What is Claimed is:

1. An immunogenic polysaccharide-protein conjugate comprising a *Staphylococcus aureus* capsular polysaccharide conjugated to a carrier protein, wherein the polysaccharide has a molecular weight of between ~~70~~50 kDa and 800 kDa or between 70 kDa and 300 kDa.

2. The immunogenic conjugate of claim 1, wherein the immunogenic conjugate has a molecular weight of between 200 kDa and 5000 kDa or between 500 kDa and 2500 kDa.

3. The immunogenic polysaccharide-protein conjugate of claim 1 or 2, wherein the capsular polysaccharide is a serotype 5 or a serotype 8 capsular polysaccharide.

4. The immunogenic conjugate of any one of claims 1-3, wherein the polysaccharide has a degree of O-acetylation between 10-100%, between 50-100%, or between 75-100%.

5. The immunogenic conjugate of any one of claims 1-4, wherein the carrier protein is CRM_{197} or pneumolysin.

6. The immunogenic conjugate of claim 5, wherein the CRM197 is covalently linked to the polysaccharide through a carbamate linkage, an amide linkage, or both.

7. The immunogenic conjugate of claim 5 or 6, wherein the molar ratio of conjugated lysines to CRM197 is about 10:1 to about 25:1.

8. The immunogenic conjugate of claim 7, wherein at least one covalent linkage between CRM197 and polysaccharide occurs at least at every 5 to 10 saccharide repeat units of the polysaccharide or every 5 saccharide repeat units of the polysaccharide.

9. The immunogenic conjugate of any one of claims 5-8, wherein the CRM197 comprises 5 to 25, 5 to 20, or 10 to 25 lysines covalently linked to the polysaccharide.

10. An immunogenic composition comprising the immunogenic conjugate of any one of claims 1-9 and a pharmaceutically acceptable carrier.

11. An immunogenic composition comprising the immunogenic conjugate of any one of claims 1-9 and at least one component selected from the group consisting of an isolated *S. aureus*

clumping factor A (ClfA) polypeptide, an isolated S. aureus clumping factor B (ClfB) polypeptide, and an isolated *S. aureus* manganese transporter protein C (MntC).

12. The immunogenic composition of claim 11, wherein the at least one component is an isolated *S. aureus* ClfA polypeptide.

13. The immunogenic composition of claim 12, which further comprises an isolated S. aureus MntC protein.

14. The immunogenic composition of claim 11 or 13, wherein the S. aureus MntC protein is a lipidated or a non-lipidated protein.

15. The immunogenic composition of any one of claims 11-14, wherein the ClfA polypeptide is a polypeptide fragment selected from the group consisting of a fibrinogen binding domain; N1, N2, and N3 domains; and N2 and N3 domains of ClfA.

16. The immunogenic composition of any one of claims 11-15, wherein the ClfA polypeptide binds to fibrinogen at a reduced level compared to binding observed to fibrinogen with native ClfA.

17. The immunogenic composition of any one of claims 11-16, wherein the ClfA polypeptide has an amino acid substitution at one or more of Tyr 338, Tyr 256, Pro 336, Lys 389, Ala 254 or Ile 387.

18. The immunogenic composition of claim 17, wherein the amino acid substitution is to Ala or Ser.

19. The immunogenic composition of claim 18, wherein the Tyr 338 is substituted to Ala.

20. The immunogenic composition of any one of claims 10 or 15-19, wherein the ClfB polypeptide is a polypeptide fragment selected from the group consisting of a fibrinogen binding domain; N1, N2, and N3 domains; and N2 and N3 domains of ClfB.

21. The immunogenic composition of any one of claims 10-20, wherein the immunogenic composition comprises less than 30% or less than 20% free type 5 or 8 polysaccharide compared to the total amount of type 5 or 8 polysaccharide.

