In an aspect, there is provided the use of photon-irradiated killed streptococcal bacteria subjected to photon-radiation at energies of at least 0.01MeV in the manufacture of a medicament for preventing or treating an infection by streptococcal bacteria in a subject, wherein the streptococcal bacteria are streptococcal derivatives comprising a genetic alteration that reduces pathogenicity, the alteration is in a gene that confers a nutrient/cofactor requirement for growth, and the gene is *S. pneumoniae* pneumococcal surface antigen A (psaA) or a homologous gene in other streptococcal bacteria.

In another aspect, there is provided a vaccine composition comprising photon-irradiated killed streptococcal bacteria subjected to photon-radiation at energies of at least 0.01MeV and a pharmaceutically-acceptable excipient, diluent and/or carrier, wherein:

(i) the photon-irradiated streptococcal bacteria comprise mutant streptococcal bacteria comprising one or more defective DNA repair proteins, and/or mutant streptococcal bacteria in which at least one type of DNA repair protein is absent; and/or

(ii) the photon-irradiated streptococcal bacteria comprise modified streptococcal bacteria comprising a sequence of DNA encoding an RNA transcript, wherein the RNA transcript comprises a region of self-complementarity capable of forming a double-stranded portion after transcription;

wherein the streptococcal bacteria are streptococcal derivatives comprising a genetic alteration that reduces pathogenicity, the alteration is in a gene that confers a nutrient/cofactor requirement for growth, and the gene is *S. pneumoniae* psaA or a homologous gene in other streptococcal bacteria. In another aspect, the present invention refers to a method of preparing the vaccine composition according to the present invention, the method comprising (i) photon-irradiating a preparation of streptococcal bacteria with photon-radiation at energies of at least 0.01MeV to thereby kill the bacteria; and (ii) combining the photon-irradiated streptococcal bacteria with a pharmaceutically-acceptable excipient, diluent and/or carrier.

Accordingly, the disclosure relates to at least the following embodiments:

CLAIMS

1. Use of photon-irradiated killed streptococcal bacteria subjected to photon-radiation at energies of at least 0.01MeV in the manufacture of a medicament for preventing or treating an infection by streptococcal bacteria in a subject, wherein the streptococcal bacteria are streptococcal derivatives comprising a genetic alteration that reduces pathogenicity, the alteration is in a gene that confers a nutrient/cofactor requirement for growth, and the gene is *S. pneumoniae* pneumococcal surface antigen A (psaA) or a homologous gene in other streptococcal bacteria.

2. The use according to claim 1, wherein:

(a) the medicament prevents or treats infection by a plurality of different streptococcal species and/or serotypes; and/or

(b) the photon-irradiated streptococcal bacteria comprise different: *Streptococcus* species, streptococcal serotypes, and/or streptococcal derivatives.

3. The use according to claim 1 or claim 2, wherein:

(a) the streptococcal infection comprises infection by one or more serotypes of *Streptococcus pneumoniae*; and/or

(b) the infection by streptococcal bacteria is any one or more of a respiratory tract infection, pneumonia, an ear infection, an ear-ache, a middle ear infection, otitis media, sinusitis, meningitis, conjunctivitis, bacteraemia, septicaemia, a joint infection, a bone infection, septic arthritis, sepsis, osteomyelitis, a soft tissue infection, cellulitis, myositis, periorbital cellulitis, an abscess, necrotising fasciitis, impetigo, peritonitis, a cardiac infection, endocarditis, and/or pericarditis.

4. The use according to any one of claims 1 to 3, wherein the photon-irradiated streptococcal bacteria comprise:

(a) at least one *Streptococcus pneumoniae* serotype, or at least one unencapsulated derivative of a *Streptococcus pneumoniae* serotype; and/or

(b) mutant streptococcal bacteria comprising:

  (i) one or more defective DNA repair proteins; and/or

  (ii) a genetic alteration causing defective DNA repair capacity.

