An example of the disclosure describes a method of eliciting an immune response to group A streptococcal bacteria in a mammal, said method including the step of administering: an isolated protein comprising a modified p145 peptide amino acid sequence comprising an amino acid substitution of residues 13 and 17 of SEQ ID NO:3; an antibody or antibody fragment that binds or is raised against the isolated protein or fragment or variant thereof; or an isolated nucleic acid encoding the isolated protein or fragment or variant thereof; to the mammal to thereby elicit the immune response.

In one ~~aspect~~example, ~~the present disclosure refers to~~ the use of an: (i) isolated protein comprising (a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18); (b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof; (ii) antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21; or (iii) isolated nucleic acid encoding the protein of (a) or (b), in the manufacture of a medicament for eliciting a mucosal immune response to group A streptococcal bacteria in a mammal; wherein the isolated protein, the antibody or antibody fragment, or the isolated nucleic acid is to be administered to the mammal to thereby elicit the mucosal immune response is described. In another example, there is described the use of an isolated protein comprising a modified p145 peptide amino acid sequence comprising an amino acid substitution of residues 13 and 17 of SEQ ID NO:3; an antibody or antibody fragment that binds or is raised against the isolated protein or fragment or variant thereof; or an isolated nucleic acid encoding the isolated protein or fragment or variant thereof in the manufacture of a medicament for eliciting a mucosal immune response to group A streptococcal bacteria in a mammal; wherein the isolated protein, the antibody or antibody fragment, or the isolated nucleic acid is to be administered to the mammal to thereby elicit the mucosal immune response.

Another example of the disclosure describes a method of inducing immunity against a group A streptococcal bacterial infection in a mammal, said method including the step of administering: an isolated protein comprising a modified p145 peptide amino acid sequence comprising an amino acid substitution of residues 13 and 17 of SEQ ID NO:3; an antibody or antibody fragment that binds or is raised against the isolated protein or fragment or variant thereof; or an isolated nucleic acid encoding the isolated protein or fragment or variant thereof;

to the mammal to thereby induce immunity against the group A streptococcal bacterial infection in the mammal.

In another ~~aspect~~example, ~~the present disclosure refers to~~ the use of an: (i) isolated protein comprising (a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18); (b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof; (ii) antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21; or (iii) isolated nucleic acid encoding the protein of (a) or (b), in the manufacture of a medicament for inducing mucosal immunity against a group A streptococcal bacterial infection in a mammal; wherein the isolated protein, the antibody or antibody fragment, or the isolated nucleic acid is to be administered to the mammal to thereby induce mucosal immunity against the group A streptococcal bacterial infection in the mammal is described. In yet another aspect, the present disclosure refers to the use of an: (i) isolated protein comprising (a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18); (b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof; ~~(ii) antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21;~~ or (ii~~i~~) isolated nucleic acid encoding the protein of (a) or (b), in the manufacture of a medicament for treating or preventing a group A streptococcal bacterial infection in a mammal; wherein the isolated protein, ~~the antibody or antibody fragment,~~ or the isolated nucleic acid is to be intramuscularly administered to the mammal to thereby prevent or treat the group A streptococcal bacterial infection in the mammal, and wherein intramuscular administration of the isolated protein or the isolated nucleic acid elicits a mucosal immune response and/or induces mucosal immunity to the group A streptococcal bacterial infection in the mammal. In one example, there is described the use of an isolated protein comprising a modified p145 peptide amino acid sequence comprising an amino acid substitution of residues 13 and 17 of SEQ ID NO:3; an antibody or antibody fragment that binds or is raised against the isolated protein or fragment or variant thereof; or an isolated nucleic acid encoding the isolated protein or fragment or variant thereof in the manufacture of a medicament for inducing mucosal immunity against a group A streptococcal bacterial infection in a mammal; wherein the isolated protein, the antibody or antibody fragment, or the isolated nucleic acid is to be administered to the

Suitably, the mucosal immune response is characterized by the production of IgG. Typically, IgA production is substantially absent or at a relatively reduced level compared to the level of IgG produced.

