that superantigen antibody titres of > 40 in the IVIG are required for clinical benefit. This is approximately the amount of specific antibody that is found in IVIG and as such multiple doses of IVIG are recommended. The high costs of IVIG, batch to batch variation [8] and difficulties in supply underscore the need for alternative adjunctive therapies.

SUMMARY

Surprisingly, the present inventors have discovered that antibodies or antibody fragments that bind a group A streptococcus M protein fragment or variant thereof with or without antibodies or antibody fragments that bind a group A streptococcus superantigen fragment or variant thereof are surprisingly efficacious against a group A streptococcus-associated disease disorder or condition such as streptococcal toxic shock syndrome.

In one aspect, the present disclosure refers to a use of an antibody or antibody fragment that binds or is raised against a group A streptococcus M protein fragment, or a variant or derivative thereof and optionally an antibody or antibody fragment that binds or is raised against a group A streptococcus superantigen protein, fragment, variant or derivative thereof, in the manufacture of a medicament for passively immunizing against, treating or preventing an invasive group A streptococcus disease (iGAS) in a mammal, such as streptococcal toxic shock syndrome (STSS), wherein the M protein fragment is or comprises a conserved region of the M protein.

In another aspect, the present disclosure refers to a use of an antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein fragment, or a variant or derivative thereof, and an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof, in the manufacture of a medicament for passively immunizing against, treating or preventing an invasive group A streptococcus disease (iGAS) in a mammal, such as streptococcal toxic shock syndrome (STSS), wherein the M protein fragment is or comprises a conserved region of the M protein.

In another aspect, the present disclosure refers to a composition formulated for administration to a mammal, said composition comprising: an antibody or antibody fragment that binds, or is raised against, a group A

streptococcus M protein fragment, or a variant or derivative thereof, wherein the M protein fragment is or comprises a conserved region of the M protein; and an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof

In a broad form, the disclosure therefore relates to use of antibodies or antibody fragments that bind a group A streptococcus M protein, fragment, variant or derivative thereof and optionally an antibody or antibody fragment that binds a group A streptococcus superantigen protein, fragment, variant or derivative thereof to passively immunize against, treat or prevent a group A streptococcus-associated disease disorder or condition such as invasive GAS (iGAS) disease inclusive of streptococcal toxic shock syndrome (STSS).

In another broad form, the disclosure relates to the use of a group A streptococcus M protein fragment, variant or derivative thereof and optionally a group A streptococcus superantigen protein, fragment, variant or derivative thereof to vaccinate or immunize against, treat or prevent a group A streptococcus-associated disease disorder or condition such as invasive GAS (iGAS) disease inclusive of streptococcal toxic shock syndrome (STSS).

An example of the disclosure provides a method of passively immunizing a mammal against streptococcal toxic shock syndrome, said method including the step of administering to the mammal: an antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein, fragment, variant or derivative thereof, to thereby passively immunize the mammal against streptococcal toxic shock syndrome in the mammal.

In one particular example, the method further includes the step of administering an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen to the mammal.

Another example of the disclosure provides a method of treating or preventing streptococcal toxic shock syndrome in a mammal, said method including the step of administering to the mammal: a group A streptococcus M protein, fragment, variant or derivative thereof and/or an antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein, fragment, variant or derivative thereof to thereby treat or prevent streptococcal toxic shock syndrome in the mammal.

In one particular example, the method further includes the step of administering a group A streptococcus superantigen protein, fragment, variant or derivative thereof and/or an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof to the mammal.

A further example of the disclosure provides a composition suitable for administration to a mammal, said composition comprising: an antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein, fragment, variant or derivative thereof.

In one example, the composition further comprises an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof.

For the aforementioned examples, the antibody or antibody fragment is suitably a monoclonal antibody or antibody fragment. In one particular example, the monoclonal antibody or antibody fragment is a recombinant humanized monoclonal antibody or fragment thereof.

In a related example, the disclosure resides in a composition suitable for administration to a mammal, said composition comprising: a group A streptococcus M protein, fragment, variant or derivative thereof and a group A streptococcus superantigen protein, fragment, variant or derivative thereof.

A further related example of the disclosure provides a monoclonal antibody or fragment thereof which binds, or is raised against, a group A streptococcus M protein, fragment, variant or derivative thereof; and/or an antibody or antibody

fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof.

Preferably, the monoclonal antibody or fragment is a recombinant humanized monoclonal antibody or fragment thereof.

