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(54) Title: CNA_B DOMAIN ANTIGENS IN VACCINES AGAINST GRAM POSITIVE BACTERIA

(57) Abstract: The invention provides protective antigens which are useful in vaccine compositions to induce protection against gram positive bacteria, particularly against S. agalactiae, S. pyogenes, S. pneumoniae, S. aureus, S. suis, and S. equi.

Cna_B DOMAIN ANTIGENS IN VACCINES AGAINST GRAM POSITIVE BACTERIA

[01] This application claims the benefit of US 61/143,859, filed on 12 January 2009, the complete contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

[02] This invention is in the fields of immunology and vaccinology. In particular, it relates to antigens derived from gram positive bacteria and their use in immunization.

BACKGROUND OF THE INVENTION

[03] Gram positive bacteria include some of the most virulent human and animal pathogens and are responsible for a long list of severe diseases and subsequent sequelae. There is a continuing need in the art for effective vaccines against gram positive bacterial infections.

BRIEF DESCRIPTION OF THE FIGURES

[04] **FIG. 1A**. Amino acid sequence (SEQ ID NO:1) of the Cna_B domain of *S. pyogenes* protein Cpa_M18 (Spy_M18_0126) cloned together with a flanking domain ("Fb signal") ("Cna_B-Fb"). **FIG. 1B**. Graphic representation of cloned domains. See Example 1.

[05] **FIG. 2**. SDS-polyacrylamide gel containing purified recombinant His-tagged Cna_B-Fb domain. See Example 1.

[06] **FIGS. 3A-D**. Western blots demonstrating that the *S. pyogenes* Cpa_M18 (Spy_M18_0126) Cna_B-Fb domain is immunogenic and that Cna_B-Fb domain antiserum recognizes Cpa and F2 (MGAS2096_Spy0119) proteins from various M strains of *S. pyogenes* (**FIGS. 3A-C**) as well as pili components of *S. agalactiae* (**FIGS. 3C-D**) and *S. pneumoniae* (**FIG. 3D**). See Example 1.

[07] **FIGS. 4A-B**. Western blots comparing reactivity of Cna_B-Fb antiserum (**FIG. 4A**) with Cpa_M18 antiserum (**FIG. 4B**). See Example 1.

[08] **FIG. 5**. Graph showing results of opsonophagocytosis assays for *S. agalactiae* strains 515 and JM using antiserum raised against recombinant Cna_B-Fb (see Example 1) and differentiated HL-60 cells. See Example 2.

[09] **FIG. 6**. Graph showing results of opsonophagocytosis assays for *S. agalactiae* mutant strain R13 (which lacks pili island 2) and its complemented strains containing *S. pyogenes* pilus M1 or *S. pyogenes* pilus M6. See Example 2.

[10] **FIG. 7**. Alignment of amino acid sequences of Cna_B domains of Cpa proteins from various *S. pyogenes* strains. Cna_B_Cpa_M5_Manfredo (Spy_M5_0104; SEQ ID NO:18), SEQ ID NO:2; Cna_B_Cpa_M28 (M28_Spy0107, SEQ ID NO:19), SEQ ID NO:3; Cna_B_Cpa_M12 (MGAS2096_Spy0113, SEQ ID NO:20), SEQ ID NO:4; Cna_B_Cpa_M1 (M5005_Spy_0107, SEQ ID NO:21), SEQ ID NO:5; Cna_B_Cpa_M3 (SpyM3_0098, SEQ ID NO:22), SEQ ID NO:6; Cna_B_Cpa_M18 (spyM18_0126, SEQ ID NO:23), SEQ ID NO:7; Cna_B_Cpa_M6 (M6_Spy0159, SEQ ID NO:24), SEQ ID NO:8; Cna_B_Cpa_M4_C (MGAS10750_Spy0115, SEQ ID NO:25), SEQ ID NO:9; Cna_B_Cpa_M2 (MGAS10270_Spy0113, SEQ ID NO:26), SEQ ID NO:10.

[11] **FIG. 8**. Alignment of amino acid sequences of Cna_B domains of pili proteins from *S. agalactiae*. Cna_B_GBS_52 (SAG_0646, SEQ ID NO:45), SEQ ID NO:27; Cna_B_GBS_150 (SAL 1482, SEQ ID NO:26), SEQ ID NO:28; Cna_B_GBS_104_1 (SAG 0649, SEQ ID NO:47), SEQ ID NO:29; Cna_B_GBS_67 (SAL 1487, SEQ ID NO:48), SEQ ID NO:30; Cna_B_GBS_1523 (SAN 1518, SEQ ID NO:49), SEQ ID NO:31; Cna_B_GBS_1524 (SAN 1519, SEQ ID NO:50), SEQ ID NO:32; Cna_B_GBS_80 (SAG 0645, SEQ ID NO:51), SEQ ID NO:33; Cna_B_GBS_104_2

(SAG 0649, SEQ ID NO:47), SEQ ID NO:34; and Cna_B_GBS_1521 (SAN 1516, SEQ ID NO:52), SEQ ID NO:35.

[12] **FIG. 9**. Alignment of amino acid sequences of GBS island 1 pili components with a Cna_B domain of *S. pyogenes* Cpa protein from strain M18. Cna_B_GBS_80 (SAG 0645, SEQ ID NO:51), SEQ ID NO:33; Cna_B_GBS_52 (SAG 0646, SEQ ID NO:45), SEQ ID NO:27; Cna_B_GBS_104_2 (SAG 0649, SEQ ID NO:47), SEQ ID NO:34; Cna_B_GBS_104_1 (SAG 0649, SEQ ID NO:47), SEQ ID NO:29; and Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:7.

[13] **FIG. 10.** Alignment of amino acid sequences of GBS island 2 pili components with a Cna_B domain of *S. pyogenes* Cpa protein from strain M18. Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:7; Cna_B_GBS_150 (SAL 1482, SEQ ID NO:46), SEQ ID NO:28; Cna_B_GBS_67 (SAL 1487, SEQ ID NO:48), SEQ ID NO:30; and Cna_B_GBS_59 (SAL 1486, SEQ ID NO:102), SEQ ID NO:103.

[14] **FIG. 11**. Alignment of amino acid sequences of GBS island 3 pili components with a Cna_B domain of *S. pyogenes* Cpa protein from strain M18. Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:7; Cna_B_GBS_1524 (SAN 1519, SEQ ID NO:50), SEQ ID NO:32; and Cna_B_GBS_1523 (SAN 1518, SEQ ID NO:49), SEQ ID NO:31.

[15] **FIG. 12**. Alignment of amino acid sequences of *S. pneumoniae* pili strain TIGR4 components with a Cna_B domain of *S. pyogenes* Cpa protein from strain M18. Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:7; RrgB (SP_0463, SEQ ID NO:63), SEQ ID NO:53; RrgA1 (SP_0462, SEQ ID NO:64), SEQ ID NO:54; RrgC2 (SP_0464, SEQ ID NO:65), SEQ ID NO:56; RrgA2 (SP_0462, SEQ ID NO:64), SEQ ID NO:57; and RrgC1 (SP_0464, SEQ ID NO:65), SEQ ID NO:58.

[16] **FIG. 13**. Alignment of amino acid sequences of *S. aureus* proteins comprising a Cna_B domain with a Cna_B domain of *S. pyogenes* Cpa protein from strain M18. Ser-Asp rich2 (SdrD MW0517, SEQ ID NO:72), SEQ ID NO:66; Ser-Asp rich3 (SdrD MW0517, SEQ ID NO:72), SEQ ID NO:67; CBP (MW2612, SEQ ID NO:73), SEQ ID NO:68; and Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:7.

[17] **FIG. 14**. Western blot demonstrating that Cna_B antiserum recognized *S. suis* recombinant proteins. Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:14; Cna_B_Bkb3 (DUF 11) 89/1591 (SEQ ID NO:83), SEQ ID NO:75: Cna_B_Bbk1 SSU05_0474 05AYH33 (SEQ ID NO:82), SEQ ID NO:76.

[18] **FIG. 15**. Western blot demonstrating that Cna_B antiserum recognizes *S. equi* recombinant proteins. Cna_B_CPA_M18 (Spy_M18_0126, SEQ ID NO:23), SEQ ID NO:14; BKB SEQ0936 (SEQ ID NO:88), SEQ ID NO:77; ancillary protein SEQ 0935 (SEQ ID NO:87), SEQ ID NO:78.

[19] **FIG. 16**. Alignment of Cna_B domains of *S. pyogenes* Cpa protein (Spy_M18_0126, SEQ ID NO:23) (SEQ ID NO:7) with Cna_B domains of two *S. suis* proteins. Cna_B_AUTOTRANSPORTER (SEQ ID NO:82), SEQ ID NO:80; Cna_B_ (SEQ ID NO:83), SEQ ID NO:81.

[20] **FIG. 17**. Alignment of Cna_B domains of *S. pyogenes* Cpa protein (Spy_M18_0126, SEQ ID NO:23) (SEQ ID NO:7) with Cna_B domains of two *S. equi* proteins. Cna_B_bkb (SEQ ID NO:88), SEQ ID NO:86; Cna_B_ap1 (SEQ ID NO:87), SEQ ID NO:84; Cna_B_ap2 (SEQ ID NO:87), SEQ ID NO:85.

[21] **FIG. 18**. FACS analysis of GAS Cna_B serum cross-reaction with selected GBS strains.

[22] **FIG. 19**. Graph showing results of ELISA assays described in Example 4.

[23] **FIG. 20**. Western blots demonstrating that antiserum against a Cna_B domain antigen recognizes GBS pili in a GBS protein extraction. "α-GAS_Cna_B_M18" is antiserum from mice immunized with Cna_B-Fb-M18, as described in Example 1.

[24] **FIG. 21**. Graph demonstrating that mice immunized with a Cna_B domain antigen show reduced skin lesion area in a GAS subcutaneous infection model. See Example 6.

[25] **FIG. 22**. Graph demonstrating that mice immunized with a Cna_B domain antigen show a reduced nasopharyngeal colonization rate when challenged with *S. aureus*. See Example 7.

[26] **FIG. 23**. Graphs demonstrating that mice immunized with a Cna_B domain antigen show reduced nasopharyngeal colonization rates when challenged with *S. aureus*. See Example 9.

[27] **FIG. 24**. Graphs demonstrating that mice born from mothers immunized with a chimeric Cna_B domain antigen show an increased survival rate over controls when immunized with a chimeric Cna_B domain antigen. See Example 1.

[28] **FIG. 25**. Graph demonstrating that mice immunized with a chimeric Cna_B domain antigen show reduced skin lesion area in a GAS subcutaneous infection model. See Example 6.

[29] **FIGS. 26A-B**. Graphic representation and amino acid sequence (SEQ ID NO:132) of the SdrD protein of *S. aureus subsp. aureus* NCTC 8325 (**FIG. 26A**); graphic representation of the same Cna_B domain antigen and its amino acid sequence (SEQ ID NO:132), indicating the Cna_B domains (**FIG. 26B**).

[30] **FIGS. 27A-C**. Cloning, expression, and purification of Cna_B domains. **FIG. 27A**, Graphic representation of cloned Cna_B domains (SEQ ID NOS:134-138) of SdrD.

FIG. 27B, amino acid sequence of the cloned domains (SEQ ID NO:133). **FIG. 27C**, SDS-polyacrylamide gel containing the purified Cna_B domains.

[31] **FIG. 28**. Graph demonstrating that Cna_B_SdrD confers protection in a mouse model against infection with *S. aureus* strain USA300.

DETAILED DESCRIPTION OF THE INVENTION

[32] A "Cna_B domain" was first described in an *S. aureus* collagen-binding surface protein as a region that does not mediate collagen binding. The structure of the repetitive B-region forms a beta sandwich structure. It is thought that this region forms a stalk in the *S. aureus* collagen-binding protein that presents the ligand binding domain away from the bacterial cell surface. Proteins containing a Cna_B domain are present in a variety of Gram positive pathogenic bacteria, including *S. aureus*, *S. pneumoniae*, *S. agalactiae* (GBS), *S. pyogenes* (GAS), *S. equi*, *S. suis*, *C. perifringens*, *L. monocytogenes*, *B. thuringiensis*, *P. acidigallici*, *E. faceium*, *B. cereus*, *S. epidermidis*, *E. faecalis*, *C. difficile*, *C. diphtheriae*, *S. gordonii*, *S. dysgalactiae*, and *C. tetani*.

[33] As described in the specific examples, below, the Cna_B domain (SEQ ID NO:7) of *S. pyogenes* Cpa protein (Spy_M18_0126, SEQ ID NO:23) is immunogenic. Specific antibodies raised against it recognize recombinant proteins of *S. pyogenes*, *S. agalactiae*, *S. pneumoniae*, *S. suis*, and *S. equi*. About half of the antibodies contained in GAS_Cpa_M18 protein serum are specific for the Cna_B domain, and antiserum raised against the Cna_B domain of *S. pyogenes* Cpa protein from strain M18 ("anti-Cna_B serum") detects in a Western blot proteins which were not detected with antiserum raised against the entire protein ("GAS_M18_cpa") and mediates the phagocytic killing of *S. agalactiae*. The Cna_B domain of Spy_M18_0126 also mediates passive protection in GBS-challenged mice. Thus, there is an advantage to raising antibodies against streptococcal Cna_B domains or Cna_B domains of other gram positive bacterial proteins (*e.g.*, *S. aureus*).

[34] The invention provides Cna_B domain antigens which are useful in vaccine compositions to induce protection against gram positive bacteria, particularly against one or more of *S. aureus*, *S. pneumoniae*, *S. agalactiae* (GBS), *S. pyogenes* (GAS), *S. equi*, and *S. suis*. The invention also provides methods of using Cna_B domain antigens to induce antibodies and to treat or protect against gram positive bacterial infections, including cross-protection between various streptococcal and/or staphylococcal species.

Cna_B domains

[35] Cna_B domains from any gram positive bacterial protein can be used in compositions and methods of the invention. Amino acid sequences of Cna_B domains from various *S. aureus*, *S. pneumoniae*, *S. agalactiae*, *S. pyogenes*, *S. suis*, and *S. equis* proteins are shown in **FIGS. 7-13**, **16**, and **17** and set forth in the sequence listing as SEQ ID NOS:2-10, 27-35, 53-57, 66, 67, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 134-138. Examples of other proteins containing Cna_B domains are shown in SEQ ID NOS:89-102 and 132. The Cna_B domains typically contain one or more sequences identified in **FIGS. 7-13** as a "G box." A consensus sequence amino acid sequence for the G boxes shown in **FIGS. 7-13** is shown in SEQ ID NO:74.

Variants

[36] In some embodiments, variants of Cna_B domains of the invention have amino acid sequences which are at least 90% identical, at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, or at least 99% identical to any of SEQ ID NOS:2-10, 27-35, 53-57, 66, 67, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 134-138. Typically any difference between the amino acid sequence of a Cna_B domain and the amino acid sequence of a variant of the Cna_B domain is due to one or more conservative amino acid substitutions (typically 1, 2, 3, 4, 5, 6, 7, or 8 substitutions). However, amino acid deletions or insertions also are possible.

[37] In some embodiments conservative amino acid substitutions are based on chemical properties and include substitution of a positively-charged amino acid for another positively charged amino acid (*e.g.*, H, K, R); a negatively-charged amino acid for another negatively charged amino acid (*e.g.*, D, E); a very hydrophobic amino acid for another very hydrophobic amino acid (*e.g.*, C, F, I, L, M, V, W); a less hydrophobic amino acid for another less hydrophobic amino acid (*e.g.*, A, G, H, P, S, T, Y); a partly hydrophobic amino acid for another partly hydrophobic amino acid (*e.g.*, K, R); an aliphatic amino acid for another aliphatic amino acid (*e.g.*, A, I, L, M, P, V); a polar amino acid for another polar amino acid (*e.g.*, A, D, E, G, H, K, N, P, Q, R, S, T, Y); an aromatic amino acid for another aromatic amino acid (*e.g.*, F, H, W, Y); and a small amino acid for another small amino acid (*e.g.*, D, N, T).

[38] In some embodiments, conservative amino acid substitutions are determined using the BLOSUM62 table. The BLOSUM62 table is an amino acid substitution matrix derived from about 2,000 local multiple alignments of protein sequence segments, representing highly conserved regions of more than 500 groups of related proteins (Henikoff & Henikoff, Proc. Natl. Acad. Sci. USA 89:10915, 1992). The BLOSUM62 substitution frequencies can be used to define conservative amino acid substitutions that may be introduced into amino acid sequences of Cna_B domains. In these embodiments a conservative substitution preferably refers to a substitution represented by a BLOSUM62 value of greater than -1. For example, an amino acid substitution is conservative if the substitution is characterized by a BLOSUM62 value of 0, 1, 2, or 3. According to this system, preferred conservative amino acid substitutions are characterized by a BLOSUM62 value of at least 1 (*e.g.*, 1, 2, or 3), while more preferred conservative amino acid substitutions are characterized by a BLOSUM62 value of at least 2 (*e.g.*, 2 or 3).

[39] Particular amino acid substitutions or alterations can be identified by aligning the Cna_B domains as shown in **FIGS. 7-13**. Cna_B domain antigens (described below) including any combination of such options is within the scope of the invention.

Cna_B domain antigens

[40] "Cna_B domain antigens" comprise one or more Cna_B domains as described above and may or may not comprise additional amino acids at the N terminus, C terminus, or both. In some embodiments, Cna_B domain antigens consist of any of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 133-138. In other embodiments, Cna_B domain antigens comprise a Cna_B domain as well as other amino acid sequences which are not directly adjacent to a Cna_B domain in a native bacterial (*e.g.*, streptococcal or staphylococcal) protein. That is, in such antigens the amino group of the N terminal amino acid of a Cna_B domain is not linked by a peptide bond to the carboxyl group of an amino acid to which it is linked in a native bacterial (*e.g.*, streptococcal or staphylococcal) protein and/or the carboxyl group of the C terminal amino acid of the Cna_B domain is not linked by a peptide bond to the amino group of an amino acid to which it is linked in a native gram positive bacterial protein, *e.g.*, a protein of *S. aureus*, *S. pneumoniae*, *S. agalactiae* (GBS), *S. pyogenes* (GAS), *S. equi*, or *S. suis*. "Native" gram positive bacterial proteins are proteins which are found in gram positive bacterial as they exist in nature; "native" streptococcal or staphylococcal proteins are proteins which are found in streptococcal or staphylococcal bacteria, respectively, as they exist in nature.

[41] In still other embodiments, Cna_B domain antigens consist of a Cna_B domain as well as additional amino acids at the N and/or C terminal(s) of the domain, provided that the Cna_B domain antigen does not consist of a full-length bacterial (*e.g.*, streptococcal or staphylococcal) protein (see Tables 1-32).

[42] In other embodiments, Cna_B domain antigens consist of polypeptides of the formula:

$$A(LB)_n$$

wherein A is a first Cna_B domain; B is a second Cna_B domain; n is an integer (typically 1-10; *e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10); and L is independently absent or is an

amino acid linker. The Cna_B domains in such antigens can be the same, different, or a mixture of some Cna_B domains which are the same and some which are different (*i.e.*, all the Cna_B domains can be different or two or more of the Cna_B domains can be the same). For example, the Cna_B domains can be domains of two or more different gram positive proteins, particularly proteins of gram positive cocci, such as streptococcal proteins, staphylococcal proteins, or of proteins of two or more different species or strains (*e.g.*, *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, *S. aureus*, *S. suis*, and/or *S. equi*).

[43] The amino acid linker, if present between any of the Cna_B domains, typically contains between 6 and 12 amino acids (*e.g.*, 6, 7, 8, 9, 10, 11, or 12). GSGGGG (SEQ ID NO:79) is an example of a useful linker. Linkers in a Cna_B domain antigen can be the same or different.

[44] Examples of Cna_B domain antigens of formula $A(LB)_n$ include proteins comprising or consisting of SEQ ID NO:108. SEQ ID NO:108 comprises, from N to C terminus, a Cna_B domain of SAG_0645 (SEQ ID NO:112), the amino acid sequence VDS, a first amino acid linker (SEQ ID NO:79), a Cna_B domain of SAN_1518 (SEQ ID NO:113), a second amino acid linker (SEQ ID NO:79), a first Cna_B domain of SAL_1487 (SEQ ID NO:110), the amino acid sequence NSG, a second Cna_B domain of SAL_1487 (SEQ ID NO:111), and the amino acid KQI.

[45] Other examples of Cna_B domain antigens of formula $A(LB)_n$ include proteins comprising or consisting of SEQ ID NO:109. SEQ ID NO:109 comprises, from N to C terminus, Cna_B domain of SAG_0645 (SEQ ID NO:112), the amino acid sequence VDS, a first amino acid linker (SEQ ID NO:79), a Cna_B domain of SAN_1518 (SEQ ID NO:113), a second amino acid linker (SEQ ID NO:79), a first Cna_B domain of SAL_1486 (114), the amino acid sequence LPL, a second Cna_B domain of SAL_1486 (SEQ ID NO:115), and the amino acid sequence DIE.

[46] Other examples of Cna_B domain antigens of formula $A(LB)_n$ include proteins which comprise or consist of SEQ ID NOS:127, 128, 129, 130, 131, 133, 134, 135, 136, 137, or 138; see Examples 8 and 10.

[47] In the Cna_B domain antigens described above, the amino acid sequences VDS, NSG, KQI, LPL, and DIE are included so as not to truncate a beta pleated sheet. It is well within the skill of the ordinary artisan to include other such amino acid sequences in Cna_B domain antigens of the invention to help preserve tertiary structure of Cna_B domains.

[48] Still other examples of Cna_B domain antigens of formula $A(LB)_n$ comprise:

a. Cna_B domains of *S. pyogenes* Spy_M18_0126 (*e.g.*, SEQ ID NO:7) and M6_Spy0159) (*e.g.*, SEQ ID NO:8), and MGAS2096_Spy0119 (*e.g.*, SEQ ID NO:121); these include Cna_B domain antigens which comprise fusions of the five Cna_B domains (SEQ ID NOS:122-126) of SEQ ID NO:121. A coding sequence for the Cna_B domain of Spy0159 is shown in SEQ ID NO:120. A coding sequence for Spy0119 is shown in SEQ ID NO:119. Nucleotides 181-390, 1576-1797, 1915-2127, 2281-2496, and 2716-2916 of SEQ ID NO:121 encode the Cna_B domains shown in SEQ ID NOS:122-126, respectively.

b. Cna_B domains of *S. aureus* SdrD (*e.g.*, SEQ ID NOS:134-138; SEQ ID NO:66 and/or 67; SEQ ID NO:139) and Cna_B_cap (*e.g.*, SEQ ID NO:68).

c. Cna_B domains of *S. pneumoniae* SP_0463) (*e.g.*, SEQ ID NO:53), Cna_B_RrgA (SP_0462) (*e.g.*, SEQ ID NO:54 and/or 56), and Cna_B_RrgC (SP_0464) (*e.g.*, SEQ ID NO:55 and/or 57).

d. Cna_B domains of Spy_M18_0126 (*e.g.*, SEQ ID NO:7), SAG 0645 (SEQ ID NO:33), RrgB (SP_0463) (*e.g.*, SEQ ID NO:53), and SdrD (*e.g.*, SEQ ID NOS:134-138; SEQ ID NO:66 and/or 67; SEQ ID NO:139).

[49] Cna_B domain antigens of the invention also can comprise any of the Cna_B domain antigens described above. In some of these embodiments, the amino group of the N terminal amino acid of the Cna_B domain is not linked by a peptide bond to the carboxyl group of an amino acid to which it is linked in a native bacterial (*e.g.*, streptococcal or staphylococcal) protein and/or the carboxyl group of the C terminal amino acid of the Cna_B domain is not linked by a peptide bond to the amino group of an amino acid to which it is linked in a native bacterial (*e.g.*, streptococcal or staphylococcal) protein.

[50] In some embodiments, one or more Cna_B domain antigens of the invention are part of a fusion polypeptide which comprises another bacterial antigen, preferably another bacterial (*e.g.*, streptococcal or staphylococcal) antigen. Suitable antigens are disclosed, *e.g.*, in WO 99/05447, WO 02/034771, WO 04/018646, WO 05/028618, WO 05/032482, WO 06/042027, and WO 06/078318.

[51] Fusion polypeptides comprising one or more Cna_B domains and other domains, such as von Willenbrand Factor A (vWFA) domains (*e.g.*, SEQ ID NOS:105, 106, 107), are also within the scope of the invention, such as:

a. a Cna_B domain of Spy_M18_0126) (*e.g.*, SEQ ID NO:7) and vWFA_cpa_M6 (M6_Spy0159) (*e.g.*, SEQ ID NO:105); and

b. a Cna_B domain of SAG 0645 (*e.g.*, SEQ ID NO:33) and vWFA_SAL_1487 (*e.g.*, SEQ ID NO:106).

[52] Such fusion polypeptides can include linker sequences between the various fusion partners and/or flanking sequences from each of the fusion partners, which can be selected from those disclosed in Tables 1-37 and 43-48, below.

Table 1. Cna_B domain antigens comprising SEQ ID NO:2 (Spy_M5_0104, SEQ ID NO:18; >gi|139472985|ref|YP_001127700.1| putative surface-anchored protein [Streptococcus pyogenes str. Manfredo])

number of additional contiguous amino acids of SEQ ID NO:18 at N terminus of SEQ ID NO:2	number of additional contiguous amino acids of SEQ ID NO:18 at C terminus of SEQ ID NO:2
0-70, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70	0-390, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390

Table 2. Cna_B domain antigens comprising SEQ ID NO:3 (M28_Spy0107, SEQ ID NO:19; >gi|71902773|ref|YP_279576.1| collagen-binding protein [Streptococcus pyogenes MGAS6180])

number of additional contiguous amino acids of SEQ ID NO:19 at N terminus of SEQ ID NO:3	number of additional contiguous amino acids of SEQ ID NO:19 at C terminus of SEQ ID NO:3
0-294, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294	0-390, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390

Table 3. Cna_B domain antigens comprising SEQ ID NO:4 (MGAS2096_Spy0113, SEQ ID NO:20; >gi|94991610|ref|YP_599709.1| fibronectin-binding protein [Streptococcus pyogenes MGAS2096])

number of additional contiguous amino acids of SEQ ID NO:20 at N terminus of SEQ ID NO:4	number of additional contiguous amino acids of SEQ ID NO:20 at C terminus of SEQ ID NO:4
0-297, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297	0-396, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396

Table 4. Cna_B domain antigens comprising SEQ ID NO:5 (M5005_Spy_0107, SEQ ID NO:21; >gi|71909921|ref|YP_281471.1| fibronectin-binding protein [Streptococcus pyogenes MGAS5005])

number of additional contiguous amino acids of SEQ ID NO:21 at N terminus of SEQ ID NO:5	number of additional contiguous amino acids of SEQ ID NO:21 at C terminus of SEQ ID NO:5
0-310, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310	0-380, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380

Table 5. Cna_B domain antigens comprising SEQ ID NO:6 (SpyM3_0098, SEQ ID NO:22; >gi|21909634|ref|NP_663902.1| putative collagen binding protein [Streptococcus pyogenes MGAS315])

number of additional contiguous amino acids of SEQ ID NO:22 at N terminus of SEQ ID NO:6	number of additional contiguous amino acids of SEQ ID NO:22 at C terminus of SEQ ID NO:6
0-288, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288	0-393, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393

Table 6. Cna_B domain antigens comprising SEQ ID NO:7 (Spy_M18_0126, SEQ ID NO:23; >gi|19745301|ref|NP_606437.1| putative collagen binding protein [Streptococcus pyogenes MGAS8232])

number of additional contiguous amino acids of SEQ ID NO:23 at N terminus of SEQ ID NO:7	number of additional contiguous amino acids of SEQ ID NO:23 at C terminus of SEQ ID NO:7
0-70, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70	0-392, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392

Table 7. Cna_B domain antigens comprising SEQ ID NO:8 (M6_Spy0159, SEQ ID NO:24; >gi|50913505|ref|YP_059477.1| collagen adhesion protein [Streptococcus pyogenes MGAS10394])

number of additional contiguous amino acids of SEQ ID NO:24 at N terminus of SEQ ID NO:8	number of additional contiguous amino acids of SEQ ID NO:24 at C terminus of SEQ ID NO:8
0-906, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723,	0-58, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58

724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906	

Table 8. Cna_B domain antigens comprising SEQ ID NO:9 (MGAS10750_Spy0115, SEQ ID NO:25; >gi|94993511|ref|YP_601609.1| Fibronectin-binding protein [Streptococcus pyogenes MGAS10750]

number of additional contiguous amino acids of SEQ ID NO:25 at N terminus of SEQ ID NO:9	number of additional contiguous amino acids of SEQ ID NO:25 at C terminus of SEQ ID NO:9
0-654, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362,	0-646, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362,

363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654	363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646

Table 9. Cna_B domain antigens comprising SEQ ID NO:10 (MGAS10270_Spy0113, SEQ ID NO:26; >gi|94989622|ref|YP_597722.1| collagen adhesion protein [Streptococcus pyogenes MGAS10270])

number of additional contiguous amino acids of SEQ ID NO:26 at N terminus of SEQ ID NO:10	number of additional contiguous amino acids of SEQ ID NO:26 at C terminus of SEQ ID NO:10
0-51, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51	0-768, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690,

	691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768

Table 10. Cna_B domain antigens comprising SEQ ID NO:27 (SAG_0646, SEQ ID NO:45; >gi|22536815|ref|NP_687666.1| cell wall surface anchor family protein [Streptococcus agalactiae 2603V/R])

number of additional contiguous amino acids of SEQ ID NO:45 at N terminus of SEQ ID NO:27	number of additional contiguous amino acids of SEQ ID NO:45 at C terminus of SEQ ID NO:27
0-169, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169	0-52, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52

Table 11. Cna_B domain antigens comprising SEQ ID NO:28 (SAL 1482, SEQ ID NO:46; GBS150= SAL_1482 (ancillary2), jcvi.org/tigr-scripts/CMR/shared/GenePage.cgi?locus=SAL_1482
>SAL_1482

number of additional contiguous amino acids of SEQ ID NO:46 at N terminus of SEQ ID NO:28	number of additional contiguous amino acids of SEQ ID NO:46 at C terminus of SEQ ID NO:28
0-160, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111,	0-75, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55,

112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160	56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75

Table 12. Cna_B domain antigens comprising SEQ ID NO:29 (SAG 0649, SEQ ID NO:47; >gi|22536818|ref|NP_687669.1| cell wall surface anchor family protein, putative [Streptococcus agalactiae 2603V/R])

number of additional contiguous amino acids of SEQ ID NO:47 at N terminus of SEQ ID NO:29	number of additional contiguous amino acids of SEQ ID NO:47 at C terminus of SEQ ID NO:29
0-51, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51	0-778, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583,

WO 2010/079464 PCT/IB2010/050110

	584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778

Table 13A. Cna_B domain antigens comprising SEQ ID NO:110 or 30 (SAL 1487, SEQ ID NO:48; GBS67= SAL_1487 (ancillary 1), jcvi.org/cgi-bin/CMR/shared/GenePage.cgi?locus=SAL_1487 >SAL_1487

number of additional contiguous amino acids of SEQ ID NO:48 at N terminus of SEQ ID NO:110 or 30	number of additional contiguous amino acids of SEQ ID NO:48 at C terminus of SEQ ID NO:110 or 30
0-52, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52	0-786, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480,