22. The immunogenic composition of any one of claims 10-21, further comprising an antigen selected from the group consisting of Opp3a, DltD, HtsA, LtaS, IsdA, IsdB, IsdC, SdrC, SdrD, SdrE, SdrF, SdrG, SdrH, SrtA, SpA, Sbi, FmtB, alpha-hemolysin (hla), beta-hemolysin, fibronectin-binding

protein A (fnbA), fibronectin-binding protein B (fnbB), coagulase, Fig, map, Panton-Valentine leukocidin (pvl), alpha-toxin and its variants, gamma toxin (hlg) and variants, ica, immunodominant ABC transporter, Mg2+ transporter, Ni ABC transporter, RAP, autolysin, laminin receptors, IsaA/PisA, IsaB/PisB , SPOIIIE, SsaA, EbpS, Sas A, SasF, SasH, EFB (FIB), SBI, Npase, EBP, bone sialo binding protein II, aureolysin precursor (AUR)/Sepp1, Cna, and fragments thereof such as M55, TSST-1, mecA, poly-N-acetylglucosamine (PNAG/dPNAG) exopolysaccharide, GehD, EbhA, EbhB, SSP-1, SSP-2, HBP, vitronectin binding protein, HarA, EsxA, EsxB, Enterotoxin A, Enterotoxin B, Enterotoxin C1, and novel autolysin.

23. The immunogenic composition of any one of claims 10-22, further comprising an adjuvant.

24. The use of the immunogenic composition of any one of claims 10-23 in the manufacture of a medicament for inducing an immune response against *Staphylococcus aureus* in a subject.

25. The use of claim 24, wherein the immune response prevents or reduces an infection, disease, condition, or at least one symptom associated with a staphylococcal organism in a subject.

26. The use of claim 34, wherein the infection, disease or condition is selected from the group consisting of invasive *Staphylococcus aureus* disease, sepsis and carriage.

27. The use of any one of claims 24-26, wherein the immune response induced comprises the generation of antibodies having opsonophagocytic activity (OPA) against *S. aureus*.

28. The use of the immunogenic composition of any one of claims 10-23 in the manufacture of a medicament for conferring passive immunity to a subject.

Claims

1. An immunogenic polysaccharide-protein conjugate comprising a *Staphylococcus aureus* capsular polysaccharide conjugated to a carrier protein, wherein the polysaccharide has a molecular weight of between 50 kDa and 800 kDa or between 70 kDa and 300 kDa.

2. The immunogenic conjugate of claim 1, wherein the immunogenic conjugate has a molecular weight of between 200 kDa and 5000 kDa or between 500 kDa and 2500 kDa.

3. The immunogenic polysaccharide-protein conjugate of claim 1 or 2, wherein the capsular polysaccharide is a serotype 5 or serotype 8 capsular polysaccharide.

4. The immunogenic conjugate of any one of claims 1-3, wherein the polysaccharide has a degree of O-acetylation between 10-100%, between 50-100%, or between 75-100%.

5. The immunogenic conjugate of any one of claims 1-4, wherein the carrier protein is CRM_{197} or pneumolysin.

6. The immunogenic conjugate of claim 5, wherein the CRM_{197} is covalently linked to the polysaccharide through a carbamate linkage, an amide linkage, or both.

7. The immunogenic conjugate of claim 5 or 6, wherein the molar ratio of conjugated lysines to CRM_{197} is about 10:1 to about 25:1.

8. The immunogenic conjugate of claim 7, wherein at least one covalent linkage between CRM_{197} and polysaccharide occurs at least at every 5 to 10 saccharide repeat units of the polysaccharide or every 5 saccharide repeat units of the polysaccharide.

9. The immunogenic conjugate of any one of claims 5-8, wherein the CRM_{197} comprises 5 to 25, 5 to 20, or 10 to 25 lysines covalently linked to the polysaccharide.

10. An immunogenic composition comprising the immunogenic conjugate of any one of claims 1-9 and a pharmaceutically acceptable carrier.

11. An immunogenic composition comprising the immunogenic conjugate of any one of claims 1-9 and at least one component selected from the group consisting of an isolated *S. aureus* clumping factor A (ClfA) polypeptide, an isolated S. aureus clumping factor B (ClfB) polypeptide, and an isolated 5. *aureus* manganese transporter protein C (MntC).