This example also provides an isolated nucleic acid encoding the recombinant humanized monoclonal antibody or fragment thereof, a genetic construct comprising the isolated nucleic acid and/or a host cell comprising the genetic construct.

In a particular example, the M protein fragment is or comprises a conserved region of the M protein. In one example, the M protein fragment is, comprises, or is contained within a p145 peptide.

In one particular example, the M protein fragment is, is contained within, or comprises, a J8 peptide, fragment, variant or derivative thereof.

In another particular example, the fragment is, is contained within, or comprises, a p17 peptide, fragment, variant or derivative thereof.

In another particular example, the superantigen is streptococcal pyrogenic exotoxin (Spe) A or SpeC.

Suitably, according to the aforementioned examples the mammal is a human.

As used herein, the indefinite articles '*a*' and '*an*' are used here to refer to or encompass singular or plural elements or features and should not be taken as meaning or defining "one" or a "single" element or feature.

Unless the context requires otherwise, the terms "*comprise*", "*comprises*" and "*comprising*", or similar terms are intended to mean a non-exclusive inclusion, such that a recited list of elements or features does not include those stated or listed elements solely, but may include other elements or features that are not listed or stated.

By "*consisting essentially of*" in the context of an amino acid sequence is meant the recited amino acid sequence together with an additional one, two or three amino acids at the N- or C-terminus.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: (A-B) Infectivity of GAS SN1 in HLA-B6 mice. Naïve HLA-B6 and B6 mice (n=10/group) were infected with GAS SN1 via skin. On day 6-post infection mice were culled and skin bacterial burdens were assessed (A). The

CLAIMS

1. Use of an antibody or antibody fragment that binds or is raised against a group A streptococcus M protein fragment, or a variant or derivative thereof and optionally an antibody or antibody fragment that binds or is raised against a group A streptococcus superantigen protein, fragment, variant or derivative thereof, in the manufacture of a medicament for passively immunizing against, treating or preventing an invasive group A streptococcus disease (iGAS) in a mammal, such as streptococcal toxic shock syndrome (STSS), wherein the M protein fragment is or comprises a conserved region of the M protein.

2. Use of an antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein fragment, or a variant or derivative thereof, and an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof, in the manufacture of a medicament for passively immunizing against, treating or preventing an invasive group A streptococcus disease (iGAS) in a mammal, such as streptococcal toxic shock syndrome (STSS), wherein the M protein fragment is or comprises a conserved region of the M protein.

3. The use of claim 1 or claim 2, wherein the iGAS is STSS.

4. A composition formulated for administration to a mammal, said composition comprising:

an antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein fragment, or a variant or derivative thereof, wherein the M protein fragment is or comprises a conserved region of the M protein; and

an antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof.

5. The use of any one of claims 1-3, or the composition of claim 4, wherein the M protein fragment is, comprises, or is contained within a p145 peptide.

6. The use of any one of claims 1-3, or the composition of claim 4, wherein the M protein fragment is, comprises, or is contained within a J8 peptide, fragment, variant or derivative thereof.

7. The use of any one of claims 1-3, or the composition of claim 4, wherein the M protein fragment is, comprises, or is contained within a p17 peptide, fragment, variant or derivative thereof.

8. The use of any one of claims 1-3, or the composition of claim 4, wherein the M protein fragment is, comprises, or is contained within an amino acid sequence selected from the group consisting of SEQ ID NOs:1-10 and 13 to 29.

9. The use of any one of claims 1-3 and 5-8, or the composition of any one of claims 4-8, wherein the superantigen is streptococcal pyrogenic exotoxin (Spe) A or SpeC.

10. The use of any one of claims 1-3 and 5-9, or the composition of any one of claims 4-9, wherein the antibody or antibody fragment that binds, or is raised against, a group A streptococcus M protein, fragment, variant or derivative thereof is a monoclonal antibody or antibody fragment.

11. The use of any one of claims 1-3 and 5-9, or the composition of any one of claims 4-9, wherein the antibody or antibody fragment that binds, or is raised against, a group A streptococcus superantigen protein, fragment, variant or derivative thereof is a monoclonal antibody or antibody fragment.

12. The use of claim 10 or claim 11, or the composition of claim 10 or claim 11, wherein the antibody or antibody fragment is a humanized monoclonal antibody or antibody fragment.

13. The use of any one of claims 1-3 and 5-12, or the composition of any one of claims 4-12, wherein the mammal is a human.