	481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786

Table 13B. Cna_B domain antigens comprising SEQ ID NO:111 (SAL 1487, SEQ ID NO:48; GBS67= SAL_1487 (ancillary 1), jcvi.org/cgi-bin/CMR/shared/GenePage.cgi?locus=SAL_1487 >SAL_1487

number of additional contiguous amino acids of SEQ ID NO:48 at N terminus of SEQ ID NO:111	number of additional contiguous amino acids of SEQ ID NO:48 at C terminus of SEQ ID NO:111
0-750, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288,	0-67, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67

289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750	

Table 14. Cna_B domain antigens comprising SEQ ID NO:31 or 113 (SAN 1518, SEQ ID NO:49; >ORF01523 cell wall surface anchor family protein, putative {Streptococcus agalactiae COH1})

number of additional contiguous amino acids of SEQ ID NO:49 at N terminus of SEQ ID NO:31 or 113	number of additional contiguous amino acids of SEQ ID NO:49 at C terminus of SEQ ID NO:31 or 113
0-365, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182,	0-50, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50

183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365	

Table 15. Cna_B domain antigens comprising SEQ ID NO:32 (SAN 1519, SEQ ID NO:50; >ORF01524 reticulocyte binding protein {Streptococcus agalactiae COH1})

number of additional contiguous amino acids of SEQ ID NO:50 at N terminus of SEQ ID NO:32	number of additional contiguous amino acids of SEQ ID NO:50 at C terminus of SEQ ID NO:32
0-1290, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363,	0-62, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62

364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000, 1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1020, 1021, 1022, 1023, 1024, 1025, 1026, 1027, 1028, 1029, 1030, 1031, 1032, 1033, 1034, 1035, 1036, 1037, 1038, 1039, 1040, 1041, 1042, 1043, 1044, 1045, 1046, 1047, 1048, 1049, 1050, 1051, 1052, 1053, 1054, 1055, 1056, 1057, 1058, 1059, 1060, 1061, 1062, 1063, 1064, 1065, 1066, 1067, 1068, 1069, 1070, 1071, 1072, 1073, 1074, 1075, 1076, 1077, 1078, 1079, 1080, 1081, 1082, 1083, 1084, 1085, 1086, 1087, 1088, 1089, 1090, 1091, 1092, 1093, 1094, 1095, 1096, 1097, 1098, 1099, 1100, 1101, 1102, 1103, 1104, 1105, 1106, 1107, 1108, 1109, 1110, 1111, 1112, 1113, 1114, 1115, 1116, 1117, 1118, 1119, 1120, 1121, 1122, 1123, 1124, 1125, 1126, 1127, 1128, 1129, 1130,	

1131, 1132, 1133, 1134, 1135, 1136, 1137, 1138, 1139, 1140, 1141, 1142, 1143, 1144, 1145, 1146, 1147, 1148, 1149, 1150, 1151, 1152, 1153, 1154, 1155, 1156, 1157, 1158, 1159, 1160, 1161, 1162, 1163, 1164, 1165, 1166, 1167, 1168, 1169, 1170, 1171, 1172, 1173, 1174, 1175, 1176, 1177, 1178, 1179, 1180, 1181, 1182, 1183, 1184, 1185, 1186, 1187, 1188, 1189, 1190, 1191, 1192, 1193, 1194, 1195, 1196, 1197, 1198, 1199, 1200, 1201, 1202, 1203, 1204,1205, 1206, 1207, 1208, 1209, 1210, 1211, 1212, 1213, 1214, 1215, 1216, 1217, 1218, 1219, 1220, 1221, 1222, 1223, 1224, 1225, 1226, 1227, 1228, 1229, 1230, 1231, 1232, 1233, 1234, 1235, 1236, 1237, 1238, 1239, 1240, 1241, 1242, 1243, 1244, 1245, 1246, 1247, 1248, 1249, 1250, 1251, 1252, 1253, 1254, 1255, 1256, 1257, 1258, 1259, 1260, 1261, 1262, 1263, 1264, 1265, 1266, 1267, 1268, 1269, 1270, 1271, 1272, 1273, 1274, 1275, 1276, 1277, 1278, 1279, 1280, 1281, 1282, 1283, 1284, 1285, 1286, 1287, 1288, 1289, 1290	

Table 16. Cna_B domain antigens comprising SEQ ID NO:33 or 112 (SAG 0645, SEQ ID NO:51; >gi|22536814|ref|NP_687665.1| cell wall surface anchor family protein [Streptococcus agalactiae 2603V/R])

number of additional contiguous amino acids of SEQ ID NO:51 at N terminus of SEQ ID NO:33 or 112	number of additional contiguous amino acids of SEQ ID NO:51 at C terminus of SEQ ID NO:33 or 112
0-394, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394	0-65, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65

Table 17. Cna_B domain antigens comprising SEQ ID NO:35 (SAN 1516, SEQ ID NO:52; >ORF01521 hypothetical protein {Streptococcus agalactiae COH1})

number of additional contiguous amino acids of SEQ ID NO:52 at N terminus of SEQ ID NO:35	number of additional contiguous amino acids of SEQ ID NO:52 at C terminus of SEQ ID NO:35
0-98, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98	0-36, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36

Table 18A. Cna_B domain antigens comprising SEQ ID NO:114 (SAL 1486, SEQ ID NO:102; GBS59= SAL_1486 (backbone), jcvi.org/cgi-bin/CMR/shared/GenePage.cgi?locus=SAL_1486 >SAL_1486

number of additional contiguous amino acids of SEQ ID NO:102 at N terminus of SEQ ID NO:114	number of additional contiguous amino acids of SEQ ID NO:102 at C terminus of SEQ ID NO:114
0-83, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83	0-503, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339,

	340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503

Table 18B. Cna_B domain antigens comprising SEQ ID NO:115 (SAL 1486, SEQ ID NO:102; GBS59= SAL_1486 (backbone), jcvi.org/cgi-bin/CMR/shared/GenePage.cgi?locus=SAL_1486 >SAL_1486

number of additional contiguous amino acids of SEQ ID NO:102 at N terminus of SEQ ID NO:115	number of additional contiguous amino acids of SEQ ID NO:102 at C terminus of SEQ ID NO:115
0-470, *e.g.,* 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416,	0-56, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56

WO 2010/079464 PCT/IB2010/050110

417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470	

Table 18C. Cna_B domain antigens comprising SEQ ID NO:116 (SAG 1407, SEQ ID NO:118)

number of additional contiguous amino acids of SEQ ID NO:118 at N terminus of SEQ ID NO:116	number of additional contiguous amino acids of SEQ ID NO:118 at C terminus of SEQ ID NO:116
0-20, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20	0-614, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554,

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	555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614

Table 18D. Cna_B domain antigens comprising SEQ ID NO:117 (SAG 1407, SEQ ID NO:118)

number of additional contiguous amino acids of SEQ ID NO:118 at N terminus of SEQ ID NO:117	number of additional contiguous amino acids of SEQ ID NO:118 at C terminus of SEQ ID NO:117
0-489, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489	0-53, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53

WO 2010/079464 PCT/IB2010/050110

Table 19. Cna_B domain antigens comprising SEQ ID NO:53 (SP_0463, SEQ ID NO:63; >gi|15900379|ref|NP_344983.1| cell wall surface anchor family protein [Streptococcus pneumoniae TIGR4])

number of additional contiguous amino acids of SEQ ID NO:63 at N terminus of SEQ ID NO:53	number of additional contiguous amino acids of SEQ ID NO:63 at C terminus of SEQ ID NO:53
0-459, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459	0-68, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68

Table 20. Cna_B domain antigens comprising SEQ ID NO:54 (SP_0462, SEQ ID NO:64; >gi|15900378|ref|NP_344982.1| cell wall surface anchor family protein [Streptococcus pneumoniae TIGR4])

number of additional contiguous amino acids of SEQ ID NO:64 at N terminus of SEQ ID NO:54	number of additional contiguous amino acids of SEQ ID NO:64 at C terminus of SEQ ID NO:54
0-60, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60	0-762, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699,

	700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762

Table 21. Cna_B domain antigens comprising SEQ ID NO:55 (SP_0464, SEQ ID NO:65; >gi|15900380|ref|NP_344984.1| cell wall surface anchor family protein [Streptococcus pneumoniae TIGR4])

number of additional contiguous amino acids of SEQ ID NO:65 at N terminus of SEQ ID NO:55	number of additional contiguous amino acids of SEQ ID NO:65 at C terminus of SEQ ID NO:55
0-271, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271	0-41, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41

Table 22. Cna_B domain antigens comprising SEQ ID NO:66 (SdrD MW0517,SEQ ID NO:72); >gi|21282246|ref|NP_645334.1| Ser-Asp rich fibrinogen-binding bone sialoprotein-binding protein [Staphylococcus aureus subsp. aureus MW2])

number of additional contiguous amino acids of SEQ ID NO:72 at N terminus of SEQ ID NO:66	number of additional contiguous amino acids of SEQ ID NO:72 at C terminus of SEQ ID NO:66
0-703, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582,	0-473, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430,

WO 2010/079464 PCT/IB2010/050110

583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703	431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473

Table 23. Cna_B domain antigens comprising SEQ ID NO:67 (SdrD MW0517,SEQ ID NO:72); >gi|21282246|ref|NP_645334.1| Ser-Asp rich fibrinogen-binding bone sialoprotein-binding protein [Staphylococcus aureus subsp. aureus MW2])

number of additional contiguous amino acids of SEQ ID NO:72 at N terminus of SEQ ID NO:67	number of additional contiguous amino acids of SEQ ID NO:72 at C terminus of SEQ ID NO:67
0-924, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459,	0-353, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179,

WO 2010/079464 PCT/IB2010/050110

460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924	180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353

Table 24. Cna_B domain antigens comprising SEQ ID NO:68 (MW2612, SEQ ID NO:73; >gi|21284341|ref|NP_647429.1| collagen adhesin precursor [Staphylococcus aureus subsp. aureus MW2])

number of additional contiguous amino acids of SEQ ID NO:73 at N terminus of SEQ ID NO:68	number of additional contiguous amino acids of SEQ ID NO:73 at C terminus of SEQ ID NO:68
0-344, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285,	0-761, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661,

286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344	662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761

Table 25. Cna_B domain antigens comprising SEQ ID NO:1 (Spy_M18_0126, SEQ ID NO:23; >gi|19745301|ref|NP_606437.1| putative collagen binding protein [Streptococcus pyogenes MGAS8232])

number of additional contiguous amino acids of SEQ ID NO:23 at N terminus of SEQ ID NO:1	number of additional contiguous amino acids of SEQ ID NO:23 at C terminus of SEQ ID NO:1
0-70, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70	0-282, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282

Table 26. Cna_B domain antigens comprising SEQ ID NO:34(SAG 0649, SEQ ID NO:47; >gi|22536818|ref|NP_687669.1| cell wall surface anchor family protein, putative [Streptococcus agalactiae 2603V/R])

number of additional contiguous amino acids of SEQ ID NO:47 at N terminus of SEQ ID NO:34	number of additional contiguous amino acids of SEQ ID NO:47 at C terminus of SEQ ID NO:34
0-748, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633,	0-62, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62

WO 2010/079464 PCT/IB2010/050110

634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748	

Table 27. Cna_B domain antigens comprising SEQ ID NO:57 (*S. pneumoniae* protein SP_0464; SEQ ID NO:65)

number of additional contiguous amino acids of SEQ ID NO:65 at N terminus of SEQ ID NO:57	number of additional contiguous amino acids of SEQ ID NO:65 at C terminus of SEQ ID NO:57
0-161, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161	0-141, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141

Table 28. Cna_B domain antigens comprising SEQ ID NO:80 (*S. suis* protein SSU05_0474[Streptococcus suis 05ZYH33 ; SEQ ID NO:82)

number of additional contiguous amino acids of SEQ ID NO:82 at N terminus of SEQ ID NO:80	number of additional contiguous amino acids of SEQ ID NO:82 at C terminus of SEQ ID NO:80
0-348, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348	0-53, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53

Table 29. Cna_B domain antigens comprising SEQ ID NO:81 (*S. suis* protein DUF11:Surface protein from Gram-positive cocci, anchor region [Streptococcus suis 89/1591; SEQ ID NO:83)

number of additional contiguous amino acids of SEQ ID NO:83 at N terminus of SEQ ID NO:81	number of additional contiguous amino acids of SEQ ID NO:83 at C terminus of SEQ ID NO:81
0-358, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358	0-124, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124

Table 30. Cna_B domain antigens comprising SEQ ID NO:84 (*S. equi* protein ancillary protein SEQ0935 undefined product 914186:916159 forward MW:73872 67; SEQ ID NO:87)

number of additional contiguous amino acids of SEQ ID NO:87 at N terminus of SEQ ID NO:84	number of additional contiguous amino acids of SEQ ID NO:87 at C terminus of SEQ ID NO:84
0-350, *e.g.* 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350	0-244, *e.g.* 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244

Table 31. Cna_B domain antigens comprising SEQ ID NO:85 (*S. equi* protein ancillary protein SEQ0935 undefined product 914186:916159 forward MW:73872 67; SEQ ID NO:87)

number of additional contiguous amino acids of SEQ ID NO:87 at N terminus of SEQ ID NO:85	number of additional contiguous amino acids of SEQ ID NO:87 at C terminus of SEQ ID NO:85
0-539, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539	0-55, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55

Table 32. Cna_B domain antigens comprising SEQ ID NO:86 (*S. equi* protein BKB SEQ0936 undefined product 916183:917625 forward MW:51902 46,3; SEQ ID NO:88)

number of additional contiguous amino acids of SEQ ID NO:88 at N terminus of SEQ ID NO:86	number of additional contiguous amino acids of SEQ ID NO:88 at C terminus of SEQ ID NO:86
0-336, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336	0-74, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74

Table 33. Cna_B domain antigens comprising SEQ ID NO:122 (*S. pyogenes* protein F2, Spy0119; SEQ ID NO:121)

number of additional contiguous amino acids of SEQ ID NO:121 at N terminus of SEQ ID NO:122	number of additional contiguous amino acids of SEQ ID NO:121 at C terminus of SEQ ID NO:122
0-59, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59	0-1030, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686,

	687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000, 1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1020, 1021, 1022, 1023, 1024, 1025, 1026, 1027, 1028, 1029, 1030

Table 34. Cna_B domain antigens comprising SEQ ID NO:123 (*S. pyogenes* protein F2, Spy0119; SEQ ID NO:121)

number of additional contiguous amino acids of SEQ ID NO:121 at N terminus of SEQ ID NO:123	number of additional contiguous amino acids of SEQ ID NO:121 at C terminus of SEQ ID NO:123
0-524, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229,	0-561, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183,

230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524	184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561

Table 35. Cna_B domain antigens comprising SEQ ID NO:124 (*S. pyogenes* protein F2, Spy0119; SEQ ID NO:121)

number of additional contiguous amino acids of SEQ ID NO:121 at N terminus of SEQ ID NO:124	number of additional contiguous amino acids of SEQ ID NO:121 at C terminus of SEQ ID NO:124
0-637, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603,	0-451, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408,

604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637	409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451

Table 36. Cna_B domain antigens comprising SEQ ID NO:125 (*S. pyogenes* protein F2, Spy0119; SEQ ID NO:121)

number of additional contiguous amino acids of SEQ ID NO:121 at N terminus of SEQ ID NO:125	number of additional contiguous amino acids of SEQ ID NO:121 at C terminus of SEQ ID NO:125
0-759, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495,	0-328, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328

496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759	

Table 37. Cna_B domain antigens comprising SEQ ID NO:126 (*S. pyogenes* protein F2, Spy0119; SEQ ID NO:121)

number of additional contiguous amino acids of SEQ ID NO:121 at N terminus of SEQ ID NO:126	number of additional contiguous amino acids of SEQ ID NO:121 at C terminus of SEQ ID NO:126
0-904, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297,	0-188, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188

298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904	

Table 43. Cna_B domain antigens comprising SEQ ID NO:134 (Cna_B domain of *S. aureus* SdrD protein, SEQ ID NO:132)

number of additional contiguous amino acids of SEQ ID NO:132 at N terminus of SEQ ID NO:134	number of additional contiguous amino acids of SEQ ID NO:132 at C terminus of SEQ ID NO:134
0-591, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591	0-683, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408,

WO 2010/079464 PCT/IB2010/050110

	409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683

Table 44. Cna_B domain antigens comprising SEQ ID NO:135 (Cna_B domain of *S. aureus* SdrD protein, SEQ ID NO:132)

number of additional contiguous amino acids of SEQ ID NO:132 at N terminus of SEQ ID NO:135	number of additional contiguous amino acids of SEQ ID NO:132 at C terminus of SEQ ID NO:135
0-703, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117,	0-572, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79,

118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703	80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540,

	541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572

Table 45. Cna_B domain antigens comprising SEQ ID NO:136 (Cna_B domain of *S. aureus* SdrD protein, SEQ ID NO:132)

number of additional contiguous amino acids of SEQ ID NO:132 at N terminus of SEQ ID NO:136	number of additional contiguous amino acids of SEQ ID NO:132 at C terminus of SEQ ID NO:136
0-814, *e.g.,* 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603,	0-461, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408,

604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814	409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461

Table 46. Cna_B domain antigens comprising SEQ ID NO:137 (Cna_B domain of *S. aureus* SdrD protein, SEQ ID NO:132)

number of additional contiguous amino acids of SEQ ID NO:132 at N terminus of SEQ ID NO:137	number of additional contiguous amino acids of SEQ ID NO:132 at C terminus of SEQ ID NO:137
0-924, *e.g.,* 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603,	0-351, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351

604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924	

Table 47. Cna_B domain antigens comprising SEQ ID NO:138 (Cna_B domain of *S. aureus* SdrD protein, SEQ ID NO:132)

number of additional contiguous amino acids of SEQ ID NO:132 at N terminus of SEQ ID NO:138	number of additional contiguous amino acids of SEQ ID NO:132 at C terminus of SEQ ID NO:138
0-1035, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603,	0-241, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241

604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000, 1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1020, 1021, 1022, 1023, 1024, 1025, 1026, 1027, 1028, 1029, 1030, 1031, 1032, 1033, 1034, 1035	

Table 48. Cna_B domain antigens comprising SEQ ID NO:139 (Cna_B domains of *S. aureus* SdrD protein, SEQ ID NO:132)

number of additional contiguous amino acids of SEQ ID NO:132 at N terminus of SEQ ID NO:139	number of additional contiguous amino acids of SEQ ID NO:132 at C terminus of SEQ ID NO:139
0-598, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74,	0-225, *e.g.*, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47,

75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598	48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225

Nucleic Acid Molecules

[53] The invention includes nucleic acid molecules which encode Cna_B domain antigens of the invention. The invention also includes nucleic acid molecules comprising nucleotide sequences having at least 95% sequence identity to such molecules. Depending on the particular sequence, the degree of sequence identity is preferably at least 95%, 96%, 97%, 98%, or 99%. Identity between nucleotide sequences is preferably determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affine gap search with parameters gap open penalty = 12 and gap extension penalty = 1.

[54] The invention also provides nucleic acid molecules which can hybridize to these molecules. Hybridization reactions can be performed under conditions of different stringency. Conditions which increase stringency of a hybridization reaction are widely known and published in the art. See, *e.g.*, page 7.52 of Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 1989. Examples of relevant conditions include (in order of increasing stringency): incubation temperatures of 25°C, 37 °C, 50 °C, 55 °C, and 68 °C; buffer concentrations of 10X SSC, 6X SSC, 1X SSC, and 0.1X SSC (where SSC is 0.15 M NaCl and 15 mM citrate buffer) and their equivalents using other buffer systems; formamide concentrations of 0%, 25%, 50%, and 75%; incubation times from 5 minutes to 24 hours; 1, 2, or more washing steps; wash incubation times of 1, 2, or 15 minutes; and wash solutions of 6X SSC, 1X SSC, 0.1X SSC, or de-ionized water. Hybridization techniques and their optimization are well known in the art. See, *e.g.*, Sambrook, 1989; Ausubel *et al.*, eds., Short Protocols in Molecular Biology, 4th ed., 1999; U.S. Patent 5,707,829; Ausubel *et al.*, eds., Current Protocols in Molecular Biology, Supplement 30, 1987.

[55] In some embodiments, nucleic acid molecules of the invention hybridize to a target under low stringency conditions; in other embodiments, nucleic acid molecules of the invention hybridize under intermediate stringency conditions; in preferred

embodiments, nucleic acid molecules of the invention hybridize under high stringency conditions. An example of a low stringency hybridization condition is 50°C and 10X SSC. An example of an intermediate stringency hybridization condition is 55°C and 1X SSC. An example of a high stringency hybridization condition is 68°C and 0.1X SSC.

Production of Cna_B domain antigens

Recombinant production

[56] The redundancy of the genetic code is well-known. Thus, any nucleic acid molecule (polynucleotide) which encodes a Cna_B domain antigen of the invention can be used to produce that protein recombinantly. Nucleic acid molecules encoding a Cna_B domain-containing protein can be isolated from the appropriate bacterium (*e.g.*, a streptococcal or staphylococcal bacterium) using standard nucleic acid purification techniques or can be synthesized using an amplification technique, such as the polymerase chain reaction (PCR), or using an automatic synthesizer. See Caruthers *et al.*, Nucl. Acids Res. Symp. Ser. 215 223, 1980; Horn *et al.* Nucl. Acids Res. Symp. Ser. 225 232, 1980; Hunkapiller *et al.*, Nature 310, 105-11, 1984; Grantham *et al.*, Nucleic Acids Res. 9, r43-r74, 1981.

[57] cDNA molecules can be made with standard molecular biology techniques, using mRNA as a template. cDNA molecules can thereafter be replicated using molecular biology techniques well known in the art. An amplification technique, such as PCR, can be used to obtain additional copies of polynucleotides of the invention, using either genomic DNA or cDNA as a template.

[58] If desired, polynucleotides can be engineered using methods generally known in the art to alter coding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of a polypeptide or mRNA product. DNA shuffling by random fragmentation and PCR reassembly of gene

fragments and synthetic oligonucleotides can be used to engineer the nucleotide sequences. For example, site directed mutagenesis can be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, introduce mutations, and so forth.

[59] Nucleic acid molecules can include a coding sequence for an N-terminal leader sequence (either the N-terminal leader sequence of a native protein comprising a Cna_B or another N-terminal leader sequence of choice). In some embodiments, sequence modifications, such as the addition of a purification tag sequence or codon optimization, are used to facilitate expression. For example, an expressed protein can comprise a tag such as polyhistidine (HIS) or glutathione S-transferase (GST). Such tags can be used to facilitate purification, detection, and stability of the expressed protein. Codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce an RNA transcript having desirable properties, such as a half life which is longer than that of a transcript generated from the naturally occurring sequence. These methods are well known in the art and are described in WO 05/032582.

Expression vectors

[60] A nucleic acid molecule which encodes a Cna_B domain antigen can be inserted into an expression vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art can be used to construct expression vectors containing coding sequences and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination.

Host cells

[61] Host cells for producing Cna_B domain antigens can be prokaryotic or eukaryotic. E. coli is a preferred host cell, but other suitable hosts include Lactococcus lactis, Lactococcus cremoris, Bacillus subtilis, Vibrio cholerae, Salmonella typhi, Salmonella typhimurium, Neisseria lactamica, Neisseria cinerea, Mycobacteria (*e.g.*, M. tuberculosis), yeasts, baculovirus, mammalian cells, etc.

[62] A host cell strain can be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed polypeptide in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post translational processing which cleaves a "prepro" form of the polypeptide also can be used to facilitate correct insertion, folding and/or function. Different host cells which have specific cellular machinery and characteristic mechanisms for post translational activities are available from the American Type Culture Collection (ATCC; 10801 University Boulevard, Manassas, VA 20110-2209) and can be chosen to ensure the correct modification and processing of a foreign protein. See WO 01/98340.

[63] Expression constructs can be introduced into host cells using well-established techniques which include, but are not limited to, transferrin-polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, "gene gun" methods, and DEAE- or calcium phosphate-mediated transfection.

[64] Host cells transformed with expression vectors can be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell can be secreted or contained intracellularly depending on the nucleotide sequence and/or the expression vector used. Those of skill in the art

understand that expression vectors can be designed to contain signal sequences which direct secretion of soluble polypeptides through a prokaryotic or eukaryotic cell membrane.

Purification

[65] Signal export sequences can be included in a recombinantly produced Cna_B domain antigen so that the antigen can be purified from cell culture medium using known methods. Alternatively, recombinantly produced Cna_B domain antigens of the invention can be isolated from engineered host cells and separated from other components in the cell, such as proteins, carbohydrates, or lipids, using methods well-known in the art. Such methods include, but are not limited to, size exclusion chromatography, ammonium sulfate fractionation, ion exchange chromatography, affinity chromatography, and preparative gel electrophoresis. A preparation of purified Cna_B domain antigens is at least 80% pure; preferably, the preparations are 90%, 95%, or 99% pure. Purity of the preparations can be assessed by any means known in the art, such as SDS-polyacrylamide gel electrophoresis. Where appropriate, Cna_B domain antigens can be solubilized, for example, with urea.

Chemical synthesis

[66] Cna_B domain antigens can be synthesized, for example, using solid phase techniques. See, *e.g.*, Merrifield, *J. Am. Chem. Soc. 85*, 2149 54, 1963; Roberge *et al.*, *Science 269*, 202 04, 1995. Protein synthesis can be performed using manual techniques or by automation. Automated synthesis can be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Optionally, portions of a Cna_B domain antigen can be synthesized separately and combined using chemical methods to produce the complete molecule.

Pharmaceutical compositions

[67] The invention provides compositions for use as medicaments. Pharmaceutical compositions of the invention are useful for raising an immune response against gram positive bacteria, particularly streptococcal or staphylococcal bacteria (*e.g.*, *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, and/or *S. aureus*). In some embodiments the compositions are useful for treating streptococcal and/or staphylococcal infections as well as reducing the risk of such infections.

[68] Pharmaceutical compositions of the invention comprise at least one active agent, which can be a Cna_B domain antigen as disclosed herein or a nucleic acid molecule encoding the Cna_B domain antigen. The disease can be, for example, bacteremia, meningitis, puerperal fever, scarlet fever, erysipelas, pharyngitis, impetigo, necrotizing fasciitis, myositis, or toxic shock syndrome.

[69] Compositions containing a Cna_B domain antigen or a nucleic acid molecule encoding a Cna_B domain antigen are preferably immunogenic compositions, and are more preferably vaccine compositions. Pharmaceutical compositions according to the invention can be either prophylactic or therapeutic, but will typically be prophylactic. A pharmaceutical composition is "prophylactic" if it reduces the risk of a gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection or reduces the severity of a gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection or a symptom of a gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection. Accordingly, the invention includes methods for the therapeutic or prophylactic treatment of a gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection. Animals, preferably mammals, most preferably humans, can be treated. The methods involve administering to the animal a therapeutic or prophylactic amount of an immunogenic composition of the invention.

[70] The pH of such compositions typically is between 6 and 8, preferably about 7. The pH can be maintained by the use of a buffer. The composition can be sterile and/or pyrogen-free. The composition can be isotonic with respect to human tissue (*e.g.*, blood).

[71] Some compositions of the invention comprise one or more Cna_B domain antigens as described herein. Other compositions of the invention comprise one or more nucleic acid molecules which encodes the antigens and, optionally, other antigens which can be included in the composition (see below). See, *e.g.*, Robinson & Torres (1997) Seminars in Immunology 9:271-283; Donnelly *et al.* (1997) Ann. Rev Immunol 15:617-648; Scott-Taylor & Dalgleish (2000) Expert Opin Investig Drugs 9:471-480; Apostolopoulos & Plebanski (2000) Curr Opin Mol Ther 2:441-447; Ilan (1999) Curr Opin Mol Ther 1:116-120; Dubensky *et al.* (2000) Mol Med 6:723-732; Robinson & Pertmer (2000) Adv Virus Res 55:1-74; Donnelly *et al.* (2000) Am J Respir Crit Care Med 162(4 Pt 2):S190-193; Davis (1999) Mt. Sinai J. Med. 66:84-90. Typically the nucleic acid molecule is a DNA molecule, *e.g.*, in the form of a plasmid. In some embodiments, compositions of the invention can comprise one or more Cna_B domain antigens and one or more nucleic acid molecules.

Additional active agents

[72] In some embodiments, compositions of the invention can include one or more additional active agents. Such agents include, but are not limited to, (a) another Cna_B domain antigen of the invention, (b) a polypeptide antigen which is useful in a pediatric vaccine, (c) a polypeptide antigen which is useful in a vaccine for elderly or immunocompromised individuals, (d) a nucleic acid molecule encoding (a)-(c), an antibody which specifically binds to (a)-(c), and a GBS polysaccharide antigen as defined below.

Antibodies

[73] Cna_B domains of gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) proteins can be used to generate antibodies, preferably protective antibodies. "Antibody" as used herein includes, but is not limited to, intact immunoglobulin molecules, as well as fragments thereof which are capable of binding a Cna_B domain. "Antibodies" therefore can include monoclonal antibodies, hybrid (chimeric) antibody molecules (*e.g.*, Winter *et al.*, Nature 349, 293-99, 1991; U.S. Patent 4,816,567); F(ab′)2 and F(ab) fragments and Fv molecules; non-covalent heterodimers (*e.g.*, Inbar *et al.*, Proc. Natl. Acad. Sci. U.S.A. 69, 2659-62, 1972; Ehrlich *et al.*, Biochem 19, 4091-96, 1980); single-chain Fv molecules (sFv) (*e.g.*, Huston *et al.*, Proc. Natl. Acad. Sci. U.S.A. 85, 5897-83, 1988); dimeric and trimeric antibody fragment constructs; minibodies (*e.g.*, Pack *et al.*, Biochem 31, 1579-84, 1992; Cumber *et al.*, J. Immunology 149B, 120-26, 1992); humanized antibody molecules (*e.g.*, Riechmann *et al.*, Nature 332, 323-27, 1988; Verhoeyan *et al.*, Science 239, 1534-36, 1988; and U.K. Patent Publication No. GB 2,276,169, published 21 September 1994); and any functional fragments obtained from such molecules, as well as antibodies obtained through non-conventional processes such as phage display.

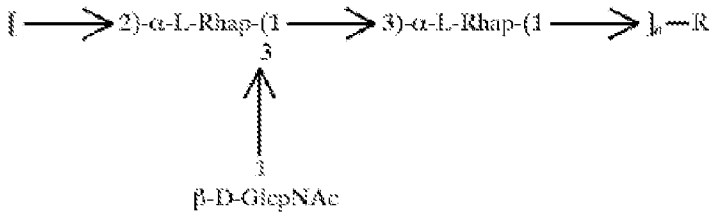
[74] An antibody binds specifically to a Cna_B domain according to the invention if it provides a detection signal at least 5-, 10-, or 20-fold higher than a detection signal provided with other proteins when used in an immunochemical assay. Preferably, an antibody that binds specifically to a Cna_B domain can immunoprecipitate that a Cna_B domain antigen from solution. In some embodiments, antibodies which bind specifically to a Cna_B domain induce opsonophagocytosis of GBS strain 515 by at least 30% (*e.g.*, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100%).

Additional antigens

[75] Compositions of the invention may be administered in conjunction with one or more antigens for use in therapeutic or prophylactic methods of the present invention. Preferred antigens include those listed below. Additionally, the compositions of the present invention may be used to treat or prevent infections caused by any of the below-listed pathogens. In addition to combination with the antigens described below, the compositions of the invention may also be combined with an adjuvant as described herein.

