raised against *S. pneumoniae*, termed anticapsular antibodies, are recognized as protective in adult and immunocompetent individuals. However, children under 2 years of age and immunocompromised individuals, including the elderly, do not respond well to T-cell independent antigens and, therefore, are not afforded optimal protection by PPV-23. A second *S. pneumoniae* vaccine, Prevnar, includes bacterial polysaccharides from 7 *S. pneumoniae* strains conjugated to the diphtheria toxoid protein. This vaccine induces both B and T cell responses. However, because it only protects against 7 pneumococcal serotypes, serotype replacement can render Prevnar ineffective. PPV-23 suffers from the same limitation. Serotype replacement has already been demonstrated in several clinical trials and epidemiologic studies, and raises the possibility that different formulations of the vaccines will need to be developed, presumably at even higher cost. Furthermore, both PPV-23 and Prevnar are expensive to manufacture, greatly limiting their availability in the developing world.

Thus, there remains a need to design more effective pharmaceutical compositions than the current strategies offer. In particular, such compositions need to incorporate novel or specific antigens that elicit an immune response against *S. pneumoniae*.

II. Summary

In a first aspect of the present disclosure, there is provided a vaccine formulation comprising a pharmaceutically acceptable carrier and

(a) one or more polypeptides comprising an amino acid sequence having at least 95% identity to any of SEQ ID NOS: 9, 10, 20, and 21 or an immunogenic fragment thereof, or

(b) one or more polypeptides comprising any of SEQ ID NOS: 9, 10, 20 and 21, or an immunogenic fragment thereof.

In a second aspect of the present disclosure, there is provided an immunogenic composition comprising a pharmaceutically acceptable carrier and two or more polypeptides having amino acid sequences comprising any of SEQ ID NOS: 1-23 and SP1574, SP1655, SP2106, SP1473, SP0605, SP1177, SP0335,

SP0906, SP1828, SP2157, SP1229, SP1128, SP1836, SP1865, SP0904, SP0765, SP1634, SP0418, SP1923, SP1313, SP0775, SP0314, SP0912, SP0159, SP0910, SP2148, SP1412, SP0372, SP1304, SP2002, SP0612, SP1988, SP0484, SP0847, SP1527, SP0542, SP0441, SP0350, SP0014, SP1965, SP0117, SP0981, SP2229, SP2136, SP1179, SP1174, SP2216, SP1393, SP0641.1, SP1384, and SP2032, or an immunogenic fragment thereof, wherein at least one of the polypeptides has an amino acid sequence having at least 95% identity to any one of SEQ ID NOS: 9, 10, 20, and 21, or comprises any one of SEQ ID NOS: 9, 10, 20 and 21.

Streptococcus pneumoniae is a major health concern, especially in very young, elderly, or immunocompromised patients. While DNA and protein sequence information for *S. pneumoniae* has been known for some time, and researchers have long attempted to produce vaccines against *S. pneumoniae*, a major problem was how to identify protective polypeptides from among the approximately 2100 genes in the *S. pneumoniae* genome. The instant application presents the results of whole-genome screens designed to identify the most immunogenic proteins in the *S. pneumoniae* genome. Several of the hits from the screen have been shown to protect against *S. pneumoniae* colonization in a mouse model. Accordingly, the present disclosure provides, *inter alia*, certain highly effective vaccines in *Streptococcus pneumoniae*. The vaccines may be used therapeutically or prophylactically. The

CLAIMS

We claim:

1. A vaccine formulation comprising a pharmaceutically acceptable carrier and

(a) one or more polypeptides comprising an amino acid sequence having at least 95% identity to any of SEQ ID NOS: 9, 10, 20, and 21 or an immunogenic fragment thereof, or

(b) one or more polypeptides comprising any of SEQ ID NOS: 9, 10, 20 and 21, or an immunogenic fragment thereof.

2. The vaccine formulation of claim 1, wherein the vaccine formulation comprises at least two different polypeptides, wherein at least one of said polypeptides has an amino acid sequence comprising one of SEQ ID NOS: 9, 10, 20, and 21 or an immunogenic fragment thereof.

3. The vaccine formulation of claim 2, wherein each of the at least two different polypeptides belongs to a different group of (i)-(vi):

(i) SEQ ID NO: 9, 10, 20, and 21 or an immunogenic fragment thereof,

(ii) one of SEQ ID NOS: 2-5 or an immunogenic fragment thereof,

(iii) one of SEQ ID NOS: 6-7 or an immunogenic fragment thereof,

(iv) SEQ ID NO: 8 or an immunogenic fragment thereof,

(v) SEQ ID NO: 1 or an immunogenic fragment thereof, and

(vi) one of SEQ ID NO: 11-13 or an immunogenic fragment thereof.