Preferably, the modified p145 peptide, fragment or variant elicits a mucosal immune response upon intramuscular administration to the mammal.

Preferably, the mammal of the aforementioned examples is a human.

In a particular example of the aforementioned examples, the modified p145 peptide, fragment or variant may be administered in combination with an immunogenic fragment of a SpyCEP protein. Preferably, the fragment of SpyCEP is, or comprises an S2 peptide (SEQ ID NO:23) or a variant such as a K4S2 peptide (SEQ ID NO:24).

In yet another aspect, the present disclosure refers to a composition comprising: (i) an isolated protein comprising: (a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18); (b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof; ~~(ii) an antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21;~~ or (~~i~~ii) an isolated nucleic acid encoding the isolated protein of (a) or (b); and an immunogenic fragment of a SpyCEP protein, ~~an antibody or antibody fragment that binds or is raised against the SpyCEP immunogenic fragment,~~ or an isolated nucleic acid that encodes the SpyCEP immunogenic fragment wherein the composition is formulated for (a) eliciting a mucosal immune response to group A streptococcal bacteria in a mammal; (b) inducing mucosal immunity against a group A streptococcal bacterial infection in a mammal; or (c) treating or preventing a group A streptococcal bacterial infection in a mammal by eliciting a mucosal immune response, or inducing mucosal immunity to the group A streptococcal bacterial infection in the mammal, and wherein the composition is formulated for intramuscular administration. In one example, there is described a composition comprising: an isolated protein comprising: an isolated protein comprising a modified p145 peptide amino acid sequence comprising an amino acid substitution of residues 13 and 17 of SEQ ID NO:3, a fragment or variant thereof, an antibody or antibody fragment that binds or is raised against the isolated protein or fragment or variant thereof or an isolated nucleic acid encoding the isolated protein or fragment or variant thereof; and an immunogenic fragment of a SpyCEP protein or variant thereof, an antibody or antibody fragment that binds or is raised against the SpyCEP

immunogenic fragment or variant thereof or an isolated nucleic acid that encodes the SpyCEP immunogenic fragment or variant thereof.

A related example of the disclosure therefore provides a composition comprising: an isolated protein comprising a modified p145 peptide amino acid sequence comprising an amino acid substitution of residues 13 and 17 of SEQ ID NO:3, a fragment or variant thereof, an antibody or antibody fragment that binds or is raised against the isolated protein or fragment or variant thereof or an isolated nucleic acid encoding the isolated protein or fragment or variant thereof; and an immunogenic fragment of a SpyCEP protein or variant thereof, an antibody or antibody fragment that binds or is raised against the SpyCEP immunogenic fragment or variant thereof or an isolated nucleic acid that encodes the SpyCEP immunogenic fragment or variant thereof.

Suitably, the modified p145 peptide amino acid sequence comprises an asparagine (N) amino acid at residue 13 and an arginine (R) amino acid at residue 17, preferably comprising the amino acid sequence set forth in SEQ ID NO:1. Preferably, the fragment of the modified p145 peptide comprises the amino acid sequence set forth in SEQ ID NO:2.

In a preferred example, the fragment of SpyCEP is, or comprises an S2 peptide comprising the amino acid sequence set forth in SEQ ID NO:23, or a variant thereof. The variant may be a K4S2 peptide comprising the amino acid sequence set forth in SEQ ID NO:24.

In another aspect, the present disclosure refers to the use of an: (i) isolated protein comprising:(a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18); (b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, or (ii) isolated nucleic acid encoding the protein of (a) or (b), in the manufacture of a medicament for preventing or treating a group A streptococcal skin infection, a group A streptococcal intranasal infection, or an invasive group A streptococcal infection in a mammal; wherein the isolated protein or the isolated nucleic acid is to be parentally administered to the mammal.