GBS polysaccharide antigen

[76] In some embodiments compositions of the invention comprise a GBS polysaccharide antigen. *S. agalactiae* GBS carbohydrate typically features a branched structure with an L-rhamnopyranose (Rhap) backbone consisting of alternating alpha-(1→2) and alpha-(1→3) links and D-N-acetylglucosamine (GlcpNAc) residues beta-(1→3)-connected to alternating rhamnose rings (Kreis *et al.*, Int. J. Biol. Macromol. 17, 117-30, 1995). GBS polysaccharide antigens useful in compositions of the invention have the formula:



(I),

wherein R is a terminal reducing L-Rhamnose or D-GlcpNAc and n is a number from about 3 to about 30.

[77] The GBS polysaccharide antigen used according to the invention may be a substantially full-length GBS carbohydrate, as found in nature, or it may be shorter than the natural length. Full-length polysaccharides may be depolymerized to give shorter fragments for

use with the invention, *e.g.*, by hydrolysis in mild acid, by heating, by sizing chromatography, etc. However, it is preferred to use saccharides of substantially full-length. In particular, it is preferred to use saccharides with a molecular weight of about 10 kDa. Molecular masses can be measured by gel filtration relative to dextran standards.

[78] The saccharide may be chemically modified relative to the GBS carbohydrate as found in nature. For example, the saccharide may be de N acetylated (partially or fully), N propionated (partially or fully), etc. The effect of de acetylation etc., for example on immunogenicity, can be assessed by routine assays.

[79] In some embodiments the GBS polysaccharide antigen is conjugated to a carrier, such as the mutated diphtheria toxin CRM197 and other carriers described below.

[80] Antigens for use with the invention include, but are not limited to, one or more of the following antigens set forth below, or antigens derived from one or more of the pathogens set forth below:

A. Bacterial Antigens

[81] Bacterial antigens suitable for use in the invention include proteins, polysaccharides, lipopolysaccharides, and outer membrane vesicles which may be isolated, purified or derived from a bacteria. In addition, bacterial antigens may include bacterial lysates and inactivated bacteria formulations. Bacteria antigens may be produced by recombinant expression. Bacterial antigens preferably include epitopes which are exposed on the surface of the bacteria during at least one stage of its life cycle. Bacterial antigens are preferably conserved across multiple serotypes. Bacterial antigens include antigens derived from one or more of the bacteria set forth below as well as the specific antigens examples identified below.

[82] *Neisseria meningitides*: *Meningitides* antigens may include proteins (such as those identified in References 1 – 7), saccharides (including a polysaccharide, oligosaccharide or lipopolysaccharide), or outer-membrane vesicles (References 8, 9, 10, 11) purified or derived from N. *meningitides* serogroup such as A, C, W135, Y, and/or B. *Meningitides* protein antigens may be selected from adhesions, autotransporters, toxins, Fe acquisition proteins, and membrane associated proteins (preferably integral outer membrane protein).

[83] *Streptococcus pneumoniae*: *Streptococcus pneumoniae* antigens may include a saccharide (including a polysaccharide or an oligosaccharide) and/or protein from *Streptococcus pneumoniae*. Saccharide antigens may be selected from serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. Protein antigens may be selected from a protein identified in WO 98/18931, WO 98/18930, US Patent No. 6,699,703, US Patent No. 6,800,744, WO 97/43303, and WO 97/37026. *Streptococcus pneumoniae* proteins may be selected from the Poly Histidine Triad family (PhtX), the Choline Binding Protein family (CbpX), CbpX truncates, LytX family, LytX truncates, CbpX truncate-LytX truncate chimeric proteins, pneumolysin (Ply), PspA, PsaA, Sp128, Sp101, Sp130, Sp125 or Sp133.

[84] *Streptococcus pyogenes* (Group A Streptococcus): Group A Streptococcus antigens may include a protein identified in WO 02/34771 or WO 2005/032582 (including GAS 40), fusions of fragments of GAS M proteins (including those described in WO 02/094851, and Dale, Vaccine (1999) 17:193-200, and Dale, Vaccine 14(10): 944-948), fibronectin binding protein (Sfb1), Streptococcal heme-associated protein (Shp), and Streptolysin S (SagA).

[85] *Moraxella catarrhalis*: *Moraxella* antigens include antigens identified in WO 02/18595 and WO 99/58562, outer membrane protein antigens (HMW-OMP), C-antigen, and/or LPS.

[86] *Bordetella pertussis*: *Pertussis* antigens include petussis holotoxin (PT) and filamentous haemagglutinin (FHA) from *B. pertussis*, optionally also combination with pertactin and/or agglutinogens 2 and 3 antigen.

[87] *Staphylococcus aureus*: *Staphylococcus aureus* antigens include *S. aureus* type 5 and 8 capsular polysaccharides optionally conjugated to nontoxic recombinant *Pseudomonas aeruginosa* exotoxin A, such as StaphVAX™, or antigens derived from surface proteins, invasins (leukocidin, kinases, hyaluronidase), surface factors that inhibit phagocytic engulfment (capsule, Protein A), carotenoids, catalase production, Protein A, coagulase, clotting factor, and/or membrane-damaging toxins (optionally detoxified) that lyse eukaryotic cell membranes (hemolysins, leukotoxin, leukocidin).

[88] *Staphylococcus epidermis*: *S. epidermidis* antigens include slime-associated antigen (SAA).

[89] *Clostridium tetani* (Tetanus): Tetanus antigens include tetanus toxoid (TT), preferably used as a carrier protein in conjunction/conjugated with the compositions of the present invention.

[90] *Cornynebacterium diphtheriae* (Diphtheria): Diphtheria antigens include diphtheria toxin, preferably detoxified, such as CRM197. Additionally antigens capable of modulating, inhibiting or associated with ADP ribosylation are contemplated for combination/co-administration/conjugation with the compositions of the present invention. The diphtheria toxoids may be used as carrier proteins.

[91] *Haemophilus influenzae B* (Hib): Hib antigens include a Hib saccharide antigen.

[92] *Pseudomonas aeruginosa*: *Pseudomonas* antigens include endotoxin A, Wzz protein, P. aeruginosa LPS, more particularly LPS isolated from PAO1 (O5 serotype), and/or Outer Membrane Proteins, including Outer Membrane Proteins F (OprF) (Infect Immun. 2001 May; 69(5): 3510-3515).

[93] *Legionella pneumophila.* Bacterial antigens may be derived from *Legionella pneumophila.*

[94] *Streptococcus agalactiae* (Group B Streptococcus): Group B Streptococcus antigens include a protein or saccharide antigen identified in WO 02/34771, WO 03/093306, WO 04/041157, or WO 2005/002619 (including proteins GBS 80, GBS 104, GBS 276 and GBS 322, and including saccharide antigens derived from serotypes Ia, Ib, Ia/c, II, III, IV, V, VI, VII and VIII).

[95] *Neiserria gonorrhoeae*: *Gonorrhoeae* antigens include Por (or porin) protein, such as PorB (see Zhu *et al.*, Vaccine (2004) 22:660 – 669), a transferring binding protein, such as TbpA and TbpB (See Price *et al.*, Infection and Immunity (2004) 71(1):277 – 283), a opacity protein (such as Opa), a reduction-modifiable protein (Rmp), and outer membrane vesicle (OMV) preparations (see Plante *et al.*, J Infectious Disease (2000) 182:848 – 855), also see *e.g.* WO99/24578, WO99/36544, WO99/57280, WO02/079243).

[96] *Chlamydia trachomatis*: *Chlamydia trachomatis* antigens include antigens derived from serotypes A, B, Ba and C (agents of trachoma, a cause of blindness), serotypes L1, L2 & L3 (associated with Lymphogranuloma venereum), and serotypes, D-K. Chlamydia trachomas antigens may also include an antigen identified in WO 00/37494, WO 03/049762, WO 03/068811, or WO 05/002619, including PepA (CT045), LcrE (CT089), ArtJ (CT381), DnaK (CT396), CT398, OmpH-like (CT242), L7/L12 (CT316), OmcA (CT444), AtosS (CT467), CT547, Eno (CT587), HrtA (CT823), and MurG (CT761).

[97] *Treponema pallidum* (Syphilis): Syphilis antigens include TmpA antigen.

[98] *Haemophilus ducreyi* (causing chancroid): *Ducreyi* antigens include outer membrane protein (DsrA).

[99] *Enterococcus faecalis* or *Enterococcus faecium*: Antigens include a trisaccharide repeat or other *Enterococcus* derived antigens provided in US Patent No. 6,756,361.

[100] *Helicobacter pylori*: *H. pylori* antigens include Cag, Vac, Nap, HopX, HopY and/or urease antigen.

[101] *Staphylococcus saprophyticus*: Antigens include the 160 kDa hemagglutinin of *S. saprophyticus* antigen.

[102] *Yersinia enterocolitica* antigens include LPS (Infect Immun. 2002 August; 70(8): 4414).

[103] *E. coli*: *E. coli* antigens may be derived from enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli* (EAggEC), diffusely adhering *E. coli* (DAEC), enteropathogenic *E. coli* (EPEC), and/or enterohemorrhagic *E. coli* (EHEC).

[104] *Bacillus anthracis* (anthrax): *B. anthracis* antigens are optionally detoxified and may be selected from A-components (lethal factor (LF) and edema factor (EF)), both of which can share a common B-component known as protective antigen (PA).

[105] *Yersinia pestis* (plague): Plague antigens include F1 capsular antigen (Infect Immun. 2003 Jan; 71(1)): 374-383, LPS (Infect Immun. 1999 Oct; 67(10): 5395), *Yersinia pestis* V antigen (Infect Immun. 1997 Nov; 65(11): 4476-4482).

[106] *Mycobacterium tuberculosis*: Tuberculosis antigens include lipoproteins, LPS, BCG antigens, a fusion protein of antigen 85B (Ag85B) and/or ESAT-6 optionally formulated in cationic lipid vesicles (Infect Immun. 2004 October; 72(10): 6148), *Mycobacterium tuberculosis* (Mtb) isocitrate dehydrogenase associated antigens (Proc Natl Acad Sci U S A. 2004 Aug 24; 101(34): 12652), and/or MPT51 antigens (Infect Immun. 2004 July; 72(7): 3829).

[107] *Rickettsia*: Antigens include outer membrane proteins, including the outer membrane protein A and/or B (OmpB) (Biochim Biophys Acta. 2004 Nov 1;1702(2):145), LPS, and surface protein antigen (SPA) (J Autoimmun. 1989 Jun;2 Suppl:81).

[108] *Listeria monocytogenes*. Bacterial antigens may be derived from *Listeria monocytogenes*.

[109] *Chlamydia pneumoniae*: Antigens include those identified in WO 02/02606.

[110] *Vibrio cholerae*: Antigens include proteinase antigens, LPS, particularly lipopolysaccharides of *Vibrio cholerae* II, O1 Inaba O-specific polysaccharides, *V. cholera* O139, antigens of IEM108 vaccine (Infect Immun. 2003 Oct;71(10):5498-504), and/or Zonula occludens toxin (Zot).

[111] *Salmonella typhi* (typhoid fever): Antigens include capsular polysaccharides preferably conjugates (Vi, *i.e.* vax-TyVi).

[112] *Borrelia burgdorferi* (Lyme disease): Antigens include lipoproteins (such as OspA, OspB, OspC and OspD), other surface proteins such as OspE-related proteins (Erps), decorin-binding proteins (such as DbpA), and antigenically variable VI proteins. , such as antigens associated with P39 and P13 (an integral membrane protein, Infect Immun. 2001 May; 69(5): 3323-3334), VlsE Antigenic Variation Protein (J Clin Microbiol. 1999 Dec; 37(12): 3997).

[113] *Porphyromonas gingivalis*: Antigens include *P. gingivalis* outer membrane protein (OMP).

[114] *Klebsiella*: Antigens include an OMP, including OMP A, or a polysaccharide optionally conjugated to tetanus toxoid.

[115] Further bacterial antigens useful in compositions of the invention may be capsular antigens, polysaccharide antigens or protein antigens of any of the above. Further bacterial antigens may also include an outer membrane vesicle (OMV) preparation. Additionally, antigens include live, attenuated, and/or purified versions of any of the aforementioned bacteria. The antigens may be derived from gram-negative or gram-positive bacteria. The antigens may be derived from aerobic or anaerobic bacteria.

[116] Additionally, any of the above bacterial-derived saccharides (polysaccharides, LPS, LOS or oligosaccharides) can be conjugated to another agent or antigen, such as a carrier protein (for example CRM197). Such conjugation may be direct conjugation effected by reductive amination of carbonyl moieties on the saccharide to amino groups on the protein, as provided in US Patent No. 5,360,897 and Can J Biochem Cell Biol. 1984 May;62(5):270-5. Alternatively, the saccharides can be conjugated through a linker, such as, with succinamide or other linkages provided in Bioconjugate Techniques, 1996 and CRC, Chemistry of Protein Conjugation and Cross-Linking, 1993.

B. Viral Antigens

[117] Viral antigens suitable for use in the invention include inactivated (or killed) virus, attenuated virus, split virus formulations, purified subunit formulations, viral proteins which may be isolated, purified or derived from a virus, and Virus Like Particles (VLPs). Viral antigens may be derived from viruses propagated on cell culture or other substrate. Alternatively, viral antigens may be expressed recombinantly. Viral antigens preferably include epitopes which are exposed on the surface of the virus during at least one stage of its life cycle. Viral antigens are preferably conserved across multiple serotypes or isolates. Viral antigens include antigens derived from one or more of the viruses set forth below as well as the specific antigens examples identified below.

[118] Orthomyxovirus: Viral antigens may be derived from an Orthomyxovirus, such as Influenza A, B and C. Orthomyxovirus antigens may be selected from one or more of the viral proteins, including hemagglutinin (HA), neuraminidase (NA), nucleoprotein (NP), matrix protein (M1), membrane protein (M2), one or more of the transcriptase components (PB1, PB2 and PA). Preferred antigens include HA and NA.

[119] Influenza antigens may be derived from interpandemic (annual) flu strains. Alternatively influenza antigens may be derived from strains with the potential to cause pandemic a pandemic outbreak (*i.e.*, influenza strains with new haemagglutinin compared to the haemagglutinin in currently circulating strains, or influenza strains which are pathogenic in avian subjects and have the potential to be transmitted horizontally in the human population, or influenza strains which are pathogenic to humans).

[120] *Paramyxoviridae* viruses: Viral antigens may be derived from *Paramyxoviridae* viruses, such as Pneumoviruses (RSV), Paramyxoviruses (PIV) and Morbilliviruses (Measles).

[121] Pneumovirus: Viral antigens may be derived from a Pneumovirus, such as Respiratory syncytial virus (RSV), Bovine respiratory syncytial virus, Pneumonia virus of mice, and Turkey rhinotracheitis virus. Preferably, the Pneumovirus is RSV. Pneumovirus antigens may be selected from one or more of the following proteins, including surface proteins Fusion (F), Glycoprotein (G) and Small Hydrophobic protein (SH), matrix proteins M and M2, nucleocapsid proteins N, P and L and nonstructural proteins NS1 and NS2. Preferred Pneumovirus antigens include F, G and M. See *e.g.*, J Gen Virol. 2004 Nov; 85(Pt 11):3229). Pneumovirus antigens may also be formulated in or derived from chimeric viruses. For example, chimeric RSV/PIV viruses may comprise components of both RSV and PIV.

[122] Paramyxovirus: Viral antigens may be derived from a Paramyxovirus, such as Parainfluenza virus types 1 – 4 (PIV), Mumps, Sendai viruses, Simian virus 5, Bovine parainfluenza virus and Newcastle disease virus. Preferably, the Paramyxovirus is PIV or Mumps. Paramyxovirus antigens may be selected from one or more of the following proteins: Hemagglutinin –Neuraminidase (HN), Fusion proteins F1 and F2, Nucleoprotein (NP), Phosphoprotein (P), Large protein (L), and Matrix protein (M). Preferred Paramyxovirus proteins include HN, F1 and F2. Paramyxovirus antigens may also be formulated in or derived from chimeric viruses. For example, chimeric RSV/PIV viruses may comprise components of both RSV and PIV. Commercially available mumps vaccines include live attenuated mumps virus, in either a monovalent form or in combination with measles and rubella vaccines (MMR).

[123] Morbillivirus: Viral antigens may be derived from a Morbillivirus, such as Measles. Morbillivirus antigens may be selected from one or more of the following proteins: hemagglutinin (H), Glycoprotein (G), Fusion factor (F), Large protein (L), Nucleoprotein (NP), Polymerase phosphoprotein (P), and Matrix (M). Commercially available measles vaccines include live attenuated measles virus, typically in combination with mumps and rubella (MMR).

[124] Picornavirus: Viral antigens may be derived from Picornaviruses, such as Enteroviruses, Rhinoviruses, Heparnavirus, Cardioviruses and Aphthoviruses. Antigens derived from Enteroviruses, such as Poliovirus are preferred.

[125] Enterovirus: Viral antigens may be derived from an Enterovirus, such as Poliovirus types 1, 2 or 3, Coxsackie A virus types 1 to 22 and 24, Coxsackie B virus types 1 to 6, Echovirus (ECHO) virus) types 1 to 9, 11 to 27 and 29 to 34 and Enterovirus 68 to 71. Preferably, the Enterovirus is poliovirus. Enterovirus antigens are preferably selected from one or more of the following Capsid proteins VP1, VP2, VP3 and VP4. Commercially available polio vaccines include Inactivated Polio Vaccine (IPV) and Oral poliovirus vaccine (OPV).

[126] Heparnavirus: Viral antigens may be derived from an Heparnavirus, such as Hepatitis A virus (HAV). Commercially available HAV vaccines include inactivated HAV vaccine.

[127] Togavirus: Viral antigens may be derived from a Togavirus, such as a Rubivirus, an Alphavirus, or an Arterivirus. Antigens derived from Rubivirus, such as Rubella virus, are preferred. Togavirus antigens may be selected from E1, E2, E3, C, NSP-1, NSPO-2, NSP-3 or NSP-4. Togavirus antigens are preferably selected from E1, E2 or E3. Commercially available Rubella vaccines include a live cold-adapted virus, typically in combination with mumps and measles vaccines (MMR).

[128] Flavivirus: Viral antigens may be derived from a Flavivirus, such as Tick-borne encephalitis (TBE), Dengue (types 1, 2, 3 or 4), Yellow Fever, Japanese encephalitis, West Nile encephalitis, St. Louis encephalitis, Russian spring-summer encephalitis, Powassan encephalitis. Flavivirus antigens may be selected from PrM, M, C, E, NS-1, NS-2a, NS2b, NS3, NS4a, NS4b, and NS5. Flavivirus antigens are preferably selected from PrM, M and E. Commercially available TBE vaccine include inactivated virus vaccines.

[129] Pestivirus: Viral antigens may be derived from a Pestivirus, such as Bovine viral diarrhea (BVDV), Classical swine fever (CSFV) or Border disease (BDV).

[130] Hepadnavirus: Viral antigens may be derived from a Hepadnavirus, such as Hepatitis B virus. Hepadnavirus antigens may be selected from surface antigens (L, M and S), core antigens (HBc, HBe). Commercially available HBV vaccines include subunit vaccines comprising the surface antigen S protein.

[131] Hepatitis C virus: Viral antigens may be derived from a Hepatitis C virus (HCV). HCV antigens may be selected from one or more of E1, E2, E1/E2, NS345 polyprotein, NS

345-core polyprotein, core, and/or peptides from the nonstructural regions (Houghton *et al.*, Hepatology (1991) 14:381).

[132] Rhabdovirus: Viral antigens may be derived from a Rhabdovirus, such as a Lyssavirus (Rabies virus) and Vesiculovirus (VSV). Rhabdovirus antigens may be selected from glycoprotein (G), nucleoprotein (N), large protein (L), nonstructural proteins (NS). Commercially available Rabies virus vaccine comprise killed virus grown on human diploid cells or fetal rhesus lung cells.

[133] Caliciviridae: Viral antigens may be derived from Calciviridae, such as Norwalk virus, and Norwalk-like Viruses, such as Hawaii Virus and Snow Mountain Virus.

[134] Coronavirus: Viral antigens may be derived from a Coronavirus, SARS, Human respiratory coronavirus, Avian infectious bronchitis (IBV), Mouse hepatitis virus (MHV), and Porcine transmissible gastroenteritis virus (TGEV). Coronavirus antigens may be selected from spike (S), envelope (E), matrix (M), nucleocapsid (N), and Hemagglutinin-esterase glycoprotein (HE). Preferably, the Coronavirus antigen is derived from a SARS virus. SARS viral antigens are described in WO 04/92360;

[135] Retrovirus: Viral antigens may be derived from a Retrovirus, such as an Oncovirus, a Lentivirus or a Spumavirus. Oncovirus antigens may be derived from HTLV-1, HTLV-2 or HTLV-5. Lentivirus antigens may be derived from HIV-1 or HIV-2. Retrovirus antigens may be selected from gag, pol, env, tax, tat, rex, rev, nef, vif, vpu, and vpr. HIV antigens may be selected from gag (p24gag and p55gag), env (gp160 and gp41), pol, tat, nef, rev vpu, miniproteins, (preferably p55 gag and gp140v delete). HIV antigens may be derived from one or more of the following strains: HIVIIIb, HIVSF2, HIVLAV, HIVLAI, HIVMN, HIV-1CM235, HIV-1US4.

[136] Reovirus: Viral antigens may be derived from a Reovirus, such as an Orthoreovirus, a Rotavirus, an Orbivirus, or a Coltivirus. Reovirus antigens may be selected from

structural proteins λ1, λ2, λ3, μ1, μ2, σ1, σ2, or σ3, or nonstructural proteins σNS, μNS, or σ1s. Preferred Reovirus antigens may be derived from a Rotavirus. Rotavirus antigens may be selected from VP1, VP2, VP3, VP4 (or the cleaved product VP5 and VP8), NSP 1, VP6, NSP3, NSP2, VP7, NSP4, or NSP5. Preferred Rotavirus antigens include VP4 (or the cleaved product VP5 and VP8), and VP7.

[137] Parvovirus: Viral antigens may be derived from a Parvovirus, such as Parvovirus B19. Parvovirus antigens may be selected from VP-1, VP-2, VP-3, NS-1 and NS-2. Preferably, the Parvovirus antigen is capsid protein VP-2.

[138] Delta hepatitis virus (HDV): Viral antigens may be derived HDV, particularly δ-antigen from HDV (see, *e.g.*, U.S. Patent No. 5,378,814).

[139] Hepatitis E virus (HEV): Viral antigens may be derived from HEV.

[140] Hepatitis G virus (HGV): Viral antigens may be derived from HGV.

[141] Human Herpesvirus: Viral antigens may be derived from a Human Herpesvirus, such as Herpes Simplex Viruses (HSV), Varicella-zoster virus (VZV), Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Human Herpesvirus 6 (HHV6), Human Herpesvirus 7 (HHV7), and Human Herpesvirus 8 (HHV8). Human Herpesvirus antigens may be selected from immediate early proteins (α), early proteins (β), and late proteins (γ). HSV antigens may be derived from HSV-1 or HSV-2 strains. HSV antigens may be selected from glycoproteins gB, gC, gD and gH, fusion protein (gB), or immune escape proteins (gC, gE, or gI). VZV antigens may be selected from core, nucleocapsid, tegument, or envelope proteins. A live attenuated VZV vaccine is commercially available. EBV antigens may be selected from early antigen (EA) proteins, viral capsid antigen (VCA), and glycoproteins of the membrane antigen (MA). CMV antigens may be selected from capsid proteins, envelope glycoproteins (such as gB and gH), and tegument proteins

[142] Papovaviruses: Antigens may be derived from Papovaviruses, such as Papillomaviruses and Polyomaviruses. Papillomaviruses include HPV serotypes 1, 2, 4, 5, 6, 8, 11, 13, 16, 18, 31, 33, 35, 39, 41, 42, 47, 51, 57, 58, 63 and 65. Preferably, HPV antigens are derived from serotypes 6, 11, 16 or 18. HPV antigens may be selected from capsid proteins (L1) and (L2), or E1 – E7, or fusions thereof. HPV antigens are preferably formulated into virus-like particles (VLPs). Polyomyavirus viruses include BK virus and JK virus. Polyomavirus antigens may be selected from VP1, VP2 or VP3.

[143] Further provided are antigens, compositions, methods, and microbes included in Vaccines, 4th Edition (Plotkin and Orenstein ed. 2004); Medical Microbiology 4th Edition (Murray *et al.* ed. 2002); Virology, 3rd Edition (W.K. Joklik ed. 1988); Fundamental Virology, 2nd Edition (B.N. Fields and D.M. Knipe, eds. 1991), which are contemplated in conjunction with the compositions of the present invention.

C. Fungal Antigens

[144] Fungal antigens for use in the invention may be derived from one or more of the fungi set forth below.

[145] Fungal antigens may be derived from Dermatophytres, including: *Epidermophyton floccusum, Microsporum audouini, Microsporum canis, Microsporum distortum, Microsporum equinum, Microsporum gypsum, Microsporum nanum, Trichophyton concentricum, Trichophyton equinum, Trichophyton gallinae, Trichophyton gypseum, Trichophyton megnini, Trichophyton mentagrophytes, Trichophyton quinckeanum, Trichophyton rubrum, Trichophyton schoenleini, Trichophyton tonsurans, Trichophyton verrucosum, T. verrucosum var. album, var. discoides, var. ochraceum, Trichophyton violaceum,* and/or *Trichophyton faviforme.*

[146] Fungal pathogens may be derived from *Aspergillus fumigatus, Aspergillus flavus, Aspergillus niger, Aspergillus nidulans, Aspergillus terreus, Aspergillus sydowi,*

Aspergillus flavatus, Aspergillus glaucus, Blastoschizomyces capitatus, Candida albicans, Candida enolase, Candida tropicalis, Candida glabrata, Candida krusei, Candida parapsilosis, Candida stellatoidea, Candida kusei, Candida parakwsei, Candida lusitaniae, Candida pseudotropicalis, Candida guilliermondi, Cladosporium carrionii, Coccidioides immitis, Blastomyces dermatidis, Cryptococcus neoformans, Geotrichum clavatum, Histoplasma capsulatum, Klebsiella pneumoniae, Paracoccidioides brasiliensis, Pneumocystis carinii, Pythiumn insidiosum, Pityrosporum ovale, Sacharomyces cerevisae, Saccharomyces boulardii, Saccharomyces pombe, Scedosporium apiosperum, Sporothrix schenckii, Trichosporon beigelii, Toxoplasma gondii, Penicillium marneffei, Malassezia spp., Fonsecaea spp., Wangiella spp., Sporothrix spp., Basidiobolus spp., Conidiobolus spp., Rhizopus spp, Mucor spp, Absidia spp, Mortierella spp, Cunninghamella spp, Saksenaea spp., Alternaria spp, Curvularia spp, Helminthosporium spp, Fusarium spp, Aspergillus spp, Penicillium spp, Monolinia spp, Rhizoctonia spp, Paecilomyces spp, Pithomyces spp, and *Cladosporium spp.*

[147] Processes for producing a fungal antigens are well known in the art (see US Patent No. 6,333,164). In a preferred method a solubilized fraction extracted and separated from an insoluble fraction obtainable from fungal cells of which cell wall has been substantially removed or at least partially removed, characterized in that the process comprises the steps of: obtaining living fungal cells; obtaining fungal cells of which cell wall has been substantially removed or at least partially removed; bursting the fungal cells of which cell wall has been substantially removed or at least partially removed; obtaining an insoluble fraction; and extracting and separating a solubilized fraction from the insoluble fraction.

D. STD Antigens

[148] The compositions of the invention may include one or more antigens derived from a sexually transmitted disease (STD). Such antigens may provide for prophylactis or

therapy for STDs such as chlamydia, genital herpes, hepatits (such as HCV), genital warts, gonorrhoea, syphilis and/or chancroid (See, WO00/15255). Antigens may be derived from one or more viral or bacterial STDs. Viral STD antigens for use in the invention may be derived from, for example, HIV, herpes simplex virus (HSV-1 and HSV-2), human papillomavirus (HPV), and hepatitis (HCV). Bacterial STD antigens for use in the invention may be derived from, for example, *Neiserria gonorrhoeae, Chlamydia trachomatis, Treponema pallidum, Haemophilus ducreyi, E. coli,* and *Streptococcus agalactiae*. Examples of specific antigens derived from these pathogens are described above.

E. Respiratory Antigens

[149] The compositions of the invention may include one or more antigens derived from a pathogen which causes respiratory disease. For example, respiratory antigens may be derived from a respiratory virus such as Orthomyxoviruses (influenza), Pneumovirus (RSV), Paramyxovirus (PIV), Morbillivirus (measles), Togavirus (Rubella), VZV, and Coronavirus (SARS). Respiratory antigens may be derived from a bacteria which causes respiratory disease, such as *Streptococcus pneumoniae, Pseudomonas aeruginosa, Bordetella pertussis, Mycobacterium tuberculosis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Bacillus anthracis,* and *Moraxella catarrhalis*. Examples of specific antigens derived from these pathogens are described above.

F. Pediatric Vaccine Antigens

[150] The compositions of the invention may include one or more antigens suitable for use in pediatric subjects. Pediatric subjects are typically less than about 3 years old, or less than about 2 years old, or less than about 1 years old. Pediatric antigens may be administered multiple times over the course of 6 months, 1, 2 or 3 years. Pediatric antigens may be derived from a virus which may target pediatric populations and/or a virus from which pediatric populations are susceptible to infection. Pediatric viral

antigens include antigens derived from one or more of Orthomyxovirus (influenza), Pneumovirus (RSV), Paramyxovirus (PIV and Mumps), Morbillivirus (measles), Togavirus (Rubella), Enterovirus (polio), HBV, Coronavirus (SARS), and Varicella-zoster virus (VZV), Epstein Barr virus (EBV). Pediatric bacterial antigens include antigens derived from one or more of *Streptococcus pneumoniae, Neisseria meningitides, Streptococcus agalactiae (*Group A Streptococcus*), Moraxella catarrhalis, Bordetella pertussis, Staphylococcus aureus, Clostridium tetani (*Tetanus*), Cornynebacterium diphtheriae (*Diphtheria*), Haemophilus influenzae B (*Hib*), Pseudomonas aeruginosa, Streptococcus agalactiae (*Group B Streptococcus*),* and *E. coli*. Examples of specific antigens derived from these pathogens are described above.

G. Antigens suitable for use in Elderly or Immunocompromised Individuals

[151] The compositions of the invention may include one or more antigens suitable for use in elderly or immunocompromised individuals. Such individuals may need to be vaccinated more frequently, with higher doses or with adjuvanted formulations to improve their immune response to the targeted antigens. Antigens which may be targeted for use in Elderly or Immunocompromised individuals include antigens derived from one or more of the following pathogens: *Neisseria meningitides, Streptococcus pneumoniae, Streptococcus agalactiae (*Group A Streptococcus*), Moraxella catarrhalis, Bordetella pertussis, Staphylococcus aureus, Staphylococcus epidermis, Clostridium tetani (Tetanus), Cornynebacterium diphtheriae (*Diphtheria*), Haemophilus influenzae B (*Hib*), Pseudomonas aeruginosa, Legionella pneumophila, Streptococcus agalactiae (Group B Streptococcus), Enterococcus faecalis, Helicobacter pylori, Clamydia pneumoniae*, Orthomyxovirus (influenza), Pneumovirus (RSV), Paramyxovirus (PIV and Mumps), Morbillivirus (measles), Togavirus (Rubella), Enterovirus (polio), HBV, Coronavirus (SARS), Varicella-zoster virus (VZV), Epstein Barr virus (EBV), Cytomegalovirus (CMV). Examples of specific antigens derived from these pathogens are described above.