5. The use according to claim 4, wherein the photon-irradiated mutant streptococcal bacteria comprise a defect in at least one gene that encodes a DNA repair protein.

6. The use according to claim 5, wherein the photon-irradiated mutant streptococcal bacteria are *Streptococcus pneumoniae* mutants comprising a defect in one or more genes selected from a gene encoding a DNA alkylation repair protein, a gene encoding DNA polymerase 4, *hexA*, *hexB*, *mutS*, *radC*, *recA*, *recF*, *recN*, *recO*, *uvrA*, *uvrB*, *uvrC* or *uvrD*.

7. The use according to claim 5 or claim 6, wherein the photon-irradiated mutant streptococcal bacteria comprise streptococcal Rx1 strain derivatives in which:

(i) psaA protein is defective and any one or more of autolysin, hemolysin, pneumolysin protein is/are defective; and/or

(ii) psaA protein is absent and any one or more of autolysin, hemolysin protein is/are absent.

8. The use according to claim 7, wherein the photon-irradiated streptococcal Rx1 strain derivatives:

(i) comprise a gene encoding defective pneumococcal surface antigen A (psaA) and any one or more of a gene encoding a defective autolysin protein, a gene encoding defective hemolysin, a gene encoding defective pneumolysin protein; or

(ii) are derivatives in which a gene encoding psaA protein and any one or more of a gene encoding autolysin, a gene encoding hemolysin protein is/are absent; and/or

(iii) comprise a gene encoding defective LytA protein, and a gene encoding defective pneumolysin; and/or

(iv) do not contain the *lytA* gene, and comprise a gene encoding a defective pneumolysin.

9. The use according to claim 7 or claim 8, wherein the autolysin is LytA.

10. The use according to any one of claims 1 to 9, wherein some or all of the photon-irradiated streptococcal bacteria comprise modified streptococcal bacteria comprising a sequence of DNA encoding an RNA transcript, wherein the RNA transcript comprises aregion of self-complementarity capable of forming a double-stranded portion after transcription.

11. The use according to claim 10, wherein the portion of the double-stranded RNA transcript is at least: 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65 or 70 base pairs in length.

12. The use according to any one of claims 1 to 11, wherein the photon-irradiated streptococcal bacteria comprise:

(a) auxotrophic mutant streptococcal bacteria; and/or

(b) at least one recombinant DNA portion encoding an antigen or a component thereof that:

(i) inactivates or attenuates the bacteria; and/or

(ii) induces or enhances an immune response in the subject.

13. The use according to claim 12, wherein the recombinant DNA portion replaces or disrupts an endogenous gene necessary for pathogenicity, infection, multiplication, growth *in vivo*, or any combination thereof.

14. The use according to any one of claims 1 to 13, wherein:

(a) the photon-irradiated streptococcal bacteria comprise whole killed streptococcal bacteria; and/or

(b) the photon-irradiated streptococcal bacteria are to be administered to the subject mucosally or intranasally; and/or

(c) the photon-irradiated streptococcal bacteria are to be administered to the subject in combination with an adjuvant; and/or

(d) one, two or three separate doses of the photon-irradiated streptococcal bacteria are to be administered to the subject; and/or

(e) the subject is a human; and/or

(f) the photon-irradiated streptococcal bacteria are to be administered a total dosage of at least: 8 kilogray (kGy), 9kGy, 10kGy, 11kGy, 12kGy, 15kGy, 20kGy, 25kGy, 30 kGy, 40kGy, or 50 kGy of photon-irradiation.

15. The use according to any one of claims 1 to 14, wherein the photon-irradiated streptococcal bacteria comprise gamma-irradiated streptococcal bacteria, X-irradiated streptococcal bacteria, or a combination thereof.