12. The immunogenic composition of claim 11, wherein the at least one component is an isolated *S. aureus* ClfA polypeptide.

13. The immunogenic composition of claim 12, which further comprises an isolated *S. aureus* MntC protein.

14. The immunogenic composition of claim 11 or 13, wherein the MntC protein is a lipidated or a non-lipidated protein.

15. The immunogenic composition of any one of claims 11 - 14, wherein the ClfA polypeptide is a
polypeptide fragment selected from the group consisting of a fibrinogen binding domain; N1, N2 and N3 domains; and N2 and N3 domains of ClfA.

16. The immunogenic composition of any one of claims 11 - 15, wherein the ClfA polypeptide binds to fibrinogen at a reduced level compared to binding observed to fibrinogen with native ClfA.

17. The immunogenic composition of any one of claims 11 - 16, wherein the ClfA polypeptide has an amino acid substitution at one or more of Tyr338, Tyr256, Pro336, Lys389, Ala254, or Ile387.

18. The immunogenic composition of claim 17, wherein the amino acid substitution is to Ala or Ser.

19. The immunogenic composition of claim 18, wherein the Tyr338 is substituted to Ala.

20. The immunogenic composition of any one of claims 11 or 15 - 19, wherein the ClfB polypeptide is a polypeptide fragment selected from the group consisting of a fibrinogen binding domain; N1, N2 and N3 domains; and N2 and N3 domains of ClfB.

21. The immunogenic composition of any one of claims 10 - 20, wherein the immunogenic compositioncomprises less than 30% or less than 20% free type 5 or 8 polysaccharide compared to the total amount of type 5 or 8 polysaccharide.

22. The immunogenic composition of any one of claims 10 - 21, further comprising an antigen selected from the group consisting of Opp3a, DltD, HtsA, LtaS, IsdB, IsdC, SdrC, SdrD, SdrE, SdrF, SdrG, SdrH, SrtA, SpA, Sbi, FmtB, alpha-hemolysin (hla), beta-hemolysin, fibronectin-binding protein A (fnbA), fibronectin-binding protein B (fnbB), coagulase, ~~Fig, map,~~ PAnton-Valentine leukocidin (pvl), alpha-toxin and its variants, gamma toxin (hlg) and variants, ica, immunodominant ABC transporter, Mg2+ transporter, Ni ABC transporter, RAP, autolysin, laminin receptors, IsaA/PisA, IsaB/PisB, SPOIIIE, SsaA, EbpS, SasA, SasF, SasH, EFB (FIB), SBI, Npase, EBP, bone sialo binding protein II, aureolysin precursor (AUR)/Sepp1, Cna, and fragments thereof such as M55, TSSST-1, mecA, poly-N-acetylglucosamine (PNAG/dPNAG) exopolysaccharide, GehD, EbhA, EbhB, SSP-1, SSP-2, HBP, vitronectin binding protein, HarA, EsxA, EsxB, Enterotoxin A, Enterotoxin B, and Enterotoxin C.

23. The immunogenic composition of any one of claims 10 – 22, further comprising an adjuvant.

24. The use of the immunogenic composition of any one of claims 10 – 23 in the manufacture of a medicament for inducing an immune response against *Staphylococcus aureus* in a subject.

25. The use of claim 24, wherein the immune response prevents or reduces an infection, disease, condition, or at least one symptom associated with a staphylococcal organism in a subject.

26. The use of claim 24, wherein the infection, disease, condition is selected from the group consisting of invasive *Staphylococcus aureus* disease, sepsis and carriage.

27. The use of any one of claims 24 - 26, wherein the immune response induced comprises the generation of antibodies having opsonophagocytic activity (OPA) against *S. aureus*.

28. The use of the immunogenic composition of any one of claims 10 – 23 in the manufacture of a medicament for conferring passive immunity to a subject.