H. Antigens suitable for use in Adolescent Vaccines

[152] The compositions of the invention may include one or more antigens suitable for use in adolescent subjects. Adolescents may be in need of a boost of a previously administered pediatric antigen. Pediatric antigens which may be suitable for use in adolescents are described above. In addition, adolescents may be targeted to receive antigens derived from an STD pathogen in order to ensure protective or therapeutic immunity before the beginning of sexual activity. STD antigens which may be suitable for use in adolescents are described above.

I. Antigen Formulations

[153] In other aspects of the invention, methods of producing microparticles having adsorbed antigens are provided. The methods comprise: (a) providing an emulsion by dispersing a mixture comprising (i) water, (ii) a detergent, (iii) an organic solvent, and (iv) a biodegradable polymer selected from the group consisting of a poly(α-hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate. The polymer is typically present in the mixture at a concentration of about 1% to about 30% relative to the organic solvent, while the detergent is typically present in the mixture at a weight-to-weight detergent-to-polymer ratio of from about 0.00001:1 to about 0.1:1 (more typically about 0.0001:1 to about 0.1:1, about 0.001:1 to about 0.1:1, or about 0.005:1 to about 0.1:1); (b) removing the organic solvent from the emulsion; and (c) adsorbing an antigen on the surface of the microparticles. In certain embodiments, the biodegradable polymer is present at a concentration of about 3% to about 10% relative to the organic solvent.

[154] Microparticles for use herein will be formed from materials that are sterilizable, non-toxic and biodegradable. Such materials include, without limitation, poly(α-hydroxy acid), polyhydroxybutyric acid, polycaprolactone, polyorthoester, polyanhydride, PACA, and polycyanoacrylate. Preferably, microparticles for use with the present

invention are derived from a poly(α-hydroxy acid), in particular, from a poly(lactide) ("PLA") or a copolymer of D,L-lactide and glycolide or glycolic acid, such as a poly(D,L-lactide-co-glycolide) ("PLG" or "PLGA"), or a copolymer of D,L-lactide and caprolactone. The microparticles may be derived from any of various polymeric starting materials which have a variety of molecular weights and, in the case of the copolymers such as PLG, a variety of lactide:glycolide ratios, the selection of which will be largely a matter of choice, depending in part on the coadministered macromolecule. These parameters are discussed more fully below.

[155] Further antigens may also include an outer membrane vesicle (OMV) preparation.

[156] Additional formulation methods and antigens (especially tumor antigens) are provided in U.S. Patent 6,884,435.

J. Antigen References

[157] The following references include antigens useful in conjunction with the compositions of the present invention:

1 International patent application WO99/24578
2 International patent application WO99/36544.
3 International patent application WO99/57280.
4 International patent application WO00/22430.
5 Tettelin *et al.* (2000) Science 287:1809-1815.
6 International patent application WO96/29412.
7 Pizza *et al.* (2000) Science 287:1816-1820.
8 PCT WO 01/52885.
9 Bjune *et al.* (1991) Lancet 338(8775).
10 Fuskasawa *et al.* (1999) Vaccine 17:2951-2958.
11 Rosenqist *et al.* (1998) Dev. Biol. Strand 92:323-333.
12 Constantino *et al.* (1992) Vaccine 10:691-698.
13 Constantino *et al.* (1999) Vaccine 17:1251-1263.
14 Watson (2000) Pediatr Infect Dis J 19:331-332.
15 Rubin (20000) Pediatr Clin North Am 47:269-285,v.
16 Jedrzejas (2001) Microbiol Mol Biol Rev 65:187-207.

17 International patent application filed on 3rd July 2001 claiming priority from GB-0016363.4;WO 02/02606; PCT IB/01/00166.
18 Kalman *et al.* (1999) Nature Genetics 21:385-389.
19 Read *et al.* (2000) Nucleic Acids Res 28:1397-406.
20 Shirai *et al.* (2000) J. Infect. Dis 181(Suppl 3):S524-S527.
21 International patent application WO99/27105.
22 International patent application WO00/27994.
23 International patent application WO00/37494.
24 International patent application WO99/28475.
25 Bell (2000) Pediatr Infect Dis J 19:1187-1188.
26 Iwarson (1995) APMIS 103:321-326.
27 Gerlich *et al.* (1990) Vaccine 8 Suppl:S63-68 & 79-80.
28 Hsu *et al.* (1999) Clin Liver Dis 3:901-915.
29 Gastofsson *et al.* (1996) N. Engl. J. Med. 334-:349-355.
30 Rappuoli *et al.* (1991) TIBTECH 9:232-238.
31 Vaccines (1988) eds. Plotkin & Mortimer. ISBN 0-7216-1946-0.
32 Del Guidice *et al.* (1998) Molecular Aspects of Medicine 19:1-70.
33 International patent application WO93/018150.
34 International patent application WO99/53310.
35 International patent application WO98/04702.
36 Ross *et al.* (2001) Vaccine 19:135-142.
37 Sutter *et al.* (2000) Pediatr Clin North Am 47:287-308.
38 Zimmerman & Spann (1999) Am Fan Physician 59:113-118, 125-126.
39 Dreensen (1997) Vaccine 15 Suppl"S2-6.
40 MMWR Morb Mortal Wkly rep 1998 Jan 16:47(1):12, 9.
41 McMichael (2000) Vaccine19 Suppl 1:S101-107.
42 Schuchat (1999) Lancer 353(9146):51-6.
43 GB patent applications 0026333.5, 0028727.6 & 0105640.7.
44 Dale (1999) Infect Disclin North Am 13:227-43, viii.
45 Ferretti *et al.* (2001) PNAS USA 98: 4658-4663.
46 Kuroda *et al.* (2001) Lancet 357(9264):1225-1240; see also pages 1218-1219.
47 Ramsay *et al.* (2001) Lancet 357(9251):195-196.
48 Lindberg (1999) Vaccine 17 Suppl 2:S28-36.
49 Buttery & Moxon (2000) J R Coil Physicians Long 34:163-168.
50 Ahmad & Chapnick (1999) Infect Dis Clin North Am 13:113-133, vii.
51 Goldblatt (1998) J. Med. Microbiol. 47:663-567.
52 European patent 0 477 508.
53 U.S. Patent No. 5,306,492.
54 International patent application WO98/42721.
55 Conjugate Vaccines (eds. Cruse *et al.*) ISBN 3805549326, particularly vol. 10:48-114.
56 Hermanson (1996) Bioconjugate Techniques ISBN: 012323368 & 012342335X.
57 European patent application 0372501.
58 European patent application 0378881.
59 European patent application 0427347.

60 International patent application WO93/17712.
61 International patent application WO98/58668.
62 European patent application 0471177.
63 International patent application WO00/56360.
64 International patent application WO00/67161.

[158] The contents of all of the above cited patents, patent applications and journal articles are incorporated by reference as if set forth fully herein.

Carrier proteins

[159] Where a saccharide or carbohydrate antigen is used, it is preferably conjugated to a carrier protein in order to enhance immunogenicity. See Ramsay *et al.* (2001) Lancet 357(9251):195-196; Lindberg (1999) Vaccine 17 Suppl 2:S28-36; Buttery & Moxon (2000) J R Coll Physicians Lond 34:163-168; Ahmad & Chapnick (1999) Infect Dis Clin North Am 13:113-133, vii; Goldblatt (1998) J. Med. Microbiol. 47:563-567; European patent 0 477 508; US Patent No. 5,306,492; WO98/42721; Conjugate Vaccines (eds. Cruse *et al.*) ISBN 3805549326, particularly vol. 10:48-114; Hermanson (1996) Bioconjugate Techniques ISBN: 0123423368 or 012342335X. Preferred carrier proteins are bacterial toxins or toxoids, such as diphtheria or tetanus toxoids. The CRM197 diphtheria toxoid is particularly preferred.

[160] Other carrier polypeptides include the N. meningitidis outer membrane protein (EP-A-0372501), synthetic peptides (EP-A-0378881 and EP-A 0427347), heat shock proteins (WO 93/17712 and WO 94/03208), pertussis proteins (WO 98/58668 and EP A 0471177), protein D from H. influenzae (WO 00/56360), cytokines (WO 91/01146), lymphokines, hormones, growth factors, toxin A or B from C. difficile (WO 00/61761), iron-uptake proteins (WO 01/72337), etc. Where a mixture comprises capsular saccharide from both serigraphs A and C, it may be preferred that the ratio (w/w) of MenA saccharide:MenC saccharide is greater than 1 (*e.g.*, 2:1, 3:1, 4:1, 5:1, 10:1 or higher). Different saccharides can be conjugated to the same or different type of carrier

protein. Any suitable conjugation reaction can be used, with any suitable linker where necessary.

[161] Toxic protein antigens may be detoxified where necessary *e.g.*, detoxification of pertussis toxin by chemical and/or genetic means.

Pharmaceutically acceptable carriers

[162] Compositions of the invention will typically, in addition to the components mentioned above, comprise one or more pharmaceutically acceptable carriers. These include any carrier which does not itself induce the production of antibodies harmful to the individual receiving the composition. Suitable carriers typically are large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and lipid aggregates (such as oil droplets or liposomes). Such carriers are well known to those of ordinary skill in the art. A composition may also contain a diluent, such as water, saline, glycerol, etc. Additionally, an auxiliary substance, such as a wetting or emulsifying agent, pH buffering substance, and the like, may be present. A thorough discussion of pharmaceutically acceptable components is available in Gennaro (2000) Remington: The Science and Practice of Pharmacy. 20th ed., ISBN: 0683306472.

Immunoregulatory Agents

Adjuvants

[163] Vaccines of the invention may be administered in conjunction with other immunoregulatory agents. In particular, compositions will usually include an adjuvant. Adjuvants for use with the invention include, but are not limited to, one or more of the following set forth below:

A. Mineral Containing Compositions

[164] Mineral containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminum salts and calcium salts. The invention includes mineral salts such as hydroxides (*e.g.* oxyhydroxides), phosphates (*e.g.* hydroxyphosphates, orthophosphates), sulfates, etc. (*e.g.* see chapters 8 & 9 of Vaccine Design… (1995) eds. Powell & Newman. ISBN: 030644867X. Plenum.), or mixtures of different mineral compounds (*e.g.* a mixture of a phosphate and a hydroxide adjuvant, optionally with an excess of the phosphate), with the compounds taking any suitable form (*e.g.* gel, crystalline, amorphous, etc.), and with adsorption to the salt(s) being preferred. The mineral containing compositions may also be formulated as a particle of metal salt (WO00/23105).

[165] Aluminum salts may be included in vaccines of the invention such that the dose of Al^{3+} is between 0.2 and 1.0 mg per dose.

[166] In one embodiment the aluminum based adjuvant for use in the present invention is alum (aluminum potassium sulfate ($AlK(SO_4)_2$)), or an alum derivative, such as that formed in-situ by mixing an antigen in phosphate buffer with alum, followed by titration and precipitation with a base such as ammonium hydroxide or sodium hydroxide.

[167] Another aluminum-based adjuvant for use in vaccine formulations of the present invention is aluminum hydroxide adjuvant ($Al(OH)_3$) or crystalline aluminum oxyhydroxide (AlOOH), which is an excellent adsorbant, having a surface area of approximately $500m^2/g$. Alternatively, aluminum phosphate adjuvant ($AlPO_4$) or aluminum hydroxyphosphate, which contains phosphate groups in place of some or all of the hydroxyl groups of aluminum hydroxide adjuvant is provided. Preferred aluminum phosphate adjuvants provided herein are amorphous and soluble in acidic, basic and neutral media.

[168] In another embodiment the adjuvant of the invention comprises both aluminum phosphate and aluminum hydroxide. In a more particular embodiment thereof, the adjuvant has a greater amount of aluminum phosphate than aluminum hydroxide, such as a ratio of 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1 or greater than 9:1, by weight aluminum phosphate to aluminum hydroxide. More particular still, aluminum salts in the vaccine are present at 0.4 to 1.0 mg per vaccine dose, or 0.4 to 0.8 mg per vaccine dose, or 0.5 to 0.7 mg per vaccine dose, or about 0.6 mg per vaccine dose.

[169] Generally, the preferred aluminum-based adjuvant(s), or ratio of multiple aluminum-based adjuvants, such as aluminum phosphate to aluminum hydroxide is selected by optimization of electrostatic attraction between molecules such that the antigen carries an opposite charge as the adjuvant at the desired pH. For example, aluminum phosphate adjuvant (isoelectric point = 4) adsorbs lysozyme, but not albumin at pH 7.4. Should albumin be the target, aluminum hydroxide adjuvant would be selected (iep 11.4). Alternatively, pretreatment of aluminum hydroxide with phosphate lowers its isoelectric point, making it a preferred adjuvant for more basic antigens.

B. Oil-Emulsions

[170] Oil-emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as 5% squalene, 0.5% polyoxyethylene (20) sorbitan monooleate (polysorbate 80, *e.g.*, TWEEN® 80), and 0.5% sorbitan trioleate (*e.g.*, SPAN® 85), such as MF59®, formulated into submicron particles using a microfluidizer). See WO90/14837. See also, Podda, Vaccine (2001) 19: 2673-2680; Frey *et al.*, Vaccine (2003) 21:4234-4237. MF59® is used as the adjuvant in the FLUAD™ influenza virus trivalent subunit vaccine.

[171] Particularly preferred adjuvants for use in the compositions are submicron oil-in-water emulsions. Preferred submicron oil-in-water emulsions for use herein are squalene/water emulsions optionally containing varying amounts of MTP-PE, such as a

submicron oil-in-water emulsion containing 4-5% w/v squalene, 0.25-1.0% w/v TWEEN™ 80 (polyoxyelthylenesorbitan monooleate), and/or 0.25-1.0% SPAN 85™ (sorbitan trioleate), and, optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-huydroxyphosphophoryloxy)-ethylamine (MTP-PE), for example, the submicron oil-in-water emulsion known as "MF59" (International Publication No. WO90/14837; US Patent Nos. 6,299,884 and 6,451,325, and Ott *et al.*, in Vaccine Design: The Subunit and Adjuvant Approach (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296). MF59 contains 4-5% w/v Squalene (*e.g.* 4.3%), 0.25-0.5% w/v TWEEN™ 80, and 0.5% w/v SPAN 85™ and optionally contains various amounts of MTP-PE, formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA). For example, MTP-PE may be present in an amount of about 0-500 µg/dose, more preferably 0-250 µg/dose and most preferably, 0-100 µg/dose. As used herein, the term "MF59-0" refers to the above submicron oil-in-water emulsion lacking MTP-PE, while the term MF59-MTP denotes a formulation that contains MTP-PE. For instance, "MF59-100" contains 100 µg MTP-PE per dose, and so on. MF69, another submicron oil-in-water emulsion for use herein, contains 4.3% w/v squalene, 0.25% w/v polyoxyethylene (20) sorbitan monooleate (polysorbate 80, *e.g.*, TWEEN® 80), and 0.75% w/v sorbitan trioleate (*e.g.*, SPAN® 85) and optionally MTP-PE. Yet another submicron oil-in-water emulsion is MF75, also known as SAF, containing 10% squalene, 0.4% polyoxyethylene (20) sorbitan monooleate (polysorbate 80, *e.g.*, TWEEN® 80), 5% pluronic-blocked polymer L121, and thr-MDP, also microfluidized into a submicron emulsion. MF75-MTP denotes an MF75 formulation that includes MTP, such as from 100-400 µg MTP-PE per dose.

[172] Submicron oil-in-water emulsions, methods of making the same and immunostimulating agents, such as muramyl peptides, for use in the compositions, are described in detail in WO90/14837 and U.S. Patents 6,299,884 and 6,451,325.

[173] Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used as adjuvants in the invention.

C. Saponin Formulations

[174] Saponin formulations, may also be used as adjuvants in the invention. Saponins are a heterologous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponins isolated from the bark of the Quillaia saponaria Molina tree have been widely studied as adjuvants. Saponins can also be commercially obtained from Smilax ornata (sarsaprilla), Gypsophilla paniculata (brides veil), and Saponaria officianalis (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs.

[175] Saponin compositions have been purified using High Performance Thin Layer Chromatography (HP-TLC) and Reversed Phase High Performance Liquid Chromatography (RP-HPLC). Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of QS21 is disclosed in U.S. Patent 5,057,540. Saponin formulations may also comprise a sterol, such as cholesterol (see WO96/33739).

[176] Combinations of saponins and cholesterols can be used to form unique particles called Immunostimulating Complexes (ISCOMs). ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylcholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of Quil A, QHA and QHC. ISCOMs are further described in EP0109942, WO96/11711 and WO96/33739. Optionally, the ISCOMS may be devoid of (an) additional detergent(s). See WO00/07621.

[177] A review of the development of saponin based adjuvants can be found in Barr, *et al.*, Advanced Drug Delivery Reviews (1998) 32:247-271. See also Sjolander, *et al.*, Advanced Drug Delivery Reviews (1998) 32:321-338.

D. Virosomes and Virus Like Particles (VLPs)

[178] Virosomes and Virus Like Particles (VLPs) can also be used as adjuvants in the invention. These structures generally contain one or more proteins from a virus optionally combined or formulated with a phospholipid. They are generally non-pathogenic, non-replicating and generally do not contain any of the native viral genome. The viral proteins may be recombinantly produced or isolated from whole viruses. These viral proteins suitable for use in virosomes or VLPs include proteins derived from influenza virus (such as HA or NA), Hepatitis B virus (such as core or capsid proteins), Hepatitis E virus, measles virus, Sindbis virus, Rotavirus, Foot-and-Mouth Disease virus, Retrovirus, Norwalk virus, human Papilloma virus, HIV, RNA-phages, Qß-phage (such as coat proteins), GA-phage, fr-phage, AP205 phage, and Ty (such as retrotransposon Ty protein p1). VLPs are discussed further in WO03/024480, WO03/024481, and Niikura *et al.*, Virology (2002) 293:273-280; Lenz *et al.*, Journal of Immunology (2001) 5246-5355; Pinto, *et al.*, Journal of Infectious Diseases (2003) 188:327-338; and Gerber *et al.*, Journal of Virology (2001) 75(10):4752-4760. Virosomes are discussed further in, for example, Gluck *et al.*, Vaccine (2002) 20:B10 – B16. Immunopotentiating reconstituted influenza virosomes (IRIV) are used as the subunit antigen delivery system in the intranasal trivalent INFLEXAL™ product {Mischler & Metcalfe (2002) Vaccine 20 Suppl 5:B17-23} and the INFLUVAC PLUS™ product.

E. Bacterial or Microbial Derivatives

[179] Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as:

(1) Non-toxic derivatives of enterobacterial lipopolysaccharide (LPS)

[180] Such derivatives include Monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 De-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acylated monophosphoryl lipid A is disclosed in EP 0 689 454. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22 micron membrane (see EP 0 689 454). Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives *e.g.* RC 529. See Johnson *et al.* (1999) Bioorg Med Chem Lett 9:2273-2278.

(2) Lipid A Derivatives

[181] Lipid A derivatives include derivatives of lipid A from Escherichia coli such as OM-174. OM-174 is described for example in Meraldi *et al.*, Vaccine (2003) 21:2485-2491; and Pajak, *et al.*, Vaccine (2003) 21:836-842.

(3) Immunostimulatory oligonucleotides

[182] Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a sequence containing an unmethylated cytosine followed by guanosine and linked by a phosphate bond). Bacterial double stranded RNA or oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

[183] The CpGs can include nucleotide modifications/analogs such as phosphorothioate modifications and can be double-stranded or single-stranded. Optionally, the guanosine may be replaced with an analog such as 2′-deoxy-7-deazaguanosine. See Kandimalla, *et al.*, Nucleic Acids Research (2003) 31(9): 2393-2400; WO02/26757 and WO99/62923 for examples of possible analog substitutions. The adjuvant effect of CpG oligonucleotides is further discussed in Krieg, Nature Medicine (2003) 9(7): 831-835;

McCluskie, *et al.*, FEMS Immunology and Medical Microbiology (2002) 32:179-185; WO98/40100; US Patent No. 6,207,646; US Patent No. 6,239,116 and US Patent No. 6,429,199.

[184] The CpG sequence may be directed to TLR9, such as the motif GTCGTT or TTCGTT. See Kandimalla, *et al.*, Biochemical Society Transactions (2003) 31 (part 3): 654-658. The CpG sequence may be specific for inducing a Th1 immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in Blackwell, *et al.*, J. Immunol. (2003) 170(8):4061-4068; Krieg, TRENDS in Immunology (2002) 23(2): 64-65 and WO01/95935. Preferably, the CpG is a CpG-A ODN.

[185] Preferably, the CpG oligonucleotide is constructed so that the 5′ end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3′ ends to form immunomers. See, for example, Kandimalla, *et al.*, BBRC (2003) 306:948-953; Kandimalla, *et al.*, Biochemical Society Transactions (2003) 31(part 3):664-658; Bhagat *et al.*, BBRC (2003) 300:853-861 and WO03/035836.

(4) ADP-ribosylating toxins and detoxified derivatives thereof.

[186] Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the invention. Preferably, the protein is derived from E. coli (*i.e.*, E. coli heat labile enterotoxin "LT), cholera ("CT"), or pertussis ("PT"). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is described in WO95/17211 and as parenteral adjuvants in WO98/42375. Preferably, the adjuvant is a detoxified LT mutant such as LT-K63, LT-R72, and LTR192G. The use of ADP-ribosylating toxins and detoxified derivatives thereof, particularly LT-K63 and LT-R72, as adjuvants can be found in the following references: Beignon *et al.*, Infection and Immunity (2002) 70(6):3012-3019; Pizza, *et al.*, Vaccine (2001) 19:2534-2541; Pizza, *et al.*, Int. J. Med. Microbiol (2000) 290(4-5):455-461; Scharton-Kersten *et al.*, Infection and Immunity

(2000) 68(9):5306-5313; Ryan *et al.*, Infection and Immunity (1999) 67(12):6270-6280; Partidos *et al.*, Immunol. Lett. (1999) 67(3):209-216; Peppoloni *et al.*, Vaccines (2003) 2(2):285-293; and Pine *et al.*, (2002) J. Control Release (2002) 85(1-3):263-270. Numerical reference for amino acid substitutions is preferably based on the alignments of the A and B subunits of ADP-ribosylating toxins set forth in Domenighini *et al.*, Mol. Microbiol (1995) 15(6):1165-1167.

F. Bioadhesives and Mucoadhesives

[187] Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable bioadhesives include esterified hyaluronic acid microspheres (Singh *et al.* (2001) J. Cont. Rele. 70:267-276) or mucoadhesives such as cross-linked derivatives of polyacrylic acid, polyvinyl alcohol, polyvinyl pyrollidone, polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention. See WO99/27960.

G. Microparticles

[188] Microparticles may also be used as adjuvants in the invention. Microparticles (*i.e.* a particle of ~100nm to ~150μm in diameter, more preferably ~200nm to ~30μm in diameter, and most preferably ~500nm to ~10μm in diameter) formed from materials that are biodegradable and non toxic (*e.g.* a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, etc.), with poly(lactide co glycolide) are preferred, optionally treated to have a negatively-charged surface (*e.g.* with SDS) or a positively-charged surface (*e.g.* with a cationic detergent, such as CTAB).

H. Liposomes

[189] Examples of liposome formulations suitable for use as adjuvants are described in US Patent No. 6,090,406, US Patent No. 5,916,588, and EP 0 626 169.

I. Polyoxyethylene ether and Polyoxyethylene Ester Formulations

[190] Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters. WO99/52549. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol (WO01/21207) as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol (WO01/21152).

[191] Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-steoryl ether, polyoxytheylene-8-steoryl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

J. Polyphosphazene (PCPP)

[192] PCPP formulations are described, for example, in Andrianov *et al.*, "Preparation of hydrogel microspheres by coacervation of aqueous polyphophazene solutions", Biomaterials (1998) 19(1-3):109-115 and Payne *et al.*, "Protein Release from Polyphosphazene Matrices", Adv. Drug. Delivery Review (1998) 31(3):185-196.

K. Muramyl peptides

[193] Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-l-alanyl-d-isoglutamine (nor-MDP), and N acetylmuramyl-l-alanyl-d-isoglutaminyl-l-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

L. Imidazoquinoline Compounds

[194] Examples of imidazoquinoline compounds suitable for use adjuvants in the invention include Imiquimod and its analogues, described further in Stanley, Clin Exp Dermatol (2002) 27(7):571-577; Jones, Curr Opin Investig Drugs (2003) 4(2):214-218; and U.S. Patents 4,689,338, 5,389,640, 5,268,376, 4,929,624, 5,266,575, 5,352,784, 5,494,916, 5,482,936, 5,346,905, 5,395,937, 5,238,944, and 5,525,612.

M. Thiosemicarbazone Compounds

[195] Examples of thiosemicarbazone compounds, as well as methods of formulating, manufacturing, and screening for compounds all suitable for use as adjuvants in the invention include those described in WO04/60308. The thiosemicarbazones are particularly effective in the stimulation of human peripheral blood mononuclear cells for the production of cytokines, such as TNF- α.

N. Tryptanthrin Compounds

[196] Examples of tryptanthrin compounds, as well as methods of formulating, manufacturing, and screening for compounds all suitable for use as adjuvants in the invention include those described in WO04/64759. The tryptanthrin compounds are particularly effective in the stimulation of human peripheral blood mononuclear cells for the production of cytokines, such as TNF- α.

[197] The invention may also comprise combinations of aspects of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention:

(1) a saponin and an oil-in-water emulsion (WO99/11241);

(2) a saponin (*e.g.*, QS21) + a non-toxic LPS derivative (*e.g.* 3dMPL) (see WO94/00153);

(3) a saponin (*e.g.*, QS21) + a non-toxic LPS derivative (*e.g.* 3dMPL) + a cholesterol;

(4) a saponin (*e.g.*, QS21) + 3dMPL + IL 12 (optionally + a sterol) (WO98/57659);

(5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions (See European patent applications 0835318, 0735898 and 0761231);

(6) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion.

(7) RIBI™ adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (DETOX™); and

(8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dPML).

(9) one or more mineral salts (such as an aluminum salt) + an immunostimulatory oligonucleotide (such as a nucleotide sequence including a CpG motif).

O. Human Immunomodulators

[198] Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as interleukins (*e.g.* IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, etc.), interferons (*e.g.* interferon-γ), macrophage colony stimulating factor, and tumor necrosis factor.

[199] Aluminum salts and MF59 are preferred adjuvants for use with injectable influenza vaccines. Bacterial toxins and bioadhesives are preferred adjuvants for use with mucosally-delivered vaccines, such as nasal vaccines.

[200] The contents of all of the above cited patents, patent applications and journal articles are incorporated by reference as if set forth fully herein.

Therapeutic methods

[201] The invention provides methods for inducing or increasing an immune response to one or more gram positive (*e.g.*, streptococcal and/or staphylococcal) bacteria (*e.g.*, *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, and/or *S. aureus*) using the compositions described above. The invention also provides the compositions described above for use in inducing or increasing an immune response to one or more gram positive (*e.g.*, streptococcal and/or staphylococcal) bacteria (*e.g.*, *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, and/or *S. aureus*). The immune response is preferably protective and can include antibodies and/or cell-mediated immunity (including systemic and mucosal immunity). Immune responses include booster responses.

[202] Teenagers and children, including toddles and infants, can receive a vaccine for prophylactic use; therapeutic vaccines typically are administered to teenagers or adults. A vaccine intended for children may also be administered to adults *e.g.*, to assess safety, dosage, immunogenicity, etc.

[203] Diseases caused by *S. agalactiae* which can be prevented or treated according to the invention include, but are not limited to, newborn sepsis, meningitis and pneumonia and pregnant women infection such as in the womb, in the amniotic fluid, following cesarean sections, and in the urinary tract.

[204] Diseases caused by *S. pneumoniae* which can be prevented or treated according to the invention include, but are not limited to, Pneumonia, bacteremia, otitis media, meningitis, sinusitis, peritonitis, and arthritis.

[205] Diseases caused by *S. pyogenes* which can be prevented or treated according to the invention include, but are not limited to, erysipelas pharyngitis (such as streptococcal sore throat),, scarlet fever, impetigo, cellulitis, septicemia, necrotizing fasciitis, myositis, toxic shock syndrome, and sequelae such as rheumatic fever and acute glomerulonephritis.

[206] Diseases caused by *S. aureus* which can be prevented or treated according to the invention include, but are not limited to, minor skin infections, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, pneumonia, meningitis, osteomyelitis, endocarditis, Toxic shock syndrome, and septicemia.

[207] Diseases caused by *S. suis* which can be prevented or treated according to the invention include, but are not limited to, *S. suis* infections in swine and meningitis, septicemia, pneumonia, endocarditis, arthritis, and septic shock in humans exposed to swine or swine products.

[208] Diseases caused by *S. equi* which can be prevented or treated according to the invention include, but are not limited to, “strangles” in equine, canine and Camelid patients (*e.g.*, horses, donkeys, mules, dogs, camels and dromedaries) and metastatic strangles.

[209] Diseases caused by *S. uberis* which can be prevented or treated according to the invention include, but are not limited to, mastitis in cattle.

[210] Diseases caused by *S. dysgalactiae* which can be prevented or treated according to the invention include, but are not limited to, mastitis in, *e.g.*, horses, cattle, and swine.

[211] Diseases caused by *S. iniae* which can be prevented or treated according to the invention include, but are not limited to, *S. iniae* infection of fish and invasive infection in humans after skin injuries during the handling of infected fish.

Tests to determine the efficacy of the immune response

[212] One way of assessing efficacy of therapeutic treatment involves monitoring bacterial infection after administration of the composition of the invention. One way of assessing efficacy of prophylactic treatment involves monitoring immune responses against the Cna_B domains in the compositions of the invention after administration of the composition.

[213] Another way of assessing the immunogenicity of the component proteins of the immunogenic compositions of the present invention is to produce Cna_B domains recombinantly and to screen patient sera or mucosal secretions by immunoblot. A positive reaction between the protein and the patient serum indicates that the patient has previously mounted an immune response to the protein in question; *i.e.*, the protein is an immunogen. This method may also be used to identify immunodominant proteins and/or epitopes.

[214] Another way of checking efficacy of therapeutic treatment involves monitoring infection after administration of the compositions of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses both systemically (such as monitoring the level of IgG1 and IgG2a production) and mucosally (such as monitoring the level of IgA production) against a Cna_B domain

after administration of the composition. Typically, serum specific antibody responses are determined post-immunization but pre-challenge whereas mucosal specific antibody body responses are determined post-immunization and post-challenge.

[215] The vaccine compositions of the present invention can be evaluated in *in vitro* and *in vivo* animal models prior to host, *e.g.*, human, administration. Particularly useful mouse models include those in which intraperitoneal immunization is followed by either intraperitoneal challenge or intranasal challenge.

[216] The efficacy of immunogenic compositions of the invention can also be determined *in vivo* by challenging animal models with gram positive (*e.g.*, staphylococcal or streptococcal) bacteria, *e.g.*, guinea pigs or mice, with the immunogenic compositions. The immunogenic compositions may or may not be derived from the same serotypes as the challenge serotypes.

[217] *In vivo* efficacy models include but are not limited to: (i) a murine infection model using human gram positive (*e.g.*, streptococcal and/or staphylococcal) bacteria serotypes; (ii) a murine disease model which is a murine model using a mouse-adapted streptococcal strain, such as the M23 strain of *S. pyogenes* which is particularly virulent in mice, and (iii) a primate model using human streptococcal isolates. Other *in vivo* models are disclosed in the Examples below.