CLAIMS

~~1. Use of an:~~

~~(i) isolated protein comprising~~

~~(a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18);~~

~~(b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof;~~

~~(ii) antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21; or~~

~~(iii) isolated nucleic acid encoding the protein of (a) or (b),~~

~~in the manufacture of a medicament for eliciting a mucosal immune response to group A streptococcal bacteria in a mammal; wherein the isolated protein, the antibody or antibody fragment, or the isolated nucleic acid is to be administered to the mammal to thereby elicit the mucosal immune response.~~

~~2. Use of an:~~

~~(i) isolated protein comprising~~

~~(a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18);~~

~~(b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof;~~

~~(ii) antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21; or~~

~~(iii) isolated nucleic acid encoding the protein of (a) or (b),~~

~~in the manufacture of a medicament for inducing mucosal immunity against a group A streptococcal bacterial infection in a mammal; wherein the isolated protein, the antibody or antibody fragment, or the isolated nucleic acid is to be administered to the mammal to thereby induce mucosal immunity against the group A streptococcal bacterial infection in the mammal.~~

1~~3~~. Use of an:

(i) isolated protein comprising

~~(~~a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18);

(b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof~~,~~

~~(ii) antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21~~; or

(i~~i~~i) isolated nucleic acid encoding the protein of (a) or (b),

in the manufacture of a medicament for treating or preventing a group A streptococcal bacterial infection in a mammal; wherein the isolated protein~~, the antibody or antibody fragment~~, or the isolated nucleic acid is to be intramuscularly administered to the mammal to thereby prevent or treat the group A streptococcal bacterial infection in the mammal, and wherein intramuscular administration of the isolated protein or the isolated nucleic acid elicits a mucosal immune response and/or induces mucosal immunity to the group A streptococcal bacterial infection in the mammal.

2. The use of claim 1, wherein the group A streptococcal bacterial infection is a group A streptococcal skin infection, a group A streptococcal intranasal infection or an invasive group A streptococcal infection.

3. The use of claim 1 or claim 2, wherein the group A streptococcal bacterial infection is selected from the group consisting of cellulitis, erysipelas, impetigo, scarlet fever, a throat infection, acute pharyngitis, bacteraemia, toxic shock syndrome, necrotizing fasciitis, acute rheumatic fever, acute glomerulonephritis and any combination thereof.

~~4. The use of claim 1, comprising an initial step of identifying a mammal requiring elicitation of a mucosal immune response to group A streptococcal bacteria.~~

~~5. The use of claim 2, comprising an initial step of identifying a mammal requiring induction of mucosal immunity to group A streptococcal bacteria.~~

~~6. The use of claim 3, comprising an initial step of identifying a mammal requiring treatment or prevention of group A streptococcal bacteria.~~

~~7. The use of any one of the preceding claims, wherein the medicament is to be administered to the mammal intramuscularly and/or subcutaneously.~~

4~~8~~. The use of any one of ~~the preceding~~ claims 1 to 3, wherein a single immunization of the mammal with said medicament provides the mammal with protection against group A streptococcal bacterial skin disease.

5. The use of any one of claims 1 to 3, wherein a single immunization of the mammal with said medicament provides the mammal with protection against a group A streptococcal skin infection.

6. The use of any one of claims 1 to 3, wherein a single immunization of the mammal with said medicament provides the mammal with protection against a group A streptococcal intranasal infection.

7. The use of any one of claims 1 to 3, wherein a single immunization of the mammal with said medicament provides the mammal with protection against an invasive group A streptococcal infection.

8~~9~~. The use of any one of ~~the preceding~~ claims 1 to 7, wherein the carrier protein~~, fragment or epitope thereof~~ comprises thyroglobulin, albumin, a toxin, a toxoid or any mutant cross-reactive material (CRM).

9. ~~, preferably~~The use of any one of claims 1 to 8, wherein the carrier protein comprises a toxin from tetanus, diphtheria, pertussis, *Pseudomonas*, *E. coli*, *Staphylococcus* or *Streptococcus*~~, or a fragment or epitope thereof, or said carrier protein comprises an amino acid sequence not found in Group A Streptococcus~~.