16. The use according to any one of claims 1 to 15, wherein the photon-irradiated streptococcal bacteria comprise streptococcal Rx1 strain derivatives: (i) comprise a gene

encoding a defective LytA protein, a gene encoding defective pneumolysin, and a gene encoding defective psaA protein;

(ii) comprise a gene encoding a defective LytA protein, a gene encoding defective pneumolysin, and in which a gene encoding psaA protein is absent;

(iii) comprise a gene encoding a defective psaA protein, a gene encoding defective pneumolysin, and in which a gene encoding LytA protein is absent; or

(iv) comprise a gene encoding defective pneumolysin, in which a gene encoding LytA protein is absent, and in which a gene encoding psaA protein is absent.

17. A vaccine composition comprising photon-irradiated killed streptococcal bacteria subjected to photon-radiation at energies of at least 0.01MeV and a pharmaceutically-acceptable excipient, diluent and/or carrier, wherein:

(i) the photon-irradiated streptococcal bacteria comprise mutant streptococcal bacteria comprising one or more defective DNA repair proteins, and/or mutant streptococcal bacteria in which at least one type of DNA repair protein is absent; and/or

(ii) the photon-irradiated streptococcal bacteria comprise modified streptococcal bacteria comprising a sequence of DNA encoding an RNA transcript, wherein the RNA transcript comprises a region of self-complementarity capable of forming a double-stranded portion after transcription;

wherein the streptococcal bacteria are streptococcal derivatives comprising a genetic alteration that reduces pathogenicity, the alteration is in a gene that confers a nutrient/cofactor requirement for growth, and the gene is *S. pneumoniae* psaA or a homologous gene in other streptococcal bacteria.

18. The vaccine composition according to claim 17, wherein:

(a) the mutant streptococcal bacteria are *Streptococcus pneumoniae* mutants comprising a defect in one or more genes selected from a gene encoding a DNA alkylation repair protein, a gene encoding DNA polymerase 4, *hexA*, *hexB*, *mutS*, *radC*, *recA*, *recF*, *recN*, *recO*, *uvrA*, *uvrB*, *uvrC* or uvrD; and/or

(b) the modified streptococcal bacteria are modified *Streptococcus pneumoniae* bacteria and the portion of the double-stranded RNA transcript is at least. 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65 or 70 base pairs in length; and/or

(c) the photon-irradiated streptococcal bacteria comprise at least one recombinant DNA portion encoding an antigen or a component thereof that:

(i) inactivates or attenuates the bacteria; or

(ii) induces or enhances an immune response in the subject; and/or

(d) the photon-irradiated streptococcal bacteria comprise streptococcal Rx1 strain derivative strains in which:

(i) a psaA protein is defective and any one or more of autolysin, hemolysin, pneumolysin protein is/are defective; and/or

(ii) a psaA protein is absent and any one or more of autolysin, hemolysin protein is/are absent.

(e) the photon-irradiated mutant streptococcal bacteria comprise streptococcal Rx1 strain derivatives which:

(i) comprise a gene encoding a defective LytA protein, a gene encoding defective pneumolysin, and a gene encoding defective psaA protein;

(ii) comprise a gene encoding a defective LytA protein, a gene encoding defective pneumolysin, and in which a gene encoding psaA protein is absent;

(iii) comprise a gene encoding a defective psaA protein, a gene encoding defective pneumolysin, and in which a gene encoding LytA protein is absent; or

(iv) comprise a gene encoding defective pneumolysin, in which a gene encoding LytA protein is absent, and in which a gene encoding psaA protein is absent.

19. The vaccine composition according to claim 17 or claim 18, wherein the photon-irradiated streptococcal bacteria comprise X-irradiated mutant streptococcal bacteria and/or X-irradiated modified streptococcal bacteria.

20. A method of preparing the vaccine composition according to any one of claims 17 to 19, the method comprising:

(i) photon-irradiating a preparation of streptococcal bacteria with photon-radiation at energies of at least 0.01MeV to thereby kill the bacteria; and

(ii) combining the photon-irradiated streptococcal bacteria with a pharmaceutically-acceptable excipient, diluent and/or carrier.