[218] The immune response may be one or both of a Th1 immune response and a Th2 response. The immune response may be an improved or an enhanced or an altered immune response. The immune response may be one or both of a systemic and a mucosal immune response. Preferably the immune response is an enhanced system and/or mucosal response.

[219] An enhanced systemic and/or mucosal immunity is reflected in an enhanced Th1 and/or Th2 immune response. Preferably, the enhanced immune response includes an increase in the production of IgG1 and/or IgG2a and/or IgA.

[220] Preferably the mucosal immune response is a Th2 immune response. Preferably, the mucosal immune response includes an increase in the production of IgA.

[221] Activated Th2 cells enhance antibody production and are therefore of value in responding to extracellular infections. Activated Th2 cells may secrete one or more of IL-4, IL-5, IL-6, and IL-10. A Th2 immune response may result in the production of IgG1, IgE, IgA and memory B cells for future protection.

[222] A Th2 immune response may include one or more of an increase in one or more of the cytokines associated with a Th2 immune response (such as IL-4, IL-5, IL-6 and IL-10), or an increase in the production of IgG1, IgE, IgA and memory B cells. Preferably, the enhanced Th2 immune response will include an increase in IgG1 production.

[223] A Th1 immune response may include one or more of an increase in CTLs, an increase in one or more of the cytokines associated with a Th1 immune response (such as IL-2, IFNγ, and TNFβ), an increase in activated macrophages, an increase in NK activity, or an increase in the production of IgG2a. Preferably, the enhanced Th1 immune response will include an increase in IgG2a production.

[224] Immunogenic compositions of the invention, in particular, immunogenic composition comprising one or more Cna_B domains of the present invention may be used either alone or in combination with other gram positive bacterial antigens (*e.g.*, streptococcal or staphylococcal antigens), optionally with an immunoregulatory agent capable of eliciting a Th1 and/or Th2 response.

[225] The invention also comprises an immunogenic composition comprising one or more immunoregulatory agent, such as a mineral salt, such as an aluminium salt and an

oligonucleotide containing a CpG motif. Most preferably, the immunogenic composition includes both an aluminium salt and an oligonucleotide containing a CpG motif. Alternatively, the immunogenic composition includes an ADP ribosylating toxin, such as a detoxified ADP ribosylating toxin and an oligonucleotide containing a CpG motif. Preferably, one or more of the immunoregulatory agents include an adjuvant. The adjuvant may be selected from one or more of the group consisting of a Th1 adjuvant and Th2 adjuvant.

[226] The compositions of the invention will preferably elicit both a cell mediated immune response as well as a humoral immune response in order to effectively address a gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection. This immune response will preferably induce long lasting (*e.g.*, neutralizing) antibodies and a cell mediated immunity that can quickly respond upon exposure to one or more gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) antigens.

[227] In one particularly preferred embodiment, the immunogenic composition comprises one or more Cna_B domain antigen(s) which elicit(s) a neutralizing antibody response and one or more Cna_B domain antigen (s) which elicit(s) a cell mediated immune response. In this way, the neutralizing antibody response prevents or inhibits an initial gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection while the cell-mediated immune response capable of eliciting an enhanced Th1 cellular response prevents further spreading of the gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infection.

[228] Compositions of the invention will generally be administered directly to a patient. The compositions of the present invention may be administered, either alone or as part of a composition, via a variety of different routes. Certain routes may be favored for certain compositions, as resulting in the generation of a more effective immune response, preferably a CMI response, or as being less likely to induce side effects, or as being easier for administration.

[229] Delivery methods include parenteral injection (*e.g.*, subcutaneous, intraperitoneal, intravenous, intramuscular, or interstitial injection) and rectal, oral (*e.g.*, tablet, spray), vaginal, topical, transdermal (*e.g.*, see WO 99/27961), transcutaneous (*e.g.*, see WO02/074244 and WO02/064162), intranasal (*e.g.*, see WO03/028760), ocular, aural, and pulmonary or other mucosal administration.

[230] By way of example, the compositions of the present invention may be administered via a systemic route or a mucosal route or a transdermal route or it may be administered directly into a specific tissue. As used herein, the term "systemic administration" includes but is not limited to any parenteral routes of administration. In particular, parenteral administration includes but is not limited to subcutaneous, intraperitoneal, intravenous, intraarterial, intramuscular, or intrasternal injection, intravenous, intraarterial, or kidney dialytic infusion techniques. Preferably, the systemic, parenteral administration is intramuscular injection. As used herein, the term "mucosal administration" includes but is not limited to oral, intranasal, intravaginal, intrarectal, intratracheal, intestinal and ophthalmic administration.

[231] Dosage treatment can be a single dose schedule or a multiple dose schedule. Multiple doses may be used in a primary immunization schedule and/or in a booster immunization schedule. In a multiple dose schedule the various doses may be given by the same or different routes *e.g.*, a parenteral prime and mucosal boost, a mucosal prime and parenteral boost, etc.

[232] The compositions of the invention may be prepared in various forms. For example, a composition can be prepared as an injectable, either as a liquid solution or a suspension. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared (*e.g.*, a lyophilized composition). A composition can be prepared for oral administration, such as a tablet or capsule, as a spray, or as a syrup (optionally flavored). A composition can be prepared for pulmonary administration, *e.g.*, as an inhaler, using a fine powder or a spray. A composition can be prepared as a suppository

or pessary. A composition can be prepared for nasal, aural or ocular administration *e.g.*, as drops. A composition can be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. Such kits may comprise one or more Cna_B domain antigens or other antigens in liquid form and one or more lyophilized antigens.

[233] Immunogenic compositions used as vaccines comprise an immunologically effective amount of one or more Cna_B domain antigens (or nucleic acid molecules encoding the antigens), as well as any other components, as needed, such as antibiotics. An "immunologically effective amount" is an amount which, when administered to an individual, either in a single dose or as part of a series, increases a measurable immune response or prevents or reduces a clinical symptom.

[234] The immunogenic compositions of the present invention may be administered in combination with an antibiotic treatment regime. In one embodiment, the antibiotic is administered prior to administration of the one or more Cna_B domain antigens (or nucleic acid molecules encoding the antigens) of the invention.

[235] In another embodiment, the antibiotic is administered subsequent to the administration of a Cna_B domain antigen of the invention. Examples of antibiotics suitable for use in the treatment of a streptococcal infection include but are not limited to penicillin or a derivative thereof or clindamycin, cephalosporins, glycopeptides (*e.g.*, vancomycin), and cycloserine.

[236] The amount of active agent in a composition varies, however, depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (*e.g.*, non-human primate, primate, etc.), the capacity of the individual's immune system to synthesize antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation,

and other relevant factors. The amount will fall in a relatively broad range which can be determined through routine trials.

Kits

[237] The invention also provides kits comprising one or more containers of compositions of the invention. Compositions can be in liquid form or can be lyophilized, as can individual antigens. Suitable containers for the compositions include, for example, bottles, vials, syringes, and test tubes. Containers can be formed from a variety of materials, including glass or plastic. A container may have a sterile access port (for example, the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle).

[238] The kit can further comprise a second container comprising a pharmaceutically-acceptable buffer, such as phosphate-buffered saline, Ringer's solution, or dextrose solution. It can also contain other materials useful to the end-user, including other buffers, diluents, filters, needles, and syringes. The kit can also comprise a second or third container with another active agent, for example an antibiotic.

[239] The kit can also comprise a package insert containing written instructions for methods of inducing immunity against streptoccal bacteria or for treating gram positive bacterial (*e.g.*, streptococcal and/or staphylococcal) infections. The package insert can be an unapproved draft package insert or can be a package insert approved by the Food and Drug Administration (FDA) or other regulatory body.

[240] All patents, patent applications, and references cited in this disclosure are expressly incorporated herein by reference. The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following specific examples, which are provided for purposes of illustration only and are not intended to limit the scope of the invention.

EXAMPLE 1

Immunogenicity of a Cna_B domain

[241] The Cna_B domain of GAS protein Cpa_M18 was cloned together with a flanking domain (Fb-signal) in a PET21b vector. See **FIGS. 1A-B**. His-tagged recombinant protein was purified using activated chelating sepharose fast flow columns. See **FIG. 2**.

[242] Antiserum against the cloned Cna_B-Fb domain was obtained by immunizing 10 CD1 female mice three times each with 20 μg of the recombinant Cna_B-Fb protein. Cna_B-Fb serum was then probed by western blot experiments against a variety of purified His-tagged recombinant proteins from different human pathogens containing a Cna_B domain. The results are shown in **FIGS. 3A-D**. These experiments demonstrate that the Cna_B domain is immunogenic and that antiserum raised against it recognizes GAS_Cpa and F2 proteins as well as pili components of *S. agalactiae* and *S. pneumoniae*, which have been reported to be protective antigens (Maione *et al.*, 2005 *Science 309*, 148-150; Rosini *et al.*, 2006 *Mol. Micro. 61*, 126-141 and Gianfaldoni *et al.*, 2007, *Infect. Immun. 75*, 1059-1062). Example 5 reports experiments designed to address the possibility that antibodies in the sera reacted with the His tag; see also **FIG. 20**.

[243] Reactivity of the Cna_B antiserum was compared to that of antiserum specific for the cpa_M18 protein using western blots. The results are shown in **FIGS. 4A-B**. Higher reactivity with all proteins tested was observed for the Cna_B antiserum. In particular, all the variants of GBS_59 (SAL 1486) tested were detected by the anti-Cna_B-Fb serum, but only one variant was detected by the anti-Cpa_M18 serum.

EXAMPLE 2

Opsonophagocytosis assays

[244] Opsonophagocytic killing of *S. agalactiae* (GBS) using specific sera and differentiated HL-60 cells was investigated *in vitro* to test whether the recombinant Cna_B-Fb domain elicited protective antibodies. GBS were grown in 5 ml of Todd Hewitt Broth (THB) to the mid exponential phase (OD_{600}=0.3), then centrifuged at 3000 x g for 10 min at 4°C, washed with PBS 1x, suspended, and diluted in OP buffer (HBSS, 0.1% gelatin, 10% fetal calf serum) to a final concentration of approximately 2 x 10^7 CFU/ml). GBS cells (approximately 2 x 10^5 CFU) were mixed with heat-inactivated mouse serum (final concentration in the reaction 1:10) on wells of a chilled 96-well microtiter plate, then differentiated HL60 (1-2 x 10^6 cells) and baby rabbit complement were added on ice with GBS cells (final reaction volume 125 µl). The mixtures were incubated for 60 min at 37°C and mixed at 400-500 x g. Phagocytosis was ended by returning the samples to ice at the end of the incubation period. Immediately before (time 0) and after 1h incubation (time 1h), a 25 µl aliquot was diluted in sterile distilled water (25 µl sample+ 225 µl water, then 1:10 and 1:100) and plated in Tryptic soy agar plates with 5% sheep blood. The plates were incubated overnight at 37°C.

[245] The results are shown in **FIG. 5**. GAS_M18_Cna_B_Fb serum mediates the killing of GBS strain 515 (which expresses the Cna_B domain in pilin proteins SAL 1482, SAL 1486 and SAL 1487) and of strain JM10098 (which expressed the protective pilins SAN 1518 and SAN 1519).

[246] Further opsonophagocytosis experiments pointed out that GAS_M18_cpa (the entire protein containing Cna_B-Fb domain) was equally able to kill bacteria, suggesting that antibodies raised against Cna_B-Fb domain are indeed responsible for bacterial killing.

[247] In the absence of a suitable opsonophagocytosis system for *S. pyogenes* (GAS), R13, a mutant strain of GBS which lacks pili, and the same GBS R13 strain complemented with GAS pilus M1 and GAS pilus M6, were tested in opsonophagocytosis experiments. The results are shown in **FIG. 6**. These experiments demonstrate that GAS_M18_Cna_B_Fb antiserum mediates the killing of the GBS R13 strain which expresses GAS pili M1 and, to a lesser extent, the killing of the GBS R13 strain which expresses pili M6.

[248] Because the Fb-signal domain is present only in GAS Cpa proteins, but not in the GBS pilins for which antibody-mediated killing was demonstrated, we focused on the Cna_B domain, which is present in all the proteins tested in Example 1. The amino acid sequences of these proteins were aligned to compare amino acid sequences of their Cna_B domains (**FIGS. 7-13**). These alignments identified a conserved region, termed herein the "G box," which has the consensus sequence GXYXLXEXXXXXGY (SEQ ID NO:74).

EXAMPLE 3

Survival of Cna_B-Fb immunized mice after GBS challenge

[249] Thirty CD1 female mice were immunized on days 1, 20, and 34 with the recombinant Cna_B-Fb domain of the *S. pyogenes* Spy_M18_0126 protein prepared as described in Example 1. Ten mice were IP injected with 20 µg of the recombinant protein in 100 µl of _PBS + 100 µl Freund's incomplete adjuvant. As positive controls, five mice were injected with 20 µg of *S. agalactiae* GBS59 (SAL_1486 protein in 100 µl of PBS + 100 µl Freund's incomplete adjuvant, and five mice were injected with 20 µg of *S. agalactiae* GBS1523 (SAN 1518) protein in 100 µl of PBS + 100 µl Freund's incomplete adjuvant. As negative controls, ten mice were injected with PBS plus Freund's incomplete adjuvant.

[250] Mice were mated after the third injection, and newborns were challenged with a lethal dose of either GBS strain A909 or GBS strain 515. Eighty newborns from mothers immunized with the Cna_B-Fb and 80 with PBS, and forty newborns each from mothers immunized with *S. agalactiae* GBS59 (SAL_1486) or *S. agalactiae* GBS1523 (SAN 1518) were challenged. Newborn survival was monitored for four days. The survival rate for newborns immunized with the Cna_B-Fb domain was 42% and 44% after challenge with strains A909 and 515, respectively. The results are shown in Table 38, below.

Table 38.

injection with	challenge strain	
	A909	515
Cna_B-Fb	42%	44%
PBS (negative) control	15%	12%
GBS1523 (SAN1518) (positive control)	79%	nd
GBS59 (SAL1486) (positive control)	nd	86%

[251] Results of a similar experiment are shown in **FIG. 24**.

EXAMPLE 4

ELISA Assays

[252] Evaluation of specific anti-Cna_B domain antibodies in GAS_Cpa_M18 serum was performed by coating both GAS_Cpa_M18 protein and Cna_B domain, which were successively challenged by serial dilutions of GAS_Cpa_M18 serum in an ELISA experiment (Tables 39 and 40). Dilutions corresponding to OD_{540} = 1 indicated the ELISA titer for each protein (Table 40). **FIG. 19** shows that when Y =1 (OD_{540}) for GAS_Cpa_M18 ELISA titer was 627.814. Similarly, when Y =1 (OD_{540}) for GAS_Cpa_M18 when challenging the coated Cna_B domain the ELISA titer resulted

318.061. This experiment showed that about half of the antibodies contained in GAS_Cpa_M18 protein serum were specific for the Cna_B domain.

Table 39.

	Cpa_M18_serum	
Coated protein	Cpa_M18 full length protein	Cna_B domain
ELISA titer	627.814	318.061

Table 40.

serum dilution	OD_{540} nm anti_cpa_M18_std	OD_{450} nm anti_cna_B
10000	3.407	3.136
20000	3.408	3.082
40000	3.282	2.553
80000	3.011	1.83
160000	2.576	1.305
320000	1.425	0.769
640000	0.815	0.508
1280000	0.505	0.295

EXAMPLE 5

FACS analysis of cross-reactivity of GAS Cna_B_Fb domain serum with GAS and GBS strains

[253] This example demonstrates that GAS Cna_B_Fb domain antiserum cross-reacts with strains of both GAS and GBS.

[254] Antiserum against the cloned Cna_B-Fb domain and against the Cna_B domain only ("Cna_B_M6"; SEQ ID NO:145) was obtained by immunizing CD1 female mice three times each with 20 µg of the recombinant Cna_B-Fb protein or 20 µg of the recombinant M6_Cna_B domain.

[255] Cross-hybridization specificity against various strains of GAS and GBS was confirmed using Fluorescence Activated Cell Sorting (FACS). A threshold of 80 channels was designated as a positive shift; 150 channels was designated as a very positive shift.

[256] The results are shown in Table 41. See also **FIG. 18**.

Table 41. MFI (Mean Fluorescence Intensity)

Sera	Strains										
	M1Wessels	M3_44	M3_43	M6_16	27_M6	28_M6	CJB111_GBS	515_GBS	JM_GBS	2177_GBS	CD_11GBS
α-CnaB_M18	220**	96*	64	\	\	\	115*	94*	45	112*	228**
α-CnaB_M6	\	\	\	362**	100*	382**	\	\	\	\	\
α-AP-1_M6	\	\	\	520	390	300	\	\	\	\	\
α-GBS_59	\	\	\	\	\	\	458	421	\	\	480
α-GBS_67	\	\	\	\	\	\	\	725	\	\	\
α-GBS_80	\	\	\	\	\	\	\	\	487	367	\
α-GBS_1523	\	\	\	\	\	\	\	\	506	517	\

* > 80

** > 150

EXAMPLE 6

In vivo protection from subcutaneous infection after intraperitoneal immunization

[257] This example demonstrates that mice immunized intraperitoneally with various Cna_B domain antigens show a reduced skin lesion area in a GAS subcutaneous infection model.

[258] Mice were immunized intraperitoneally with 20 μg of Cna_B-Fb_M18 domain three times on days 1, 21 and 35 and challenged two weeks after the third immunization by subcutaneous injection of 10^9 cfu of *S. pyogenes* strain SF370_M1. Lesion areas were measured by evaluating the number of pixels in pictures of the lesions using the QUANTITY ONE® method (Bio-Rad). Phosphate buffered saline (PBS) was used as a negative control, and M1 protein ("emm-1") was used as a positive control. Results from immunizations with the GAS Cna_B domain antigen "Cna_B-Fb_M18" are shown in **FIGS. 21** and **25**. Results from immunizations with a GBS chimeric Cna_B domain antigen are shown in **FIG. 25**. The chimeric GBS Cna_B domain antigen was "GBS_59(515)-linker-GBS_67" (SEQ ID NO:129), which is described in Example 8.

EXAMPLE 7

In vivo protection from S. aureus challenge after intraperitoneal immunization

[259] This example demonstrates that intraperitoneal immunization with a Cna_B domain antigen protects against *S. aureus* colonization in a mouse renal abscess model

[260] Mice (10 mice for each experiment) were immunized with a Cna_B domain antigen (Cna_B-Fb_M18; 20μg/mouse) or with various *S. aureus* antigens with the following schedule: at day 0 first immunization and at day 14 second immunization. Challenge was performed at day 24. Immunizations were done intraperitoneally. Immunized animals were challenged on day 24 by intravenous injection of a bacterial suspension of *S. aureus* Newman strain. Cultures of Newman strain were centrifuged, washed twice, and diluted

in PBS before challenge. On day 28, mice were euthanized. Kidneys were removed and homogenized in 1% TRITON® X-100, aliquots diluted and plated on agar media for triplicate determination of CFU. PBS was used as a negative control. The results are shown in **FIG. 22** ("Cna_B" is Cna_B-Fb_M18).

EXAMPLE 8

Cloning and expression of chimeric Cna_B domain antigens

[261] The following chimeric Cna_B domain antigens were cloned and expressed in a pET15 expression vector using GBS59-Cna_B as first domain due to its high degree of solubility.

[262] SEQ ID NO:127, shown below, is the amino acid sequence of a His-tagged Cna_B domain antigen ("GBS_59(515)-linker-GBS_80"; SEQ ID NO:140) containing the Cna_B domain of SAL 1486 ("GBS59") from GBS strain 515, a linker sequence, and the Cna_B domain of SAG 0645 ("GBS80") from GBS strain 2603V/R.. The six histidine residues upstream from the chimeric sequence are bolded. The amino acid linker sequence is bolded. The underlined amino acids were added to encourage protein folding.

HHHHHHLAGATFLVKKDGKYLARKSGVATDAEKAAVDSTKSALDAAVKAYNDLTKEKQEG
QDGKSALATVSEKQKAYNDAFVKANYSYEWVEDKNAKNVVKLISNDKGQFEITGLTEGQY
SLEETQAPTGYAKLSGDVSFNVNATSYSKGSAQDIE**GSGGGG**LGGAEFDLLASDGTAVKW
TDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETK
APEGYVIPDKEIEFTVSQTSYNTKPTDITVDS

[263] SEQ ID NO:128, shown below, is the amino acid sequence of a His-tagged Cna_B domain antigen ("GBS_59(515)-linker-GBS_1523"; SEQ ID NO:141) containing the Cna_B domain of SAL 1486 ("GBS59") from GBS strain 515, a linker sequence, and the Cna_B domain of SAN 1518 ("GBS1523") from GBS strain COH1. The six histidine residues upstream from the chimeric sequence are bolded. The amino acid

linker sequence is bolded. The underlined amino acids were added to encourage protein folding.

HHHHHHLAGATFLVKKDGKYLARKSGVATDAEKAAVDSTKSALDAAVKAYNDLTKEKQEG
QDGKSALATVSEKQKAYNDAFVKANYSYEWVEDKNAKNVVKLISNDKGQFEITGLTEGQY
SLEETQAPTGYAKLSGDVSFNVNATSYSKGSAQDIE**GSGGGG**LQGAIFVLKNATGQFLNF
NDTNNVEWGTEANATEYTTGADGIITITGLKEGTYYLVEKKAPLGYNLLDNSQKVILGDG
ATDTTNSD

[264] SEQ ID NO:129, shown below, is the amino acid sequence of a His-tagged Cna_B domain antigen ("GBS_59(515)-linker-GBS_67"; SEQ ID NO:142) containing the Cna_B domain of SAL 1486 ("GBS59") from GBS strain 515, a linker sequence, and the two Cna_B domains of SAL 1487 ("GBS67") from GBS strain 515 (the second domain is italicized).. The six histidine residues upstream from the chimeric sequence are bolded. The amino acid linker sequence is bolded. The underlined amino acids were added to encourage protein folding.

HHHHHHLAGATFLVKKDGKYLARKSGVATDAEKAAVDSTKSALDAAVKAYNDLTKEKQEG
QDGKSALATVSEKQKAYNDAFVKANYSYEWVEDKNAKNVVKLISNDKGQFEITGLTEGQY
SLEETQAPTGYAKLSGDVSFNVNATSYSKGSAQDIE**GSGGGG**LSKATFVLKTTAHPESKI
EKVTAELTGEATFDNLIPGDYTLSEETAPEGYKKTNQTWQVKVESNGKTTIQNSG*LKGAT*
FELQEFNEDYKLYLPIKNNNSKVVTGENGKISYKDLKDGKYQLIEAVSPEDYQKITNKPI
*LTFEVVKGSIKNIIAVN*KQI

[265] SEQ ID NO:130, shown below, is the amino acid sequence of a His-tagged Cna_B domain antigen ("GBS_59(515)-GBS_80-linker-GBS_1523-linker";SEQ ID NO:143) containing the Cna_B domain of SAL 1486 ("GBS59") from GBS strain 515, the Cna_B domain of SAG 0645 from GBS strain 2603V/R, a linker sequence, the Cna_B domain of SAN 1518 from GBS strain COH1, and another linker sequence. The six histidine residues upstream from the chimeric sequence are bolded. The amino acid linker sequence is bolded. The underlined amino acids were added to encourage protein folding.

HHHHHHLAGATFLVKKDGKYLARKSGVATDAEKAAVDSTKSALDAAVKAYNDLTKEKQEG
QDGKSALATVSEKQKAYNDAFVKANYSYEWVEDKNAKNVVKLISNDKGQFEITGLTEGQY
SLEETQAPTGYAKLSGDVSFNVNATSYSKGSAQDIELGGAEFDLLASDGTAVKWTDALIK

ANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYV
IPDKEIEFTVSQTSYNTKPTDITVDS**GSGGGG**LQGAIFVLKNATGQFLNFNDTNNVEWGT
EANATEYTTGADGIITITGLKEGTYYLVEKKAPLGYNLLDNSQKVILGDGATDTTNSD**GS
GGGG**

[266] SEQ ID NO:131, shown below, is the amino acid sequence of a His-tagged Cna_B domain antigen ("SA Cna_B-SdrD"; SEQ ID NO:144) containing Cna_B domains of *S. aureus* SdrD protein and including "linker" amino acids (bolded) which occur naturally in the SdrD protein. The six histidine residues upstream from the chimeric sequence are bolded.

HHHHHHVGNVTVTVFDNNTNTKVGEAVTKEDGSYLIPNLPNGDYRVEFSNLPKGYEVTPS
KQGNNEELDSNGLSSVITVN**GKDNLSADLGIYKPKYNLGDYVWEDTNKNGIQDQDEKG**IS
GVTVTLKDENGNVLKTVTTDADGKYKFTDLDNGNYKVEFTTPEGYTPTTVTSGSDIEKDS
NGLTTTGVIN**GADNMTLDSGFYKTPKYNLGNYVWEDTNKDGKQDSTEKG**ISGVTVTLKNE
NGEVLQTTKTDKDGKYQFTGLENGTYKVEFETPSGYTPTQVGSGTDEGIDSNGTSTTGVI
K**DKDNDTIDSGFYKPTYNLGDYVWEDTNKNGVQDKDEKG**ISGVTVTLKDENDKVLKTVTT
DENGKYQFTDLNNGTYKVEFETPSGYTPTSVTSGNDTEKDSNGLTTTGVIK**DADNMTLDS
GFYKTPKYSLGDYVWYDSNKDGKQDSTEKG**IKDVKVTLLNEKGEVIGTTKTDENGKYCFD
NLDSGKYKVIFEKPAGLTQTVTNTTEDDKDADGGEVDVTIT

EXAMPLE 9

Intraperitoneal immunization with a Cna_B domain antigen protects against S. aureus colonization in a mouse renal abscess model.

[267] This example demonstrates that intraperitoneal immunization with a Cna_B domain antigen protects against *S. aureus* colonization in a mouse renal abscess model.

[268] Mice (10 mice for each experiment) were immunized with a Cna_B domain antigen (Cna_B-Fb_M18; 20μg/mouse) with the following schedule: at day 0 first immunization and at day 14 second immunization. Challenge was performed at day 24. Immunizations were done intraperitoneally. Immunized animals were challenged on day 24 by intravenous injection of a bacterial suspension of *S. aureus* Newman strain. Cultures of Newman strain were centrifuged, washed twice, and diluted in PBS before challenge. On day 28, mice were euthanized. Kidneys were removed and homogenized in 1% TRITON® X-100, aliquots diluted and plated on agar media for triplicate

determination of CFU. The *Staphylococcus* protein IsdB was used as a positive control, and alum was the negative control. Mice immunized with the Cna_B domain antigen showed reduced renal colonization rate after *S. aureus* challenge. The results are shown in **FIG. 23**.

EXAMPLE 10

Cna_B_SdrD confers protection in a sepsis mouse model against S. aureus infection

[269] This example demonstrates that a Cna_B domain antigen (**FIG. 27**; SEQ ID NO:132) comprising Cna_B domains (SEQ ID NOS:134-138) of the *S. aureus* protein SdrD (**FIGS. 26A, B**) confers protection in a sepsis mouse model against *S. aureus* infection.

[270] Groups of 14 mice each were immunized with the Cna_B_SdrD antigen (20 μg/mouse in alum) or a mutant form of *S. aureus* α-hemolysin (20 μg/mouse in alum) which cannot form pores (Hla_{H35L}; *see, e.g.*, Wardenburg & Schneewind, "Vaccine protection against *Staphlococcus aureus* pneumonia," Exp Med. 2008 February 18; 205(2): 287–294). Control mice were injected with alum.

[271] Mice were immunized with the following schedule: at day 0 first immunization and at day 14 second immunization. Challenge was performed at day 24. Immunizations were done intraperitoneally. Immunized animals were challenged on day 24 by intraperitoneal injection of a bacterial suspension of *S. aureus* strain USA300. Cultures of USA300 strain were centrifuged, washed twice and diluted in PBS before challenge. Mice were daily monitored for 14 days and euthanized at the appearance of humane endpoints, in agreement with Novartis Animal Welfare Policies. The percent survival two weeks after challenge with *S. aureus* strain USA300 is shown in **FIG. 28**. These results demonstrate that immunization with Cna_B_SdrD confers an high protection against *S. aureus* challenge suggesting this domain as a potential very good vaccine candidate.