10. The use of ~~claim 8 or~~ claim 9, wherein the carrier protein is diphtheria toxoid.

11. The use of any one of ~~the preceding~~ claims 1 to 10, wherein the medicament further comprises an immunogenic fragment of a SpyCEP protein or wherein an immunogenic fragment of a SpyCEP protein is to be co-administered to the mammal.

12. The use of claim 11, wherein the immunogenic fragment of the SpyCEP protein comprises:

(i) the SpyCEP peptide of SEQ ID NO:23;

(ii) a SpyCEP peptide variant consisting of an amino acid sequence at least 90% identical to SEQ ID NO: 23;

(iii) the SpyCEP peptide of (i) or the SpyCEP peptide variant of (ii) further consisting of one or a plurality of lysine residues at an N- and/or C-terminus thereof;

(iv) the K4S2 peptide of SEQ ID NO:24; or

(v) any one of (i) to (iv) conjugated to a carrier protein~~, fragment or epitope thereof~~.

13. A composition comprising:

(i) an isolated protein comprising:

(a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18);

(b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, fragment or epitope thereof; or

~~(ii) an antibody or antibody fragment that binds or is raised against the sequence of SEQ ID NO: 1 or SEQ ID NO: 21; or~~

(~~i~~iii) an isolated nucleic acid encoding the isolated protein of (a) or (b); and an immunogenic fragment of a SpyCEP protein, ~~an antibody or antibody fragment that binds or is raised against the SpyCEP immunogenic fragment,~~ or an isolated nucleic acid that encodes the SpyCEP immunogenic fragment,

wherein the composition is formulated for (a) eliciting a mucosal immune response to group A streptococcal bacteria in a mammal; (b) inducing mucosal immunity against a group A streptococcal bacterial infection in a mammal; or (c) treating or preventing a group A streptococcal bacterial infection in a mammal by eliciting a mucosal immune response, or inducing mucosal immunity to the group A streptococcal bacterial infection in the mammal~~.~~

~~14. The composition of claim 13, being~~, and wherein the composition is formulated for intramuscular ~~and/or subcutaneous~~ administration.

14~~15~~. The composition of claim 13~~ or 14~~, being formulated to achieve protection against group A streptococcal bacterial skin disease by way of single immunization of the mammal.

15. The composition of claim 13, being formulated to achieve protection against group A streptococcal skin infection by way of a single immunization of the mammal.

16. The composition of claim 13, being formulated to achieve protection against group A streptococcal intranasal infection by way of a single immunization of the mammal.

17. The composition of claim 13, being formulated to achieve protection against invasive group A streptococcal infection by way of a single immunization of the mammal.

18~~16~~. The composition of any one of claims 13~~13~~-17~~15~~, wherein the immunogenic fragment of the SpyCEP protein comprises:

(i) the SpyCEP peptide of SEQ ID NO: 23;

(ii) a SpyCEP peptide variant consisting of an amino acid sequence at least 90% identical to SEQ ID NO: 23;

(iiii) the SpyCEP peptide of (i) or the SpyCEP peptide variant of (ii) further consisting of one or a plurality of lysine residues at an N- and/or C-terminus thereof;

(iv) the K4S2 peptide of SEQ ID NO:24; or

(v) any one of (i) to (iv) conjugated to a carrier protein, fragment or epitope thereof.

19~~17~~. The use of any one of claims 1-12, or the composition of any one of claims 13-18~~16~~, wherein ~~said~~ the sequence is SEQ ID NO:1 (p*17).

20. Use of an:

(i) isolated protein comprising:

(a) the sequence of SEQ ID NO: 1 (p*17) or SEQ ID NO: 21 (p*18);

(b) the sequence of SEQ ID NO: 1 or SEQ ID NO: 21 conjugated to a carrier protein, or

(ii) isolated nucleic acid encoding the protein of (a) or (b),

in the manufacture of a medicament for preventing or treating a group A streptococcal skin infection, a group A streptococcal intranasal infection, or an invasive group A streptococcal infection in a mammal; wherein the isolated protein or the isolated nucleic acid is to be parentally administered to the mammal.