4. The vaccine formulation of claim 1, wherein the vaccine formulation comprises at least three different polypeptides, wherein at least one of said polypeptides has an amino acid sequence comprising one of SEQ ID NOS: 9, 10, 20, and 21.

5. The vaccine formulation of claim 4, wherein each of the at least three different polypeptides belongs to a different group of (i)-(vi):

(i) SEQ ID NO: 9, 10, 20, and 21 or an immunogenic fragment thereof,

(ii) one of SEQ ID NOS: 2-5 or an immunogenic fragment thereof,

(iii) one of SEQ ID NOS: 6-7 or an immunogenic fragment thereof,

(iv) SEQ ID NO: 8 or an immunogenic fragment thereof,

(v) SEQ ID NO: 1 or an immunogenic fragment thereof, and

(vi) one of SEQ ID NO: 11-13 or an immunogenic fragment thereof.

6. The vaccine formulation of any of claims 1-5, wherein the immunogenic fragment of SEQ ID NO: 9, 10, 20, or 21 is a truncated fragment of any of SEQ ID NOS: 9, 10, 20 or 21 having from 1-20 amino acid residues removed from the N-terminus, C-terminus, or both.

7. The vaccine formulation of claim 1, wherein the vaccine formulation comprises one or more polypeptides having an amino acid sequence consisting of any of SEQ ID NOS: 9, 10, 20 and 21.

8. The vaccine formulation of claim 1, which further comprises a polypeptide having an amino acid sequence comprising SEQ ID NO: 6.

9. The vaccine formulation of claim 1, which further comprises a polypeptide having an amino acid sequence comprising SEQ ID NO: 7.

10. The vaccine formulation of claim 1, which further comprises a polypeptide having an amino acid sequence comprising SEQ ID NO: 12.

11. The vaccine formulation of claim 1, which further comprises a polypeptide having an amino acid sequence comprising SEQ ID NO: 13.

12. The vaccine formulation of claim 1, wherein the vaccine formulation comprises a polypeptide consisting of SEQ ID NO: 6 and a polypeptide consisting of SEQ ID NO: 9.

13. The vaccine formulation of claim 1, wherein the vaccine formulation comprises a polypeptide consisting of SEQ ID NO: 7 and a polypeptide consisting of SEQ ID NO: 10.

14. The vaccine formulation of any of claims 1-13, which contains substantially no other *S. pneumoniae* polypeptides other than polypeptides having an amino acid sequence comprising any of SEQ ID NOS: 1-13, 20, and 21.

15. The vaccine formulation of claim 1, which further comprises one or more polypeptides having an amino acid sequence comprising any of SEQ ID NOS: 2, 22, and 23 or an immunogenic fragment thereof.

16. The vaccine formulation of any of claims 1-15, wherein the polypeptide is conjugated to an immunogenic carrier.

17. The vaccine formulation of any of claims 1-5, wherein the formulation comprises at least one lipidated polypeptide.

18. The vaccine formulation of any of claims 1-17, further comprising an adjuvant.

19. The vaccine formulation of claim 18, wherein the adjuvant is an agonist of toll-like receptors (TLRs).

20. The vaccine formulation of claim 18, wherein the adjuvant is alum.

21. The vaccine formulation of claim 18, wherein the vaccine formulation comprises 1-1000 μg of the polypeptide and 1-250 μg of the adjuvant.

22. The vaccine formulation of any of claims 1-21, which induces a T_H17 cell response at least 1.5-fold after contacting T_H17 cells.

23. The vaccine formulation of any of claims 1-21, wherein the vaccine formulation inhibits infection by *S. pneumoniae* in an uninfected subject.

24. The vaccine formulation of any of claims 1-21, wherein the vaccine formulation inhibits *S. pneumoniae* colonization in an individual.

25. The vaccine formulation of any of claims 1-21, wherein the vaccine formulation inhibits *S. pneumoniae* symptoms.

26. An immunogenic composition comprising a pharmaceutically acceptable carrier and two or more polypeptides having amino acid sequences comprising any of SEQ ID NOS: 1-23 and SP1574, SP1655, SP2106, SP1473, SP0605, SP1177, SP0335, SP0906, SP1828, SP2157, SP1229, SP1128, SP1836, SP1865, SP0904, SP0765, SP1634, SP0418, SP1923, SP1313, SP0775, SP0314, SP0912, SP0159,

SP0910, SP2148, SP1412, SP0372, SP1304, SP2002, SP0612, SP1988, SP0484, SP0847, SP1527, SP0542, SP0441, SP0350, SP0014, SP1965, SP0117, SP0981, SP2229, SP2136, SP1179, SP1174, SP2216, SP1393, SP0641.1, SP1384, and SP2032, or an immunogenic fragment thereof, wherein at least one of the polypeptides has an amino acid sequence having at least 95% identity to any one of SEQ ID NOS: 9, 10, 20, and 21, or comprises any one of SEQ ID NOS: 9, 10, 20 and 21.