Table 42. Sequence identifiers

sequence of	SEQ ID NO:	Figure
Cpa_M18 Cna_B and Fb	1	1
Cna_B_CPA_M5_MANFREDO (Spy_M5_0104)	2	7
Cna_B_CPA_M28 (M28_Spy0107)	3	7
Cna_B_CPA_M12 (MGAS2096_Spy0113)	4	7
Cna_B_CPA_M1 (M5005_Spy_0107)	5	7
Cna_B_CPA_M3 (SpyM3_0098)	6	7
Cna_B_CPA_M18 (Spy_M18_0126)	7	7, 9, 10, 11, 12, 13, 16, 17
Cna_B_CPA_M6 (M6_Spy0159)	8	7
Cna_B_CPA_M4_C (MGAS10750_Spy0115)	9	7
Cna_B_CPA_M28 (MGAS10270_Spy0113)	10	7
G box	11	7
G box	12	7
G box	13	7
G box	14	7, 14, 15
G box	15	7
G box	16	7
G box	17	7
Spy_M5_0104	18	--
M28_Spy0107	19	--
MGAS2096_Spy0113	20	--
M5005_Spy_0107	21	--

SpyM3_0098	22	--
Spy_M18_0126	23	--
M6_Spy0159	24	--
MGAS10750_Spy0115	25	--
MGAS10270_Spy0113	26	--
Cna_B_GBS_52 (SAG_0646)	27	8, 9
Cna_B_GBS_150 (SAL 1482)	28	8, 10
Cna_B_GBS_104_1 (SAG 0649)	29	8, 9
Cna_B_GBS_67 (SAL 1487)	30	8, 10
Cna_B_GBS_1523 (SAN 1518)	31	8, 11
Cna_B_GBS_1524 (SAN 1519)	32	8, 11
Cna_B_GBS_80 (SAG 0645)	33	8, 9
Cna_B_GBS_104_2 (SAG 0649)	34	8, 9
Cna_B_GBS_1521 (SAN 1516)	35	8
G box	36	8
G box	37	8
G box	38	8
G box	39	8
G box	40	8
G box	41	8
G box	42	8
G box	43	8
G box	44	8
SAG_0646	45	--
SAL 1482	46	--
SAG 0649	47	--

SAL 1487	48	--
SAN 1518	49	--
SAN 1519	50	--
SAG 0645	51	--
SAN 1516	52	--
Cna_B domain RRGB (SP_0463)	53	12
Cna_B domain RRGA1 (SP_0462)	54	12
Cna_B domain RRGC2 (SP_0464)	55	12
Cna_B domain RRGA2 (SP_0462)	56	12
Cna_B domain RRGC1 (SP_0464)	57	12
G box	58	12
G box	59	12
G box	60	12
G box	61	12
G box	62	12
SP_0463	63	--
SP_0462	64	--
SP_0464	65	--
Cna_B domain Ser-Asp rich2 (SdrD MW0517)	66	13
Cna_B domain Ser-Asp rich3 (SdrD MW0517)	67	13
Cna_B domain CBP (MW2612)	68	13
G box	69	13
G box	70	13
G box	71	13
SdrD MW0517	72	--

MW2612	73	--
G box consensus sequence	74	--
Cna_B_Bkb3 (DUF 11) 89/1591	75	14
Cna_B_Bkb1 SSU05_0474 05ZYH33	76	14
BKB SEQ0936	77	15
G box	78	15
linker	79	--
Cna_B_autotransporter (SSU05_0474[Streptococcus suis 05ZYH33]	80	16
Cna_B (Protein of unknown function DUF11:Surface protein from Gram-positive cocci, anchor region [Streptococcus suis 89/1591]	81	16
SSU05_0474[Streptococcus suis 05ZYH33	82	--
Protein of unknown function DUF11:Surface protein from Gram-positive cocci, anchor region [Streptococcus suis 89/1591	83	--
Cna_B_ ap1 (SEQ0935*)	84	17
Cna_B_ ap2 (SEQ0935*)	85	17
Cna_B_ bkb (SEQ0936**)	86	17
* SEQ0935 ancillary protein SEQ0935 undefined product 914186:916159 forward MW:73872 67	87	--
** SEQ0936 BKB SEQ0936 undefined product 916183:917625 forward MW:51902 46,3	88	--
S. suis strain 05ZYH33	89	--
S. suis strain 05ZYH33	90	--

S. suis strain 05ZYH33	91	--
S. suis strain 05ZYH33	92	--
S. suis strain 98HAH33	93	--
S. suis strain 98HAH33	94	--
S. suis strain 98HAH33	95	--
Streptococcus suis 89/1591	96	--
S. suis strain 05ZYH33	97	--
S. equi FszE: Sez_1828	98	--
S. equi FszD: Sez_1822	99	--
S. equi FszC: Sez_1821	100	--
S. equi FbpZ: Sez_1825	101	--
GBS59 (SAL 1486)	102	--
SAL 1486 Cna_B	103	13
SAL 1486 G Box	104	13
Cpa_M6 S. pyogenes vWFA (M6_Spy0159)	105	--
SAL_1487 cell wall surface anchor family protein vWFA	106	--
Ancillary pilus subunit S. pneumoniae vWFA RrgA (SP_0462)	107	--
multi-Cna_B domain antigen	108	--
multi-Cna_B domain antigen	109	--
Cna_B domain of SAL_1487	110	--
Cna_B domain of SAL_1487	111	--
Cna_B domain of SAG 0645	112	--
Cna_B domain of SAL_1518	113	--
Cna_B domain of SAL_1486	114	--

Cna_B domain of SAL_1486	115	--
Cna_B domain of SAG_1407	116	--
Cna_B domain of SAG_1407	117	--
SAG_1407	118	--
nucleotide sequence encoding GAS protein F2 Spy0119	119	--
Cna_B_M6 Spy_0159	120	--
GAS protein F2 Spy0119	121	--
Cna_B domain 1 of NO:121	122	--
Cna_B domain 2 of NO:121	123	--
Cna_B domain 3 of NO:121	124	--
Cna_B domain 4 of NO:121	125	--
Cna_B domain 5 of NO:121	126	--
His-tagged GBS_59(515)-linker-GBS_80	127	--
His-tagged GBS_59(515)-linker-GBS_1523	128	--
His-tagged GBS_59(515)-linker_GBS_67	129	--
His-tagged GBS_59(515)-GBS_80-linker-GBS_1523-linker	130	--
His-tagged SA Cna_B-SdrD	131	--
SA SdrD protein	132	27
Cna_B_SdrD antigen (Example 10)	133	28
Cna_B domain of SdrD	134	27B
Cna_B domain of SdrD	135	27B
Cna_B domain of SdrD	136	27B
Cna_B domain of SdrD	137	27B

Cna_B domain of SdrD	138	27B
Cna_B_SdrD antigen (Example 10)	139	28
GBS_59(515)-linker-GBS_80	140	--
GBS_59(515)-linker-GBS_1523	141	--
GBS_59(515)-linker_GBS_67	142	--
GBS_59(515)-GBS_80-linker-GBS_1523-linker	143	--
SA Cna_B-SdrD	144	--
Cna_B_M6	145	--

CLAIMS

1. A Cna_B domain antigen comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 134-144, wherein the amino group of the N terminal amino acid of the amino acid sequence is not linked by a peptide bond to the carboxyl group of an amino acid to which it is linked in a native gram positive bacterial protein and/or the carboxyl group of the C terminal amino acid of the amino acid sequence is not linked by a peptide bond to the amino group of an amino acid to which it is linked in a native gram positive bacterial protein.

2. The Cna_B domain antigen of claim 1 which comprises two amino acid sequences selected from the group consisting of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 134-144.

3. The Cna_B domain antigen of claim 1 which comprises the amino acid sequence SEQ ID NO:1.

4. The Cna_B domain antigen of claim 1 which consists of the amino acid sequence SEQ ID NO:1.

5. A Cna_B domain antigen which comprises a first Cna_B domain of a first gram positive bacterial protein and a second Cna_B domain of a second gram positive bacterial protein, wherein the first and second gram positive proteins are different proteins.

6. The Cna_B domain antigen of claim 5 wherein the first gram positive bacterial protein is a streptococcal protein.

7. The Cna_B domain antigen of claim 5 wherein the first gram positive bacterial protein is a staphylococcal protein.

8. The Cna_B domain antigen of claim 5 wherein the first Cna_B domain comprises the amino acid sequence SEQ ID NO:74.

9. The Cna_B domain antigen of claim 5 wherein the first Cna_B domain is an amino acid sequence selected from the group consisting of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 134-144.

10. A Cna_B domain antigen which comprises two identical Cna_B domains.

11. A Cna_B domain antigen which comprises the amino acid sequence SEQ ID NO:74, wherein the amino group of the N terminal amino acid of the amino acid sequence is not linked by a peptide bond to the carboxyl group of an amino acid to which it is linked in a native gram positive bacterial protein and/or the carboxyl group of the C terminal amino acid of the amino acid sequence is not linked by a peptide bond to the amino group of an amino acid to which it is linked in a native gram positive bacterial protein.

12. A Cna_B domain antigen which consists of an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:1 and 0-70 additional contiguous amino acids of SEQ ID NO:18 at the N terminus of SEQ ID NO:1 and/or 0-282 additional contiguous amino acids of SEQ ID NO:18 at the C terminus of SEQ ID NO:1;

(b) SEQ ID NO:2 and 0-70 additional contiguous amino acids of SEQ ID NO:18 at the N terminus of SEQ ID NO:2 and/or 0-390 additional contiguous amino acids of SEQ ID NO:18 at the C terminus of SEQ ID NO:2;

(c) SEQ ID NO:3 and 0-294 additional contiguous amino acids of SEQ ID NO:19 at the N terminus of SEQ ID NO:3 and/or 0-390 additional contiguous amino acids of SEQ ID NO:19 at the C terminus of SEQ ID NO:3;

(d) SEQ ID NO:4 and 0-297 additional contiguous amino acids of SEQ ID NO:20 at the N terminus of SEQ ID NO:4 and/or 0-396 additional contiguous amino acids of SEQ ID NO:20 at the C terminus of SEQ ID NO:4;

(e) SEQ ID NO:5 and 0-310 additional contiguous amino acids of SEQ ID NO:21 at the N terminus of SEQ ID NO:5 and/or 0-380 additional contiguous amino acids of SEQ ID NO:21 at the C terminus of SEQ ID NO:5;

(f) SEQ ID NO:6 and 0-288 additional contiguous amino acids of SEQ ID NO:22 at the N terminus of SEQ ID NO:6 and/or 0-393 additional contiguous amino acids of SEQ ID NO:22 at the C terminus of SEQ ID NO:6;

(g) SEQ ID NO:7 and 0-70 additional contiguous amino acids of SEQ ID NO:23 at the N terminus of SEQ ID NO:7 and/or 0-392 additional contiguous amino acids of SEQ ID NO:23 at the C terminus of SEQ ID NO:7;

(h) SEQ ID NO:8 and 0-906 additional contiguous amino acids of SEQ ID NO:24 at the N terminus of SEQ ID NO:8 and/or 0-58 additional contiguous amino acids of SEQ ID NO:24 at the C terminus of SEQ ID NO:8;

(i) SEQ ID NO:9 and 0-654 additional contiguous amino acids of SEQ ID NO:25 at the N terminus of SEQ ID NO:9 and/or 0-646 additional contiguous amino acids of SEQ ID NO:25 at the C terminus of SEQ ID NO:9;

(j) SEQ ID NO:10 and 0-51 additional contiguous amino acids of SEQ ID NO:26 at the N terminus of SEQ ID NO:10 and/or 0-768 additional contiguous amino acids of SEQ ID NO:26 at the C terminus of SEQ ID NO:10;

(k) SEQ ID NO:27 and 0-169 additional contiguous amino acids of SEQ ID NO:45 at the N terminus of SEQ ID NO:27 and/or 0-52 additional contiguous amino acids of SEQ ID NO:45 at the C terminus of SEQ ID NO:27;

(l) SEQ ID NO:28 and 0-160 additional contiguous amino acids of SEQ ID NO:46 at the N terminus of SEQ ID NO:28 and/or 0-75 additional contiguous amino acids of SEQ ID NO:46 at the C terminus of SEQ ID NO:28;

(m) SEQ ID NO:29 and 0-51 additional contiguous amino acids of SEQ ID NO:47 at the N terminus of SEQ ID NO:29 and/or 0-778 additional contiguous amino acids of SEQ ID NO:47 at the C terminus of SEQ ID NO:29;

(n) SEQ ID NO:30 and 0-52 additional contiguous amino acids of SEQ ID NO:48 at the N terminus of SEQ ID NO:30 and/or 0-786 additional contiguous amino acids of SEQ ID NO:48 at the C terminus of SEQ ID NO:30;

(o) SEQ ID NO:31 and 0-365 additional contiguous amino acids of SEQ ID NO:49 at the N terminus of SEQ ID NO:31 and/or 0-50 additional contiguous amino acids of SEQ ID NO:49 at the C terminus of SEQ ID NO:31;

(p) SEQ ID NO:32 and 0-1290 additional contiguous amino acids of SEQ ID NO:50 at the N terminus of SEQ ID NO:32 and/or 0-62 additional contiguous amino acids of SEQ ID NO:50 at the C terminus of SEQ ID NO:32;

(q) SEQ ID NO:33 and 0-394 additional contiguous amino acids of SEQ ID NO:51 at the N terminus of SEQ ID NO:33 and/or 0-65 additional contiguous amino acids of SEQ ID NO:51 at the C terminus of SEQ ID NO:33;

(r) SEQ ID NO:35 and 0-98 additional contiguous amino acids of SEQ ID NO:52 at the N terminus of SEQ ID NO:35 and/or 0-36 additional contiguous amino acids of SEQ ID NO:52 at the C terminus of SEQ ID NO:35;

(s) SEQ ID NO:53 and 0-459 additional contiguous amino acids of SEQ ID NO:63 at the N terminus of SEQ ID NO:53 and/or 0-68 additional contiguous amino acids of SEQ ID NO:63 at the C terminus of SEQ ID NO:53;

(t) SEQ ID NO:54 and 0-60 additional contiguous amino acids of SEQ ID NO:64 at the N terminus of SEQ ID NO:54 and/or 0-762 additional contiguous amino acids of SEQ ID NO:64 at the C terminus of SEQ ID NO:54;

(u) SEQ ID NO:55 and 0-271 additional contiguous amino acids of SEQ ID NO:65 at the N terminus of SEQ ID NO:55 and/or 0-41 additional contiguous amino acids of SEQ ID NO:65 at the C terminus of SEQ ID NO:55;

(v) SEQ ID NO:66 and 0-703 additional contiguous amino acids of SEQ ID NO:72 at the N terminus of SEQ ID NO:66 and/or 0-473 additional contiguous amino acids of SEQ ID NO:72 at the C terminus of SEQ ID NO:66;

(w) SEQ ID NO:67 and 0-924 additional contiguous amino acids of SEQ ID NO:72 at the N terminus of SEQ ID NO:67 and/or 0-353 additional contiguous amino acids of SEQ ID NO:72 at the C terminus of SEQ ID NO:67;

(x) SEQ ID NO:68 and 0-344 additional contiguous amino acids of SEQ ID NO:73 at the N terminus of SEQ ID NO:68 and/or 0-761 additional contiguous amino acids of SEQ ID NO:73 at the C terminus of SEQ ID NO:68;

(y) SEQ ID NO:34 and 0-748 additional contiguous amino acids of SEQ ID NO:47 at the N terminus of SEQ ID NO:34 and/or 0-62 additional contiguous amino acids of SEQ ID NO:47 at the C terminus of SEQ ID NO:34;

(z) SEQ ID NO:57 and 0-161 additional contiguous amino acids of SEQ ID NO:65 at the N terminus of SEQ ID NO:57 and/or 0-141 additional contiguous amino acids of SEQ ID NO:65 at the C terminus of SEQ ID NO:57;

(aa) SEQ ID NO:80 and 0-348 additional contiguous amino acids of SEQ ID NO:82 at the N terminus of SEQ ID NO:80 and/or 0-53 additional contiguous amino acids of SEQ ID NO:82 at the C terminus of SEQ ID NO:80;

(bb) SEQ ID NO:81 and 0-358 additional contiguous amino acids of SEQ ID NO:83 at the N terminus of SEQ ID NO:81 and/or 0-124 additional contiguous amino acids of SEQ ID NO:83 at the C terminus of SEQ ID NO:81;

(cc) SEQ ID NO:84 and 0-350 additional contiguous amino acids of SEQ ID NO:87 at the N terminus of SEQ ID NO:84 and/or 0-244 additional contiguous amino acids of SEQ ID NO:87 at the C terminus of SEQ ID NO:84;

(dd) SEQ ID NO:85 and 0-539 additional contiguous amino acids of SEQ ID NO:87 at the N terminus of SEQ ID NO:85 and/or 0-55 additional contiguous amino acids of SEQ ID NO:87 at the C terminus of SEQ ID NO:85;

(ee) SEQ ID NO:86 and 0-336 additional contiguous amino acids of SEQ ID NO:88 at the N terminus of SEQ ID NO:86 and/or 0-74 additional contiguous amino acids of SEQ ID NO:88 at the C terminus of SEQ ID NO:86;

(ff) SEQ ID NO:122 and 0-59 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:122 and/or 0-1030 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:122;

(gg) SEQ ID NO:123 and 0-524 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:123 and/or 0-561 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:123;

(hh) SEQ ID NO:124 and 0-637 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:124 and/or 0-451 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:124;

(ii) SEQ ID NO:125 and 0-759 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:125 and/or 0-328 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:125;

(jj) SEQ ID NO:126 and 0-904 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:126 and/or 0-188 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:126;

(kk) SEQ ID NO:134 and 0-591 additional contiguous amino acids of SEQ ID NO:132 at the N terminus or SEQ ID NO:134 and/or 0-683 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:134;

(ll) SEQ ID NO:135 and 0-703 additional contiguous amino acids of SEQ ID NO:132 at the N terminus or SEQ ID NO:135 and/or 0-572 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:135;

(mm) SEQ ID NO:136 and 0-814 additional contiguous amino acids of SEQ ID NO:132 at the N terminus or SEQ ID NO:136 and/or 0-461additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:136;

(nn) SEQ ID NO:137 and 0-924 additional contiguous amino acids of SEQ ID NO:132 at the N terminus or SEQ ID NO:137 and/or 0-351 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:137;

(oo) SEQ ID NO:138 and 0-1035 additional contiguous amino acids of SEQ ID NO:132 at the N terminus or SEQ ID NO:138 and/or 0-241 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:138; and

(pp) SEQ ID NO:139 and 0-598 additional contiguous amino acids of SEQ ID NO:132 at the N terminus or SEQ ID NO:134 and/or 0-225 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:134.

13. The Cna_B domain antigen of claim 12 which consists of an amino acid sequence selected from the group consisting of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 75, 76, 80, 81, 84-86, 110-117, and 139-144.

14. A Cna_B domain antigen which comprises an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:1 and 0-70 additional contiguous amino acids of SEQ ID NO:18 at the N terminus of SEQ ID NO:1 and/or 0-282 additional contiguous amino acids of SEQ ID NO:18 at the C terminus of SEQ ID NO:1;

(b) SEQ ID NO:2 and 0-70 additional contiguous amino acids of SEQ ID NO:18 at the N terminus of SEQ ID NO:2 and/or 0-390 additional contiguous amino acids of SEQ ID NO:18 at the C terminus of SEQ ID NO:2;

(c) SEQ ID NO:3 and 0-294 additional contiguous amino acids of SEQ ID NO:19 at the N terminus of SEQ ID NO:3 and/or 0-390 additional contiguous amino acids of SEQ ID NO:19 at the C terminus of SEQ ID NO:3;

(d) SEQ ID NO:4 and 0-297 additional contiguous amino acids of SEQ ID NO:20 at the N terminus of SEQ ID NO:4 and/or 0-396 additional contiguous amino acids of SEQ ID NO:20 at the C terminus of SEQ ID NO:4;

(e) SEQ ID NO:5 and 0-310 additional contiguous amino acids of SEQ ID NO:21 at the N terminus of SEQ ID NO:5 and/or 0-380 additional contiguous amino acids of SEQ ID NO:21 at the C terminus of SEQ ID NO:5;

(f) SEQ ID NO:6 and 0-288 additional contiguous amino acids of SEQ ID NO:22 at the N terminus of SEQ ID NO:6 and/or 0-393 additional contiguous amino acids of SEQ ID NO:22 at the C terminus of SEQ ID NO:6;

(g) SEQ ID NO:7 and 0-70 additional contiguous amino acids of SEQ ID NO:23 at the N terminus of SEQ ID NO:7 and/or 0-392 additional contiguous amino acids of SEQ ID NO:23 at the C terminus of SEQ ID NO:7;

(h) SEQ ID NO:8 and 0-906 additional contiguous amino acids of SEQ ID NO:24 at the N terminus of SEQ ID NO:8 and/or 0-58 additional contiguous amino acids of SEQ ID NO:24 at the C terminus of SEQ ID NO:8;

(i) SEQ ID NO:9 and 0-654 additional contiguous amino acids of SEQ ID NO:25 at the N terminus of SEQ ID NO:9 and/or 0-646 additional contiguous amino acids of SEQ ID NO:25 at the C terminus of SEQ ID NO:9;

(j) SEQ ID NO:10 and 0-51 additional contiguous amino acids of SEQ ID NO:26 at the N terminus of SEQ ID NO:10 and/or 0-768 additional contiguous amino acids of SEQ ID NO:26 at the C terminus of SEQ ID NO:10;

(k) SEQ ID NO:27 and 0-169 additional contiguous amino acids of SEQ ID NO:45 at the N terminus of SEQ ID NO:27 and/or 0-52 additional contiguous amino acids of SEQ ID NO:45 at the C terminus of SEQ ID NO:27;

(l) SEQ ID NO:28 and 0-160 additional contiguous amino acids of SEQ ID NO:46 at the N terminus of SEQ ID NO:28 and/or 0-75 additional contiguous amino acids of SEQ ID NO:46 at the C terminus of SEQ ID NO:28;

(m) SEQ ID NO:29 and 0-51 additional contiguous amino acids of SEQ ID NO:47 at the N terminus of SEQ ID NO:29 and/or 0-778 additional contiguous amino acids of SEQ ID NO:47 at the C terminus of SEQ ID NO:29;

(n) SEQ ID NO:30 and 0-52 additional contiguous amino acids of SEQ ID NO:48 at the N terminus of SEQ ID NO:30 and/or 0-786 additional contiguous amino acids of SEQ ID NO:48 at the C terminus of SEQ ID NO:30;

(o) SEQ ID NO:31 and 0-365 additional contiguous amino acids of SEQ ID NO:49 at the N terminus of SEQ ID NO:31 and/or 0-50 additional contiguous amino acids of SEQ ID NO:49 at the C terminus of SEQ ID NO:31;

(p) SEQ ID NO:32 and 0-1290 additional contiguous amino acids of SEQ ID NO:50 at the N terminus of SEQ ID NO:32 and/or 0-62 additional contiguous amino acids of SEQ ID NO:50 at the C terminus of SEQ ID NO:32;

(q) SEQ ID NO:33 and 0-394 additional contiguous amino acids of SEQ ID NO:51 at the N terminus of SEQ ID NO:33 and/or 0-65 additional contiguous amino acids of SEQ ID NO:51 at the C terminus of SEQ ID NO:33;

(r) SEQ ID NO:35 and 0-98 additional contiguous amino acids of SEQ ID NO:52 at the N terminus of SEQ ID NO:35 and/or 0-36 additional contiguous amino acids of SEQ ID NO:52 at the C terminus of SEQ ID NO:35;

(s) SEQ ID NO:53 and 0-459 additional contiguous amino acids of SEQ ID NO:63 at the N terminus of SEQ ID NO:53 and/or 0-68 additional contiguous amino acids of SEQ ID NO:63 at the C terminus of SEQ ID NO:53;

(t) SEQ ID NO:54 and 0-60 additional contiguous amino acids of SEQ ID NO:64 at the N terminus of SEQ ID NO:54 and/or 0-762 additional contiguous amino acids of SEQ ID NO:64 at the C terminus of SEQ ID NO:54;

(u) SEQ ID NO:55 and 0-271 additional contiguous amino acids of SEQ ID NO:65 at the N terminus of SEQ ID NO:55 and/or 0-41 additional contiguous amino acids of SEQ ID NO:65 at the C terminus of SEQ ID NO:55;

(v) SEQ ID NO:66 and 0-703 additional contiguous amino acids of SEQ ID NO:72 at the N terminus of SEQ ID NO:66 and/or 0-473 additional contiguous amino acids of SEQ ID NO:72 at the C terminus of SEQ ID NO:66;

(w) SEQ ID NO:67 and 0-924 additional contiguous amino acids of SEQ ID NO:72 at the N terminus of SEQ ID NO:67 and/or 0-353 additional contiguous amino acids of SEQ ID NO:72 at the C terminus of SEQ ID NO:67;

(x) SEQ ID NO:68 and 0-344 additional contiguous amino acids of SEQ ID NO:73 at the N terminus of SEQ ID NO:68 and/or 0-761 additional contiguous amino acids of SEQ ID NO:73 at the C terminus of SEQ ID NO:68;

(y) SEQ ID NO:34 and 0-748 additional contiguous amino acids of SEQ ID NO:47 at the N terminus of SEQ ID NO:34 and/or 0-62 additional contiguous amino acids of SEQ ID NO:47 at the C terminus of SEQ ID NO:34;

(z) SEQ ID NO:57 and 0-161 additional contiguous amino acids of SEQ ID NO:65 at the N terminus of SEQ ID NO:57 and/or 0-141 additional contiguous amino acids of SEQ ID NO:65 at the C terminus of SEQ ID NO:57;

(aa) SEQ ID NO:80 and 0-348 additional contiguous amino acids of SEQ ID NO:82 at the N terminus of SEQ ID NO:80 and/or 0-53 additional contiguous amino acids of SEQ ID NO:82 at the C terminus of SEQ ID NO:80;

(bb) SEQ ID NO:81 and 0-358 additional contiguous amino acids of SEQ ID NO:83 at the N terminus of SEQ ID NO:81 and/or 0-124 additional contiguous amino acids of SEQ ID NO:83 at the C terminus of SEQ ID NO:81;

(cc) SEQ ID NO:84 and 0-350 additional contiguous amino acids of SEQ ID NO:87 at the N terminus of SEQ ID NO:84 and/or 0-244 additional contiguous amino acids of SEQ ID NO:87 at the C terminus of SEQ ID NO:84;

(dd) SEQ ID NO:85 and 0-539 additional contiguous amino acids of SEQ ID NO:87 at the N terminus of SEQ ID NO:85 and/or 0-55 additional contiguous amino acids of SEQ ID NO:87 at the C terminus of SEQ ID NO:85;

(ee) SEQ ID NO:86 and 0-336 additional contiguous amino acids of SEQ ID NO:88 at the N terminus of SEQ ID NO:86 and/or 0-74 additional contiguous amino acids of SEQ ID NO:88 at the C terminus of SEQ ID NO:86;

(ff) SEQ ID NO:122 and 0-59 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:122 and/or 0-1030 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:122;

(gg) SEQ ID NO:123 and 0-524 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:123 and/or 0-561 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:123;

(hh) SEQ ID NO:124 and 0-637 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:124 and/or 0-451 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:124;

(ii) SEQ ID NO:125 and 0-759 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:125 and/or 0-328 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:125;

(jj) SEQ ID NO:126 and 0-904 additional contiguous amino acids of SEQ ID NO:121 at the N terminus of SEQ ID NO:126 and/or 0-188 additional contiguous amino acids of SEQ ID NO:121 at the C terminus of SEQ ID NO:126;

(kk) SEQ ID NO:134 and 0-591 additional contiguous amino acids of SEQ ID NO:132 at the N terminus of SEQ ID NO:134 and/or 0-683 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:134;

(ll) SEQ ID NO:135 and 0-703 additional contiguous amino acids of SEQ ID NO:132 at the N terminus of SEQ ID NO:135 and/or 0-572 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:135;

(mm) SEQ ID NO:136 and 0-814 additional contiguous amino acids of SEQ ID NO:132 at the N terminus of SEQ ID NO:136 and/or 0-461additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:136;

(nn) SEQ ID NO:137 and 0-924 additional contiguous amino acids of SEQ ID NO:132 at the N terminus of SEQ ID NO:137 and/or 0-351 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:137;

(oo) SEQ ID NO:138 and 0-1035 additional contiguous amino acids of SEQ ID NO:132 at the N terminus of SEQ ID NO:138 and/or 0-241 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:138; and

(pp) SEQ ID NO:139 and 0-598 additional contiguous amino acids of SEQ ID NO:132 at the N terminus of SEQ ID NO:139 and/or 0-225 additional contiguous amino acids of SEQ ID NO:132 at the C terminus of SEQ ID NO:139,

wherein the amino group of the N terminal amino acid of the amino acid sequence is not linked by a peptide bond to the carboxyl group of an amino acid to which it is linked in a native gram positive bacterial protein and/or the carboxyl group of the C terminal amino acid of the amino acid sequence is not linked by a peptide bond to the amino group of an amino acid to which it is linked in a native gram positive bacterial protein.

15. A Cna_B domain antigen which consists of:

$$A(LB)_n$$

wherein:

A is a first Cna_B domain;

B is a second Cna_B domain;

n is 1-10; and

L is independently absent or an amino acid linker.

16. The Cna_B domain antigen of claim 15 which comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:127-131 and 133-144.

17. The Cna_B domain antigen of claim 15 wherein the first Cna_B domain and at least one second Cna_B domain are domains of two different gram positive bacterial proteins.

18. The Cna_B domain antigen of claim 17 wherein the two different gram positive proteins are from two different species of streptococcus.

19. The Cna_B domain antigen of claim 17 wherein at least one of the gram positive bacterial proteins is from a bacterium selected from the group consisting of *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, *S. aureus*, *S. suis*, and *S. equi.*

20. A Cna_B domain antigen which comprises:

$$A(LB)_n$$

wherein:

A is a first Cna_B domain;

B is a second Cna_B domain;

n is 1-10; and

L is independently absent or an amino acid linker; and

wherein the amino group of the N terminal amino acid of the first Cna_B domain is not linked by a peptide bond to the carboxyl group of an amino acid to which it is linked in a native gram positive bacterial protein and/or the carboxyl group of the C terminal amino acid of the second Cna_B domain is not linked by a peptide bond to the amino group of an amino acid to which it is linked in a native gram positive bacterial protein.

21. A Cna_B domain antigen consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 75, 76, 80, 81, 84-86, 110-117, 122-126, and 133-144.

22. A fusion polypeptide, comprising:

a Cna_B domain antigen of any of claims 1-21; and

a bacterial antigen.

23. The Cna_B domain antigen of any of claims 1-21 or the fusion polypeptide of claim 22 which is coupled to a carrier protein.

24. A nucleic acid molecule which encodes the isolated Cna_B domain antigen of any of claims 1-21 or the fusion polypeptide of claim 22.

25. The nucleic acid molecule of claim 24 which is an expression vector.

26. A host cell comprising an expression vector which encodes the Cna_B domain antigen of any of claims 1-21 or the fusion polypeptide of claim 22.

27. A method of producing a Cna_B domain antigen or a fusion polypeptide, comprising:

culturing the host cell of claim 26 under conditions under which the expression vector expresses the Cna_B domain antigen or the fusion polypeptide; and

recovering the Cna_B domain antigen or the fusion polypeptide.

28. An isolated antibody which binds selectively to one or more Cna_B domains, wherein each Cna_B domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:1-10, 27-35, 53-57, 66-68, 74-76, 80, 81, 84-86, 110-117, 122-126, and 134-144.

29. The isolated antibody of claim 28 which binds to a polypeptide comprising the amino acid sequence SEQ ID NO:1.

30. The isolated antibody of claim 28 or 29 which is a monoclonal antibody.

31. The isolated antibody of any of claims 28-30 which induces opsonophagocytosis of GBS strain 515 by at least 30%.

32. A composition comprising:

an active agent selected from the group consisting of:

the Cna_B domain antigen of any of claims 1-21;

the fusion polypeptide of claim 22;

the nucleic acid molecule of claim 24; and

the isolated antibody of claim 28; and

a pharmaceutically acceptable carrier.

33. A kit comprising:

(a) a container comprising the composition of claim 32; and

(b) instructions for using the composition to raise an immune response against a gram positive bacterial protein comprising a Cna_B domain.

34. The Cna_B domain antigen of any of claims 1-21 or the fusion polypeptide of claim 22 for use in treating infection by a gram positive bacterium.

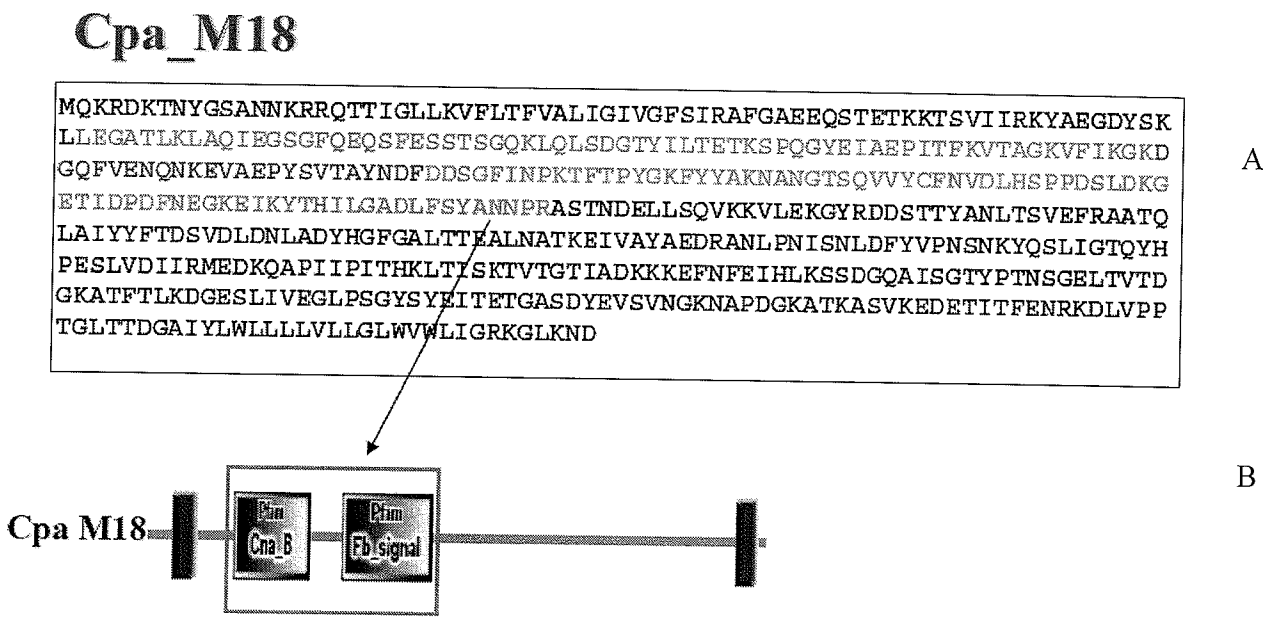
35. The Cna_B domain antigen of claim 34 wherein the gram positive bacterium is selected from the group consisting of *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, *S. aureus*, *S. suis*, and *S. equi*.

