a component of a recombinant virus, and

the recombinant virus of each said dose transiently expresses the interleukin-4 receptor antagonist in a subject to which the composition is to be administered.

17. The composition according to claim 16, wherein the antigen is a viral antigen.

18. The composition according to claim 16 or claim 17, wherein the antigen is a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

19. The composition according to any one of claims 16 to 18, wherein the IL-4R antagonist is an interleukin-4 receptor alpha chain (IL-4Rα) antagonist capable of binding to IL-4Rα and preventing IL-4R signalling.

20. The composition according to any one of claims 16 to 19, wherein the IL-4R antagonist is a human interleukin-4 molecule lacking a signal peptide and comprising one or more mutations selected from: a mutation at residue 121, a mutation at residue 124, a deletion of one or more residues after position 123, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

21. The composition according to claim 20, wherein the mutation is selected from: R121D, Y124D, a deletion of a fragment encoded by exon 2 of an interleukin-4 gene, or any combination thereof.

22. The composition according to claim 16, wherein the recombinant virus is selected from the group consisting of a poxvirus, an attenuated vaccinia virus (e.g. NYVAC), a fowlpox virus, a canarypox virus, an adenovirus, a live-attenuated virus, and a modified vaccinia Ankara (MVA) virus.

23. Use of the composition according to any one of claims 16 to 22 in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for preventing or treating an infection in a subject, wherein the pharmaceutical composition or the combination of pharmaceutical compositions is or are to be administered to the subject as a primer dose and a booster dose.

24. Use of the composition according to any one of claims 16 to 22 in the manufacture of a pharmaceutical composition or a combination of pharmaceutical compositions for vaccinating a subject against an infection, wherein the pharmaceutical composition or the combination of pharmaceutical compositions is or are to be administered as a primer dose and a booster dose to the subject.

25. The use according to claim 23 or claim 24, wherein the infection is human immunodeficiency virus infection and the composition comprises a human immunodeficiency virus antigen selected from a gag, pol, or env gene product, or any combination thereof.

26. The use according to any one of claims 1 to 10, wherein the recombinant virus is selected from the group consisting of a poxvirus, an attenuated vaccinia virus (e.g.

NYVAC), a fowlpox virus, a canarypox virus, an adenovirus, a live- attenuated virus, and a modified vaccinia Ankara (MVA) virus.

27. The use according to any one of claims 1 to 15, or 23 to 26, wherein the antigen and the interleukin-4 receptor are encoded by the same polynucleotide.

28. The use according to any one of claims 1 to 15, or 23 to 27, wherein the recombinant virus of the priming dose and the booster dose transiently expresses the interleukin-4 receptor antagonist in the subject for a period of less than less than 1, 2, 3, 4, 5, 6, or 7 days.

29. The use according to any one of claims 1 to 15, 23 to 28, wherein the priming dose is to be administered to the subject mucosally and the booster dose is to be administered to the subject intramuscularly, subcutaneously or intravenously.

30. The composition according to any one of claims 16 to 22, wherein the antigen and the interleukin-4 receptor are encoded by the same polynucleotide.

31. The composition according to any one of claims 16 to 22, or 30, wherein the recombinant virus of each said dose transiently expresses the interleukin-4 receptor antagonist in a subject to which the composition is to be administered for a period of less than less than 1, 2, 3, 4, 5, 6, or 7 days.

32. The composition according to any one of claims 16 to 22, 30, or 31, wherein the priming dose is formulated for mucosal administration and the booster dose is formulated for intramuscular, subcutaneous, or intravenous administration.