36. A method of reducing infection by a gram positive bacterium, comprising administering to an individual in need thereof an effective amount of the Cna_B domain antigen of any of claims 1-21 or the fusion polypeptide of claim 22.

37. The method of claim 36 wherein the gram positive bacterium is selected from the group consisting of *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, *S. aureus*, *S. suis*, and *S. equi*.

38. The Cna_B domain antigen of any of claims 1-21 which is an isolated antigen.

FIG. 1


Cpa_M18
MQKRDKTNYGSANNKRRQTTIGLLKVFLTFVALIGIVGFSIRAFGAEEQSTETKKTSVIIRKYAEGDYSK
LLEGATLKLAQIEGSGFQEQSFESSTSGQKLQLSDGTYILTETKSPQGYEIAEPITFKVTAGKVFIKGKD
GQFVENQNKEVAEPYSVTAYNDFDDSGFINPKTFTPYGKFYYAKNANGTSQVVYCFNVDLHSPPDSLDKG
ETIDPDFNEGKEIKYTHILGADLFSYANNPRASTNDELLSQVKKVLEKGYRDDSTTYANLTSVEFRAATQ
LAIYYFTDSVDLDNLADYHGFGALTTEALNATKEIVAYAEDRANLPNISNLDFYVPNSNKYQSLIGTQYH
PESLVDIIRMEDKQAPIIPITHKLTISKTVTGTIADKKKEFNFEIHLKSSDGQAISGTYPTNSGELTVTD
GKATFTLKDGESLIVEGLPSGYSYEITETGASDYEVSVNGKNAPDGKATKASVKEDETITFENRKDLVPP
TGLTTDGAIYLWLLLLVLLGLWVWLIGRKGLKND
A
B
Cpa M18
Pfam
Cna_B
Pfam
Fb_signal

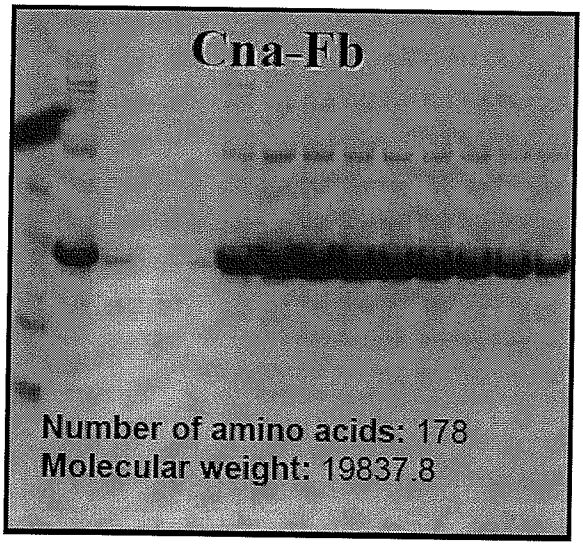

Cna-Fb
Number of amino acids: 178
Molecular weight: 19837.8

FIG. 2

FIG. 3

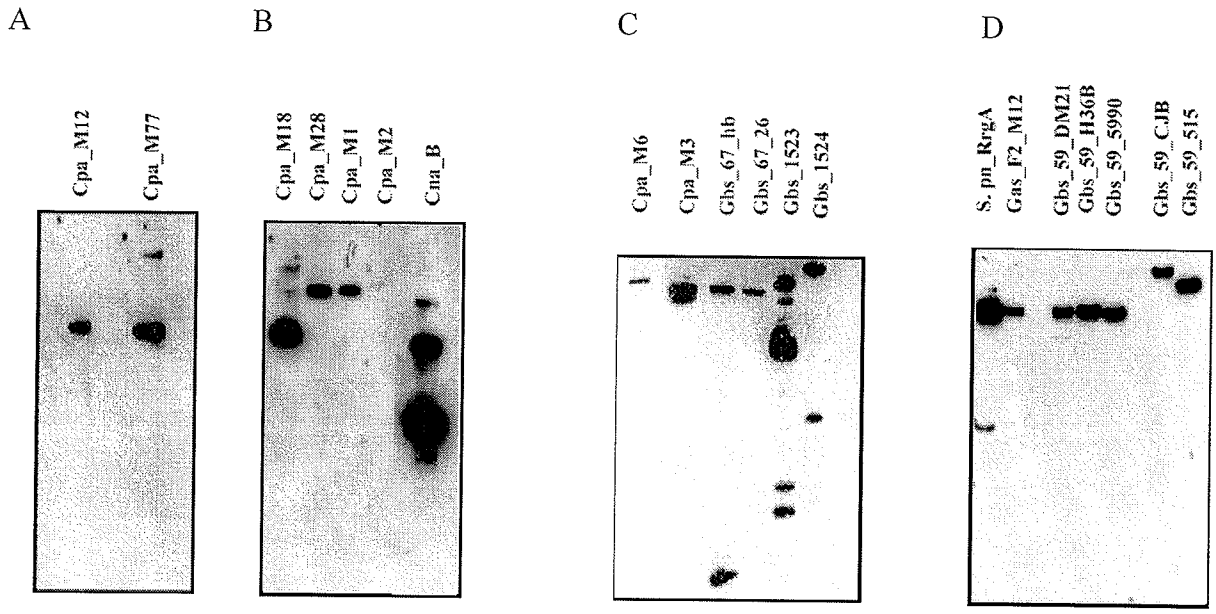
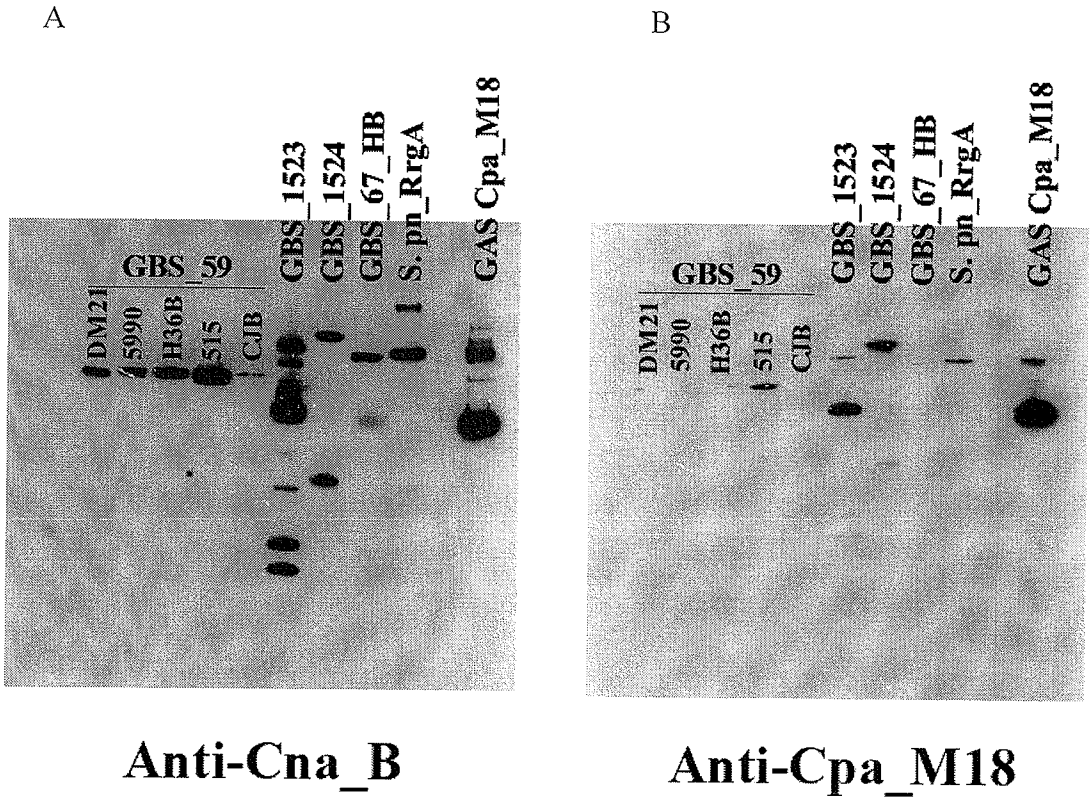

A
B
C
D
Cpa_M12
Cpa_M77
Cpa_M18
Cpa_M28
Cpa_M1
Cpa_M2
Cna_B
Cpa_M6
Cpa_M3
Gbs_67_hb
Gbs_67_26
Gbs_1523
Gbs_1524
S. pn_RrgA
Gas_F2_M12
Gbs_59_DM21
Gbs_59_H36B
Gbs_59_5990
Gbs_59_CJB
Gbs_59_515

FIG. 4


A
B
GBS_59
DM21
5990
H36B
515
CJB
GBS_1523
GBS_1524
GBS_67_HB
S. pn_RrgA
GAS
Cpa_M18
Anti-Cna_B
Anti-Cpa_M18


GBS 515
GBS JM
log Difference T0-T1
1,4
1,2
1,0
0,8
0,6
0,4
0,2
0,0
-0,2
-0,4
-0,6
-0,8
-1,0
-1,2
Preimmune sera
No HL60 cells
cps1a
59 1:10
59 1:30
GAS CNA 1:10
1523 1:10
1523 1:30
80 1:10
80 1:30
GAS CNA 1:10
no serum
cps1a
59 1:10
GAS CNA 1:10
1523 1:10
80 1:10
GAS CNA 1:10
cps1a
59 1:10
GAS CNA 1:10
1523 1:10
80 1:10
GAS CNA 1:10
no serum

FIG. 5

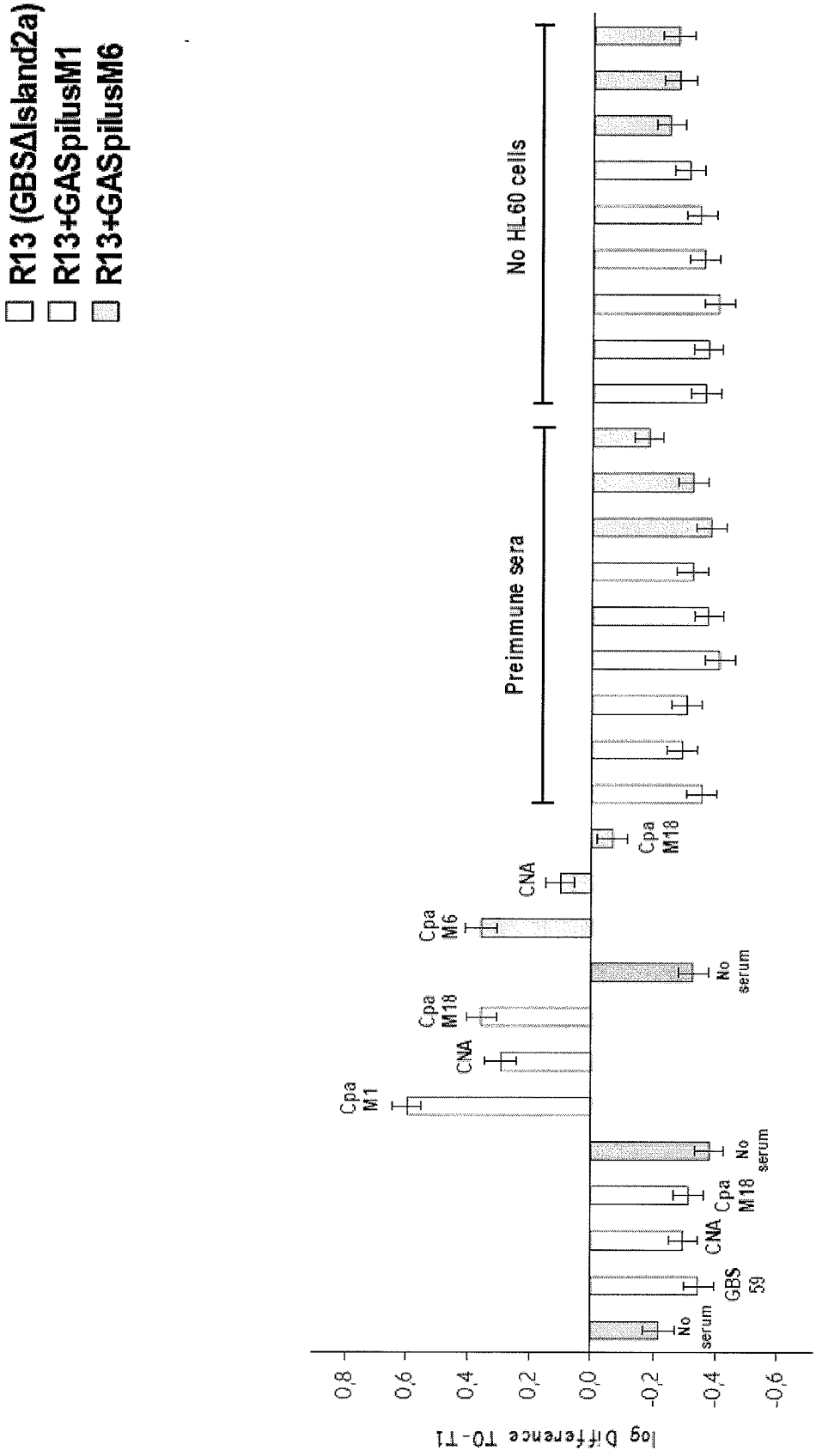

R13 (GBSΔIsland2a)
R13+GASpilusM1
R13+GASpilusM6
No HL60 cells
Preimmune sera
log Difference T0-T1
0,8
0,6
0,4
0,2
0,0
-0,2
-0,4
-0,6
No serum
GBS 59
CNA
Cpa M18
No serum
CNA
Cpa M18
Cpa M1
CNA
Cpa M18
Cpa M6
No serum
Cpa M18

FIG. 6

```
CNA_B_CPA_M5_MANFREDO   LEGATLRLT-GEDIPDFQEKVFQSNGIGEKIELSNG-TYILIEISSPDGY 48
CNA_B_CPA_M28           LEGATLRLT-GEDIPDFQEKVFQSNGIGEKIELSNG-TYILIEISSPDGY 48
CNA_B_CPA_M12           LEGATLRLT-GEDILDFQEKVFQSNGIGEKIELSNG-TYILIEISSPDGY 48
CNA_B_CPA_M1            LEGATLQLT-GDNVNSFQARVFSSNDIGERIELSDG-TYILIELNSPAGY 48
CNA_B_CPA_M3            LEGATLKLA-QIEGSGFQEKIFDSNKSGEKVELPNG-TYVLSELKPPQGY 48
CNA_B_CPA_M18           LEGATLKLA-QIEGSGFQEQSFESSISGQKLQLSDG-TYILIETKSPQGY 48
CNA_B_CPA_M6            LAGVEFELRKEDKKIVWEKGTIGSNGQLNFKYLQHGKTYYLYETKAKLGY 50
CNA_B_CPA_M4_C          LAGAKFQLE-SNKGVVLIIGEIDG-KGEYIFINLPFG-DYILIEIAAPKGY 47
CNA_B_CPA_M2            LGKATFVLKNDHDKSEISHEIVEGSGEAAFENIKFG-NYILIEKIAPIGY 49
                        *  . : *      .         .      :  *  * * *   .  **

CNA_B_CPA_M5_MANFREDO   KITE-PIKFRVVN-K--------- 61
CNA_B_CPA_M28           KIAE-PIKFRVVN-K--------- 61
CNA_B_CPA_M12           KIAE-PIKFRVVN-K--------- 61
CNA_B_CPA_M1            SIAE-PITFKVEAGKVYTIIDGK 70
CNA_B_CPA_M3            GVAT-PITFKVAAE---------- 61
CNA_B_CPA_M18           EIAE-PITFKVIA----------- 60
CNA_B_CPA_M6            TLPENPWEVAVANNGDIKVK--- 70
CNA_B_CPA_M4_C          ILDKTPRSIAIGDIVDKE----- 65
CNA_B_CPA_M2            KKIDKIWKVKVADNGAITIE--- 69
                            .   .  :
```

FIG. 7

```
CNA_B_GBS_52       LAGVVFELYEKNGRTP-IRVKNGVHSQDIDAAK----------HLEIDSSGHIRISG---- 46
CNA_B_GBS_150      LSGVIFVLYD-NQNQP-VRFKNGRFTTDQDGIT----------SLVIDDKGEIEVEG---- 45
CNA_B_GBS_104_1    LGKATFVLKNDND----------------KSETS----------HETVEGSGEATFEN---- 32
CNA_B_67           LSKATFVLKTTAHP---------------ESKIE----------KVTAELTGEATFDN---- 33
CNA_B_GBS_1523     LQGATFVLKNATGQFLNFNDINNVEWGTEANAT----------EYTTGADGTITTTG---- 47
CNA_B_GBS_1524     LAGAVFDIYESDANGN----------KASHPMYS----------GLVTNDKGLLLVDANNYL 42
CNA_B_GBS_80       LGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYA 60
CNA_B_GBS_104_2    LLGAKFQLQIEKDFSG---------YKQFVPEGS----------DVTTKNDGKIYFKA---- 39
CNA_B_GBS_1521     LTKAVHKTQP-------------------LQTFD------------NLPAEG-TVANN---- 26
                   *  . .                                          *

CNA_B_GBS_52       ---LIHGD---YVLKEIETQSGYQIGQAETAVTIEKSKIVTVTI----- 84
CNA_B_GBS_150      ---LLFGK---YTFREAKALTGYKISMKDAVV------------------ 71
CNA_B_GBS_104_1    ---IKFGD---YTLREETAPTGYKKTDKTWKVK---------------- 59
CNA_B_67           ---LIFGD---YTLSEETAPEGYKKTNQTWQVKV--------------- 61
CNA_B_GBS_1523     ---LKIGT---YYLVEKKAPLGYNLLDNSQKVTLGDGATDTTNS----- 85
CNA_B_GBS_1524     S--LPVGK---YYLIETKAPPGYLLPKNDISVLVISIGVTEEQ------ 80
CNA_B_GBS_80       VDANAFGTAVTYKLKETKAPEGYVIPDKEIEFT---------------- 93
CNA_B_GBS_104_2    ---LQIGN---YKLYEISSPDGYIEVKTKPVVTFTIQNGEVTNLK---- 78
CNA_B_GBS_1521     ---LPQGI---YLFIQTKTAQGYEIMSPFILSIPKDGKYDTTTPTVIHQ 69
                      *      * : :  :  **
```

FIG. 8

```
CNA_B_GBS_80        LGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDG-TFEIKGLAY 59
CNA_B_GBS_52        LAGVVFELYEKNG------RTPIRVKNG---VHSQDID-AAKHLETDSSG-HIRISGLIH 49
CNA_B_GBS_104_2     LLGAKFQLQIEKD------------FSG----YKQFVP-EGSDVTTKNDG-KIYFKALQD 42
CNA_B_GBS_104_1     LGKATFVLKNDND-------------KS-----------ETSHETVEGSG-EATFENIKP 35
CNA_B_M18           LEGATLKLAQIEG-------------SG----------FQEQSFESSTSGQKLQLSD--- 34
                    *  . : *   ..               ..                    .*    :.

CNA_B_GBS_80        AVDANAEGTAVTYKLKETKAPEGYVIPDKE--IEFTVSQT 97
CNA_B_GBS_52        -------G---DYVLKEIETQSGYQIGQAE--TAVTIEKS 77
CNA_B_GBS_104_2     -------G---NYKLYEISSPDGYIEVKTKPVVTFTIQNG 72
CNA_B_GBS_104_1     -------G---DYTLREETAPIGYKKTDKT--WKVKVADN 63
CNA_B_M18           -------G---TYILTETKSPQGYEIAEPI---TFKVTA- 60
                           *    * * *  :  **     .     ..:
```

FIG. 9

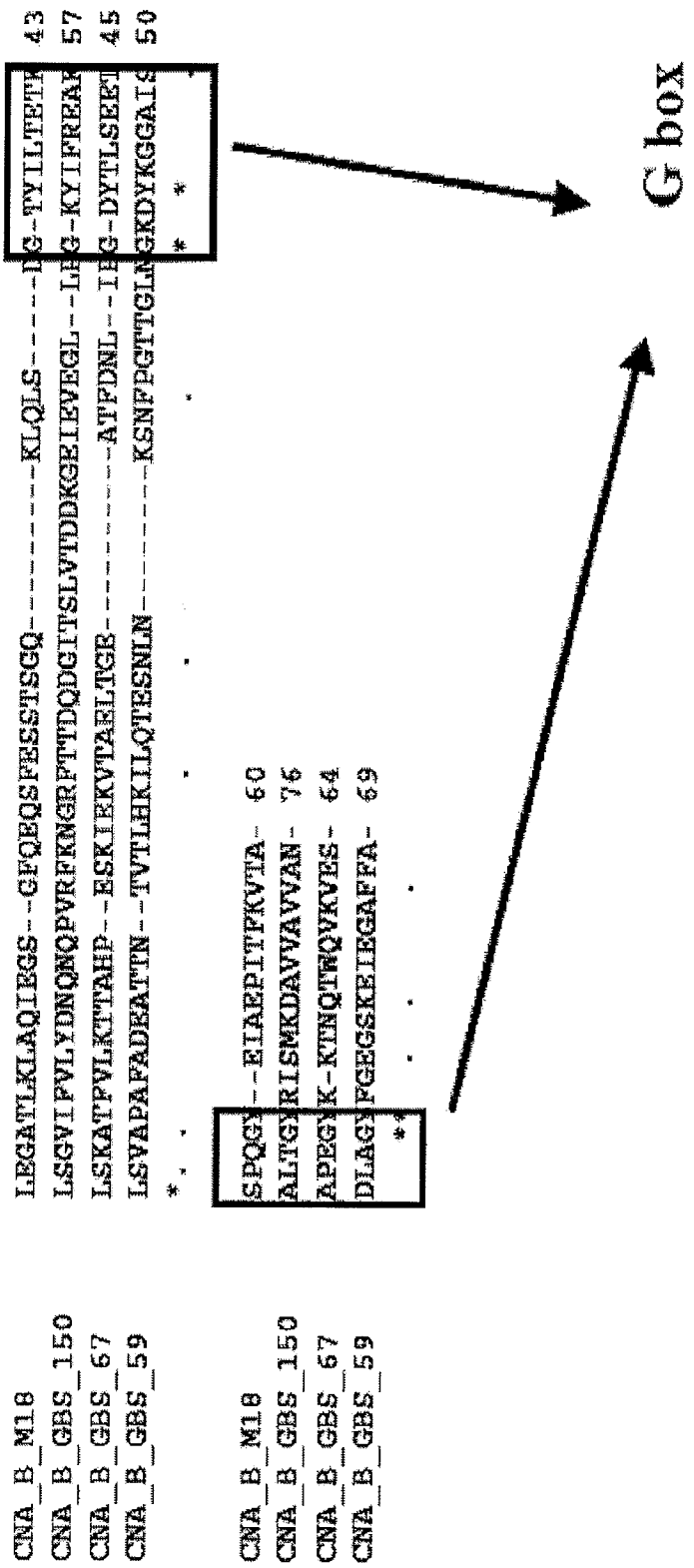

CNA_B_M18 LEGATLKLAQIEGS--GPQEQSPESSTSGQ----------KLQLS-----IG-TYILTETH 43
CNA_B_GBS_150 LSGVIPVLYDNQMQPVRPKNGRPTTDQDGITSLVTDDKGEIEVEGL--LE-G-KYIFREAK 57
CNA_B_GBS_67 LSKATPVLKTTAHP--ESKIEKVTAELTGB----------ATPDNL--IE-G-DYTLSEET 45
CNA_B_GBS_59 LSVAPAFADEATTN--TVTLEKILQTESNLN----------KSNPPGTTGLM-GKDYKGGAIS 50
CNA_B_M18 SPQGY--EIAEPITPKVTA- 60
CNA_B_GBS_150 ALTGYRISMKDAVVAVVAN- 76
CNA_B_GBS_67 APEGYK-KTNQTWQVKVES- 64
CNA_B_GBS_59 DLAGYPGEGSKEIEGAFFA- 69
G box

FIG. 10

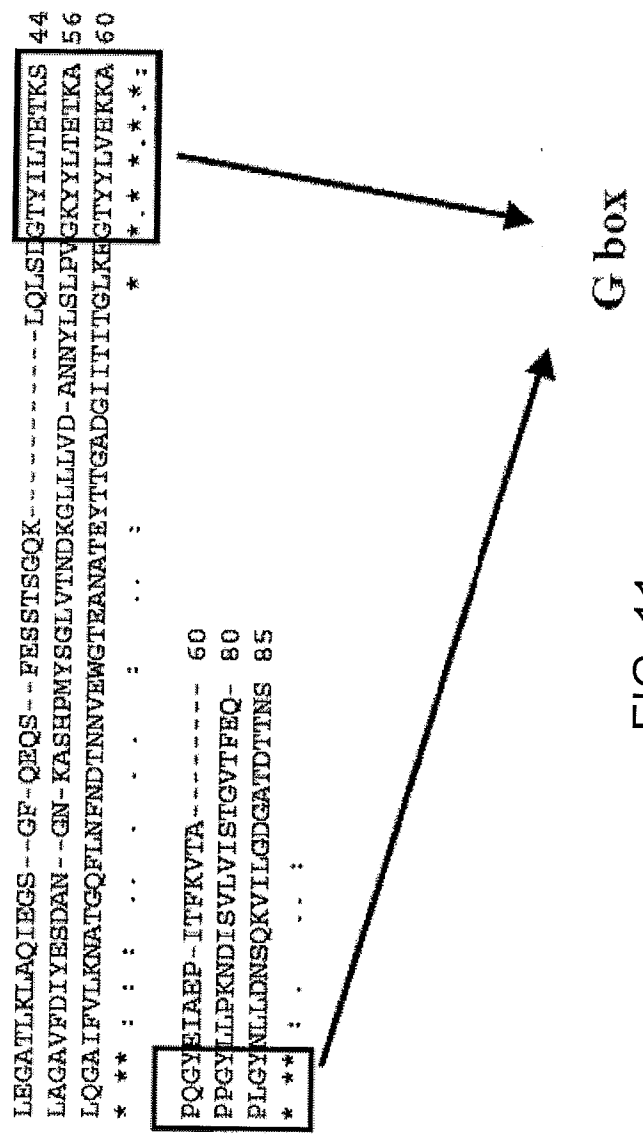

CNA_B_M18 LEGATLKLAQIEGS--GF-QEQS--FESSTSGQK----------LQLSIGTYILTETKS 44
CNA_B_GBS_1524 LAGAVFDIYESDAN--GN-KASHDMYSGLVTNDKGLLLVD-ANNYLSLPVGKYYLTETKA 56
CNA_B_GBS_1523 LQGAIFVLKNATGQFLNFNDTNNVEWGTEANATEYTTGADGIITTTGLKEGTYYLVEKKA 60
* ** : : : .. . . . : .. : * *.*.*.*:
CNA_B_M18 PQGYEIAEP-ITFKVTA-------- 60
CNA_B_GBS_1524 PPGYLLPKNDISVLVISTGVTFEQ- 80
CNA_B_GBS_1523 PLGYNLLDNSQKVILGDGATDTTNS 85
* ** : . . : :
G box

FIG. 11

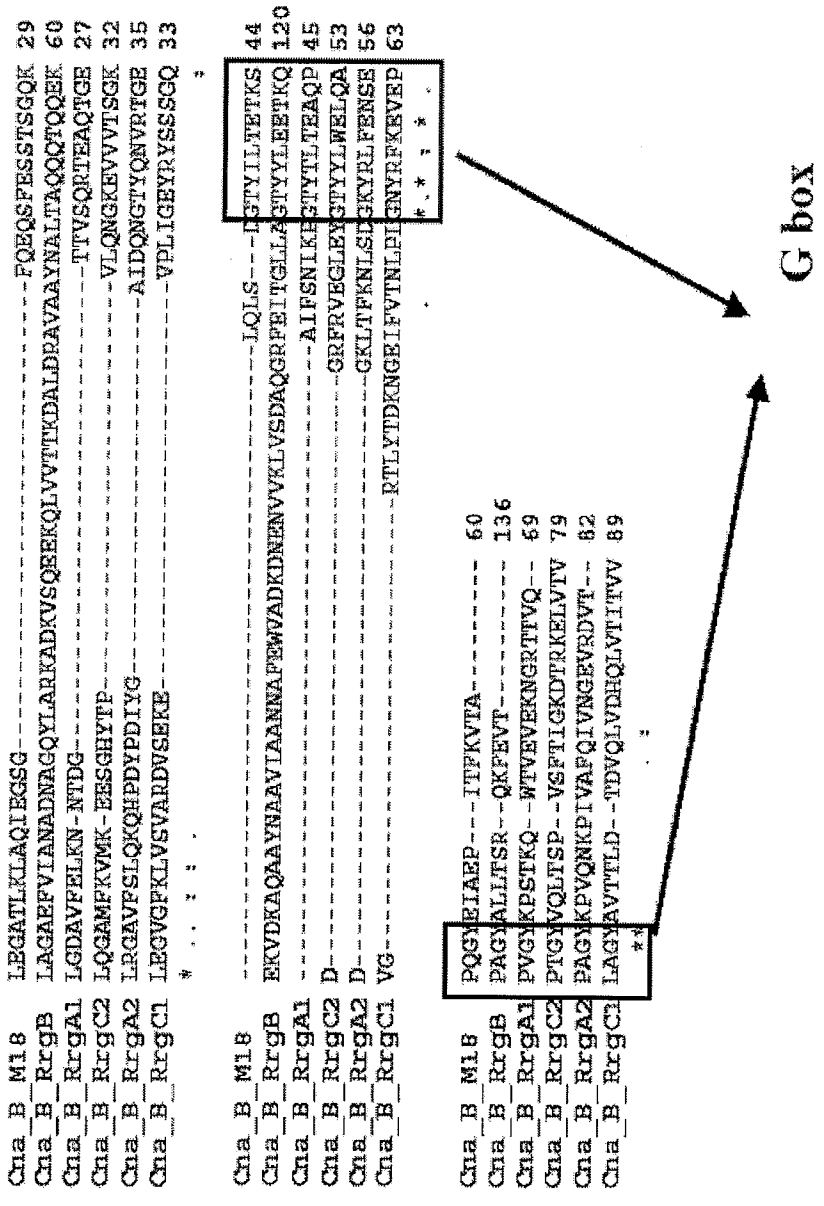

Cna_B_M18 LEGATLKLAQIEGSG----------PQEQSFESSTSGQK 29
Cna_B_RrgB LAGAEFVIANADNAGQYLARKADKVSQEEKQLVVTTKDALDPAVAAYNALTAQQQTQQEK 60
Cna_B_RrgA1 LGDAVFELKN-NTDG----------TTVSQRTEAQTGE 27
Cna_B_RrgC2 LQGAMFKVMK-EESGHYTP----------VLQNGKEVVVTSGK 32
Cna_B_RrgA2 LRGAVFSLQKQHPDYPDIYG----------AIDQNGTYQNVRTGE 35
Cna_B_RrgC1 LEGVGFKLVSVARDVSEKE----------VPLIGEYRYSSSGQ 33
Cna_B_M18 ----------LQLS---DSTYILLTETKS 44
Cna_B_RrgB EKVDKAQAAYNAAVIAANNAPEWVADKDNENVVKLVSDAQGRFEITGLLASTYYLEETKQ 120
Cna_B_RrgA1 ----------AIFSNIKESTYTLTEAQP 45
Cna_B_RrgC2 D----------GRFRVEGLEYSTYYLWELQA 53
Cna_B_RrgA2 D----------GKLTFKNLSDSKYRLFENSE 56
Cna_B_RrgC1 VG----------RTLYTDKNGEIFVTNLPDSNYRFKEVEP 63
Cna_B_M18 PQGYEIAEP---ITPKVTA---------- 60
Cna_B_RrgB PAGYALLTSR--QKPEVT---------- 136
Cna_B_RrgA1 PVGYKPSTKQ--WTVEVEKNGSTTVQ-- 69
Cna_B_RrgC2 PTGYVQLTSP--VSFTIGKDTFRKELVTV 79
Cna_B_RrgA2 PAGYKPVQNKPIVAFQIVNGEVRDVTI-- 82
Cna_B_RrgC2 LAGYAVTTLD--TDVQLVDHQLVTITVV 89
G box

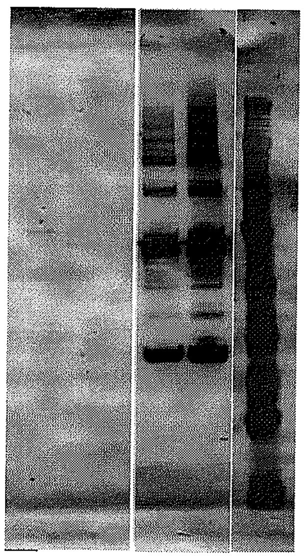
FIG. 12

```
Ser-Asp rich2   ISGVTVTLKNENGEVLQT------TKTDKDGKYQFTGLENGTYKV-EFETPSGYTPTQVG 53
Ser-Asp rich3   ISGVTVTLKDENDKVLKT------VTTDENGKYQFTDLNNGTYKV-EFETPSGYTPTSVT 53
Cna_B_cbp       IANVKFKLSKKDGSVVKDNQKEIEIITDANGIANIKALPSGDYILKEIEAPAPYTFDKDK 60
Cna_B_M18       LEGATLKLAQIEGSGFQE------QSFESSTSGQKLQLSDGTYILTETKSPQGYEIAEPI 54
                : .....* . :.. .:           : .  :  * ** : *  ::*  *  .

Ser-Asp rich2   SG--TDE---------- 58
Ser-Asp rich3   SG--NDTEKDSNGLTTT 68
Cna_B_cbp       EYPFTMKDTDNQGYFT- 76
Cna_B_M18       TF--KVTA--------- 60
```

FIG. 13

anti-Cna_B

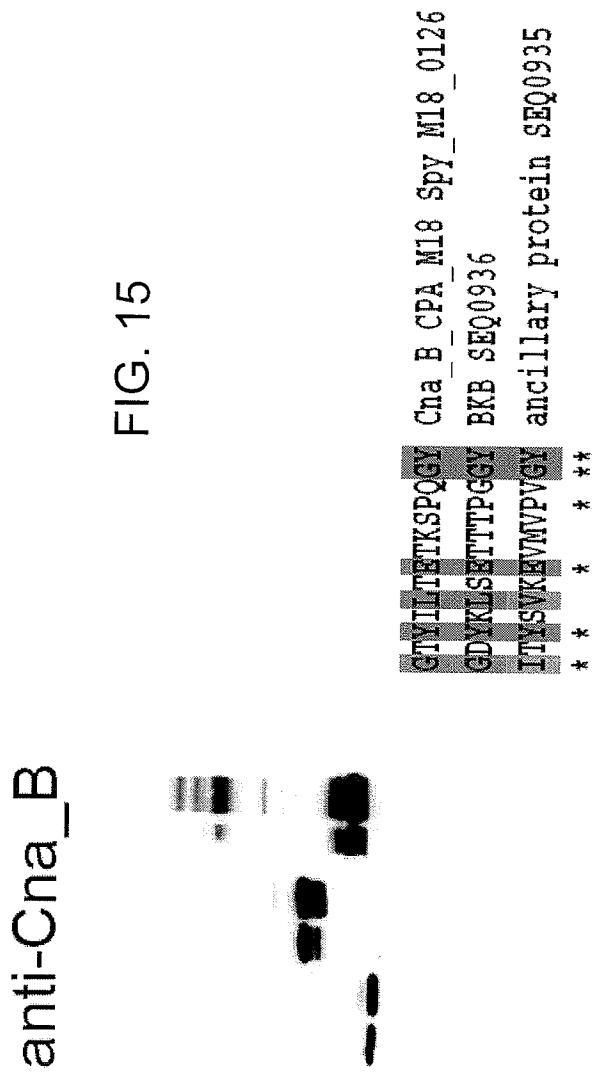


Bkb pilus 3
Bkb pilus 1
Cna_B_M18 10 ng
Cna_B_M18 20 ng

```
GTYILTETKSPQGY   Cna_B_CPA_M18 Spy_M18_0126
GTYYLKEITAPTGY   Cna_B_Bkb3 (DUF 11) 89/1591
TTYYLEEMKAPNGY   Cna_B_Bkb1 SSU05_0474 05ZYH33
 ** * *    * **
```

FIG. 14

FIG. 15


Cna_B_CPA_M18_Spy_M18_0126
BKB SEQ0936
ancillary protein SEQ0935
anti-Cna_B
Bkb Seq_0936 10 ng
Bkb Seq_0936 50 ng
AP Seq_093610 ng
AP Seq_0936 50 ng
Cna_B_M18 10 ng
Cna_B_M18 50ng

```
Cna_B_AUTOTRANSPORTER    LTGAEFKLYDAANNGTEIKVVKESDGVYRVAQADEQGVVIEAGEVVIKGL 50
Cna_B_                   LAGAVFGIYSDAETKQLVDIVTTNADGYAISTKVGKG------------- 37
Cna_B_CPA_M18            LEGATLKLAQIEGSGFQEQSFESSTSGQKLQLSDG--------------- 35
                         * ** : : .    .      . .   . .    :

Cna_B_AUTOTRANSPORTER    KHSTTYYLEEMKAPNGYNILTER-QSIE-- 77
Cna_B_                   ----TYYLKEITAPTGYSLNTNV-YTAEAS 62
Cna_B_CPA_M18            ----TYILTETKSPQGYEIAEPITFKVTA- 60
                             ** * *  .:* **.:      .
```

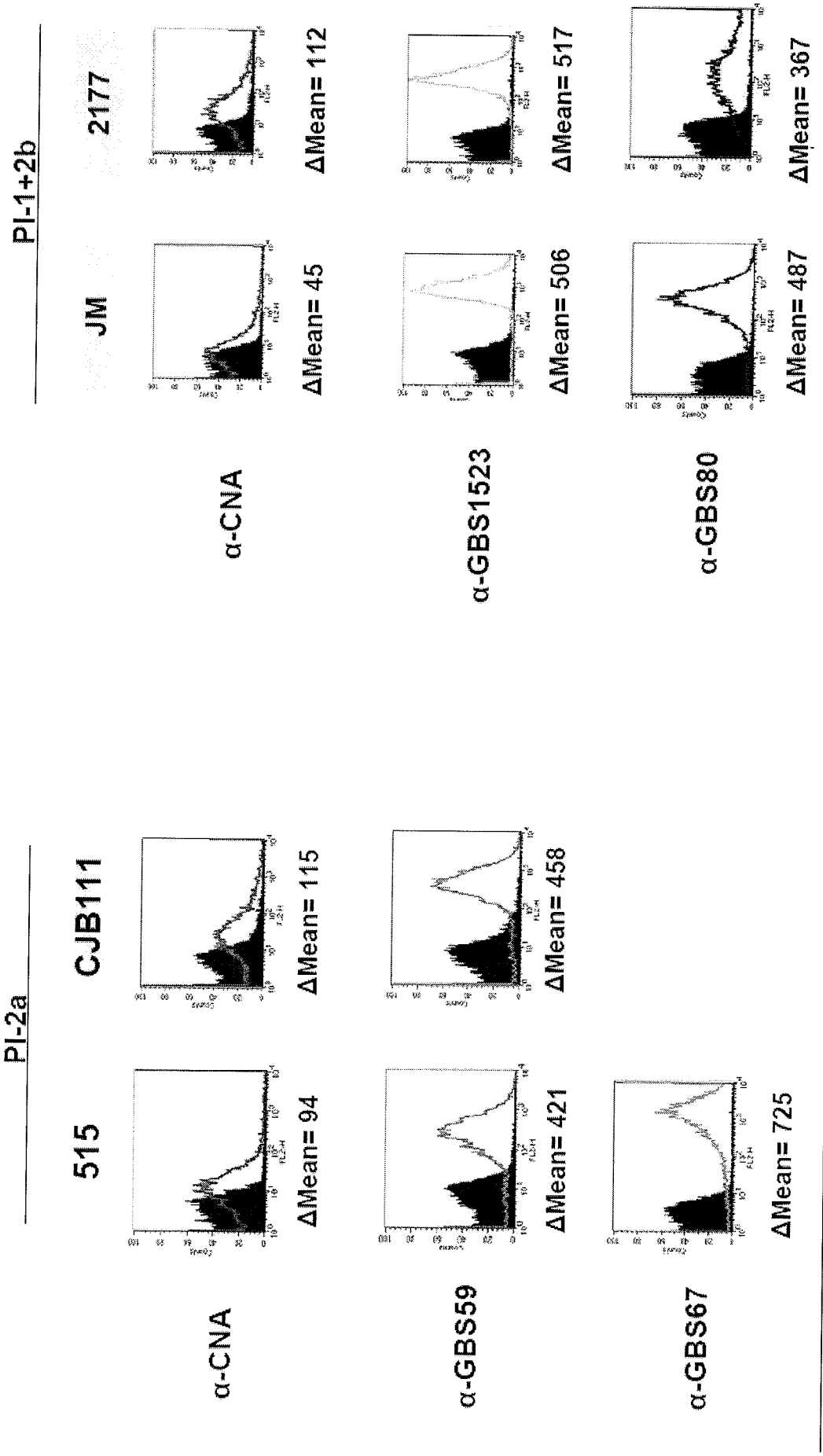
FIG. 16

```
CNA_B_bkb        -LKGAGFTLYKLVKGDNGEEKY-QIVQEIKAGDTTSFEFVGLDAGDYKLSETTTPGGYNT 58
CNA_B_CPA_M18    -LEGATLKLAQIE-G-SGFQE--QSFESSTSGQK-----LQLSDGTYILTETKSPQGYEI 50
CNA_B_ap1        -LYANDQKVNDKTIELSDTNSWQASFGKLDKYDS------QNQKITYSVKEVMVPVGYQS 53
CNA_B_ap2        LLKADGKVIREHQMTPDQQGKWEYTFDQLPVYQT-------GKKISYSIEEKQVA-GYQA 52
                  *  .    : .     .    .     .  .    :.          .   * : *   . **:

CNA_B_bkb        IA-DVMFSIVA 68
CNA_B_CPA_M18    AE-PITFKVTA 60
CNA_B_ap1        QV-EGDSGV-- 61
CNA_B_ap2        PVYEVDEGL-- 61
                     :
```

FIG. 17

FIG. 18


PI-2a
515
CJB111
α-CNA
ΔMean= 94
ΔMean= 115
α-GBS59
ΔMean= 421
ΔMean= 458
α-GBS67
ΔMean= 725
PI-1+2b
JM
2177
α-CNA
ΔMean= 45
ΔMean= 112
α-GBS1523
ΔMean= 506
ΔMean= 517
α-GBS80
ΔMean= 487
ΔMean= 367

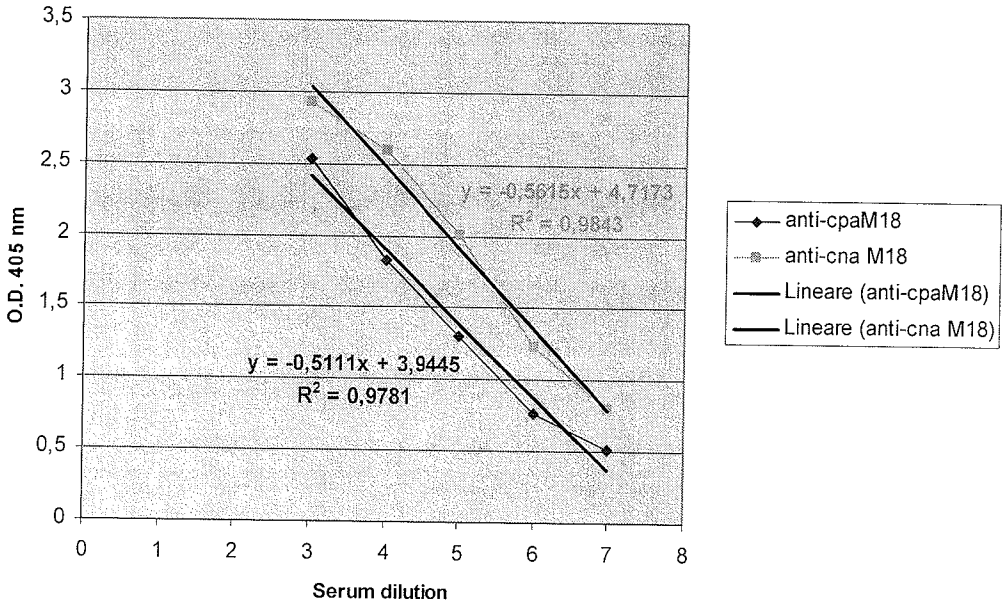
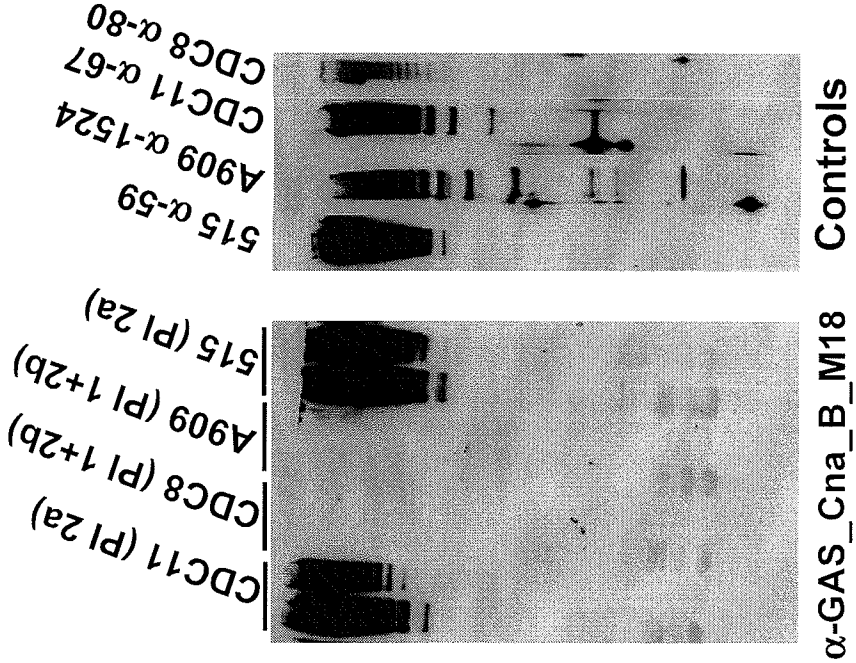


FIG. 19

Y= 1
1= -0.511x + 3.9445
2.9445 = 0.511 x
X = 5.76
6 : 3200 = 5.76 : x
X = 3072

Y= 1
1= -0.5615x + 4.7173
3.7173 = 0.5615 x
X = 6.58
7 : 6400 = 6.58 : x
X = 6016

FIG. 20


CDC8 α-80
CDC11 α-67
A909 α-152A
515 α-59
Controls
515 (PI 2a)
A909 (PI 1+2b)
CDC8 (PI 1+2b)
CDC11 (PI 2a)
α-GAS_Cna_B_M18

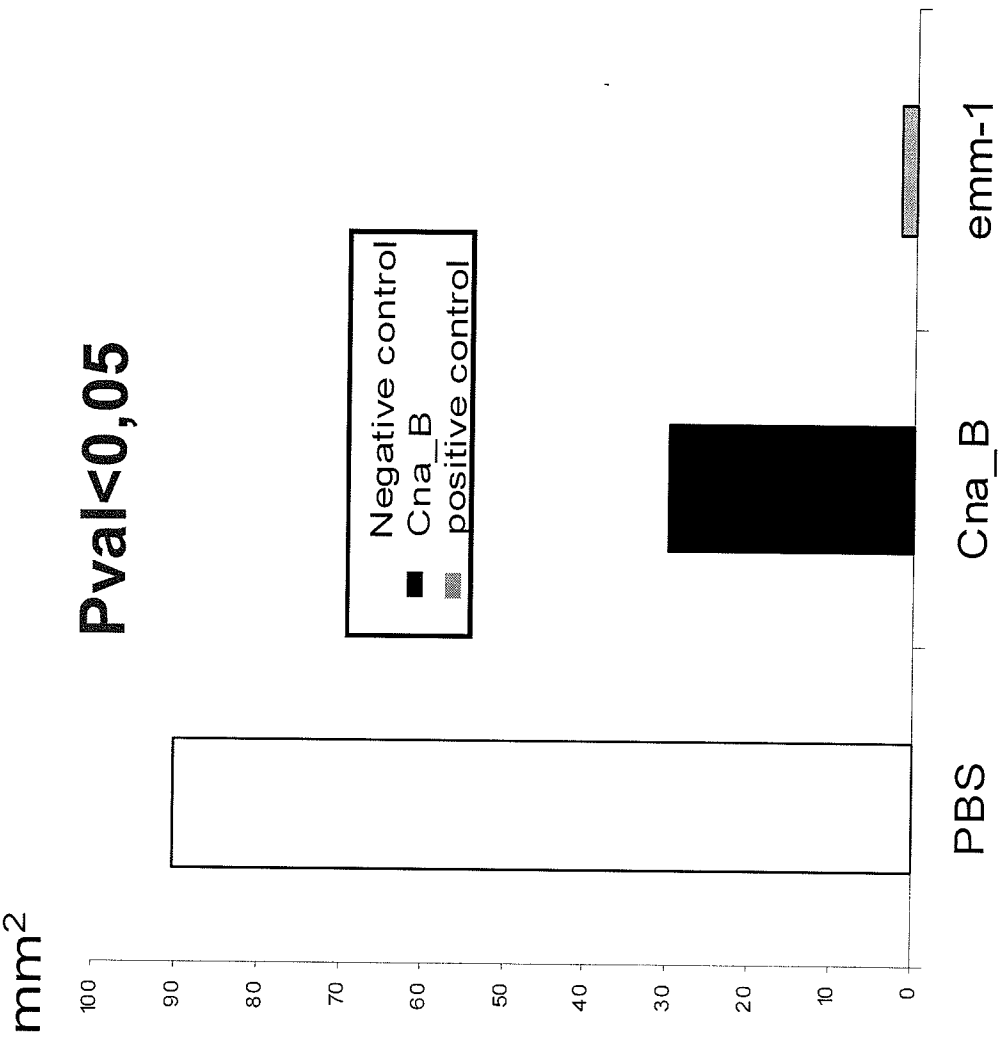

Pval<0,05
Negative control
Cna_B
positive control
mm2
100
90
80
70
60
50
40
30
20
10
0
PBS
Cna_B
emm-1

FIG. 21

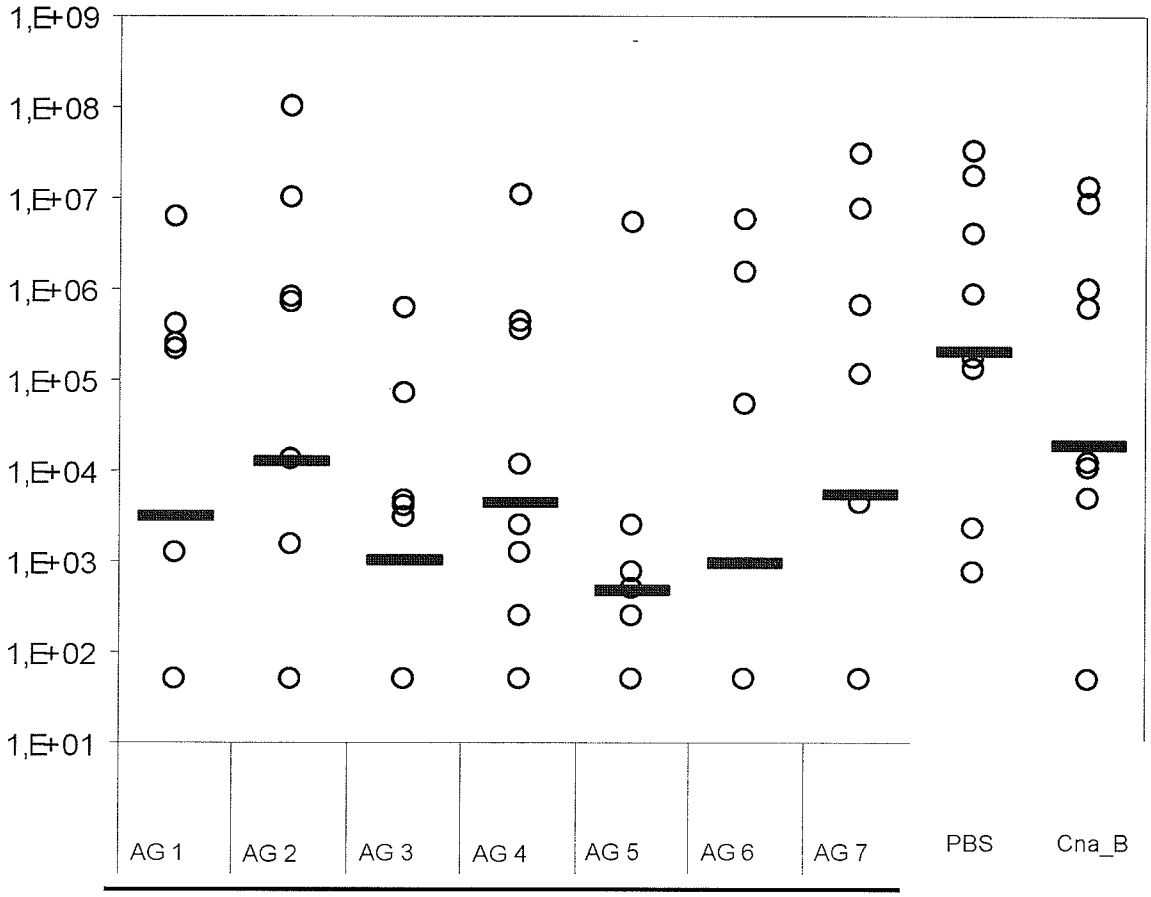

1,E+09
1,E+08
1,E+07
1,E+06
1,E+05
1,E+04
1,E+03
1,E+02
1,E+01
AG 1
AG 2
AG 3
AG 4
AG 5
AG 6
AG 7
PBS
Cna_B
S. aureus antigens (AG)

FIG. 22

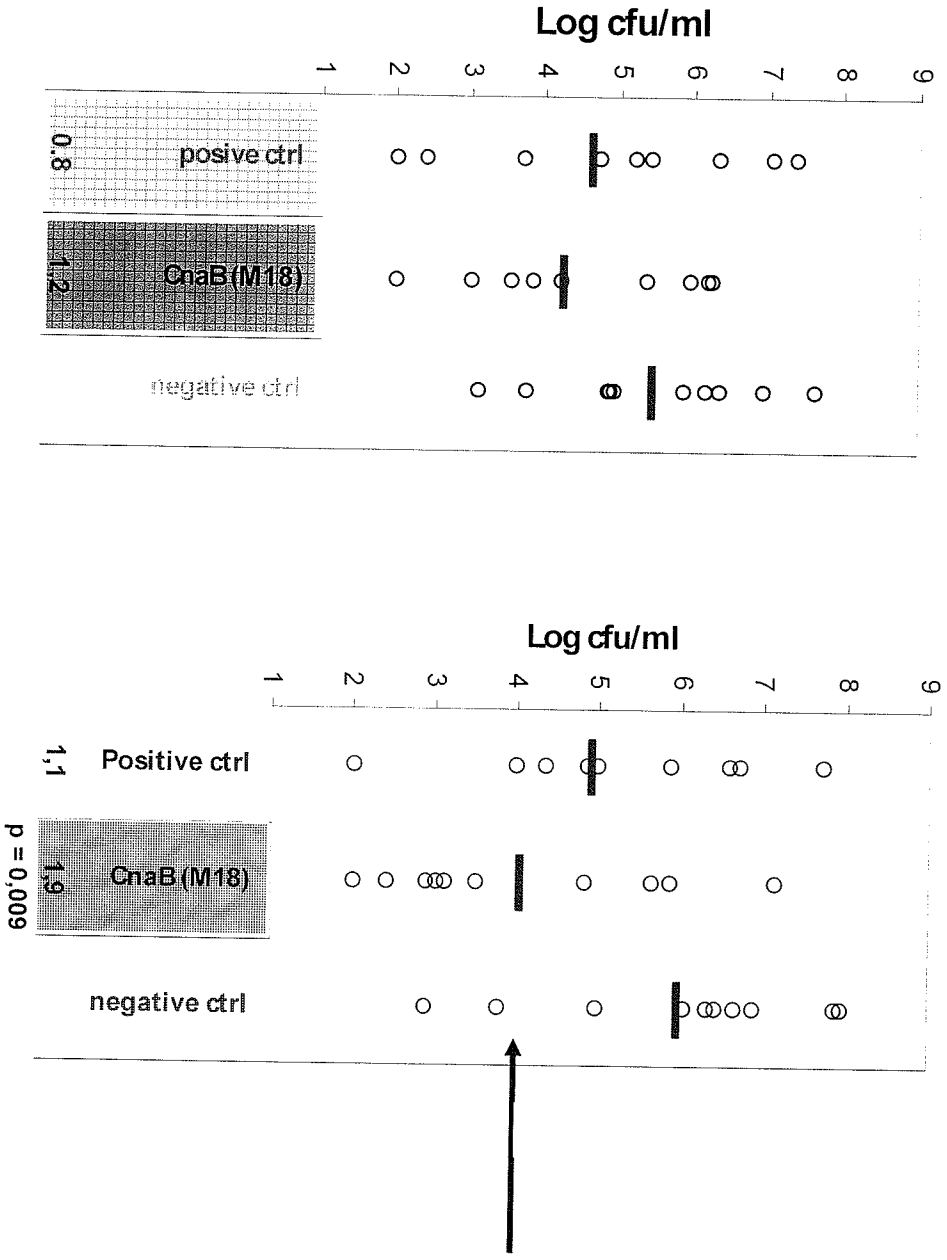

Log cfu/ml
1
2
3
4
5
6
7
8
9
0.8
posive ctrl
1,2
CnaB (M18)
negative ctrl
Log cfu/ml
1
2
3
4
5
6
7
8
9
1,1
Positive ctrl
p = 0,009
1,9
CnaB (M18)
negative ctrl

FIG. 23

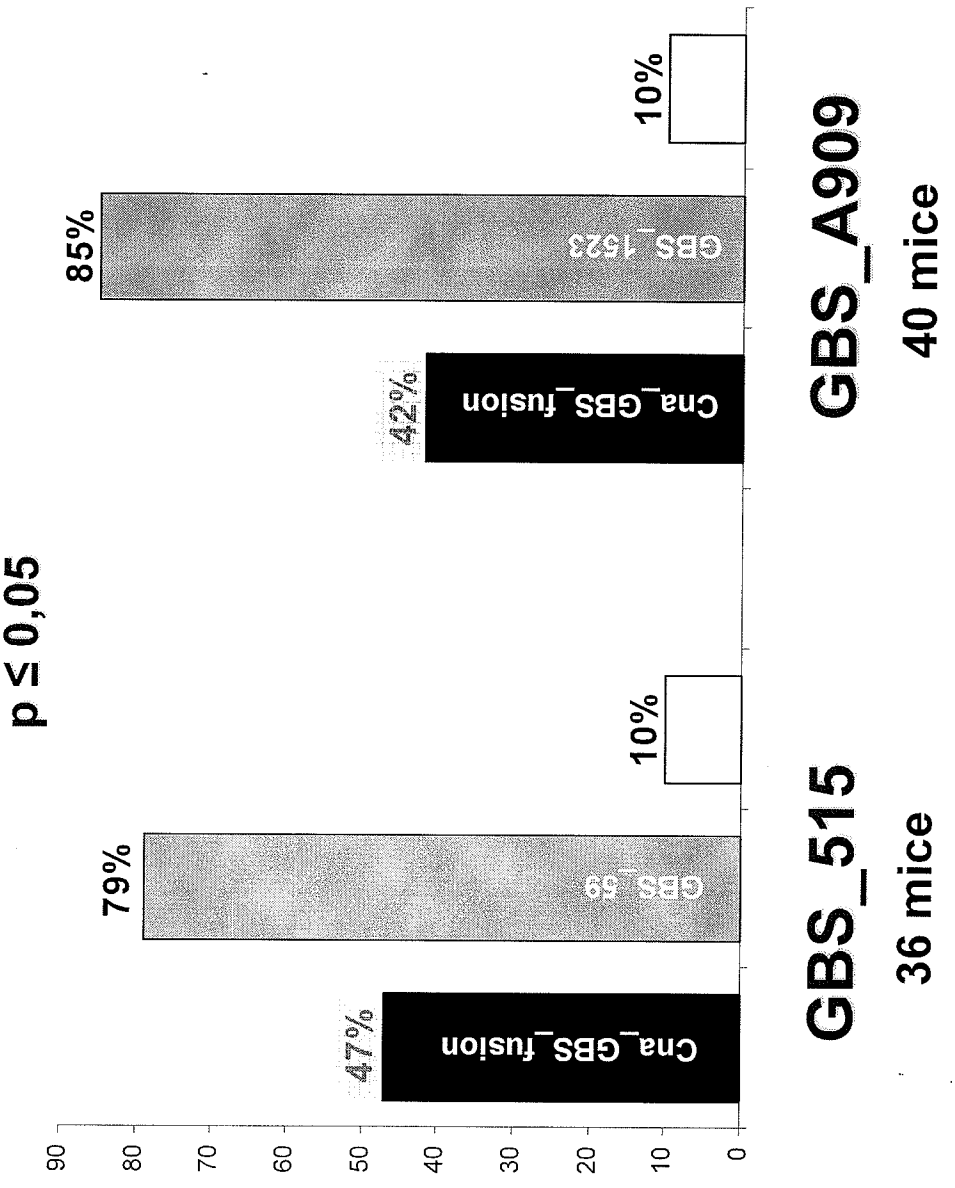

p ≤ 0,05
90
80
70
60
50
40
30
20
10
0
47%
Cna_GBS_fusion
79%
GBS_59
10%
GBS_515
36 mice
42%
Cna_GBS_fusion
85%
GBS_1523
10%
GBS_A909
40 mice

FIG. 24

FIG. 25

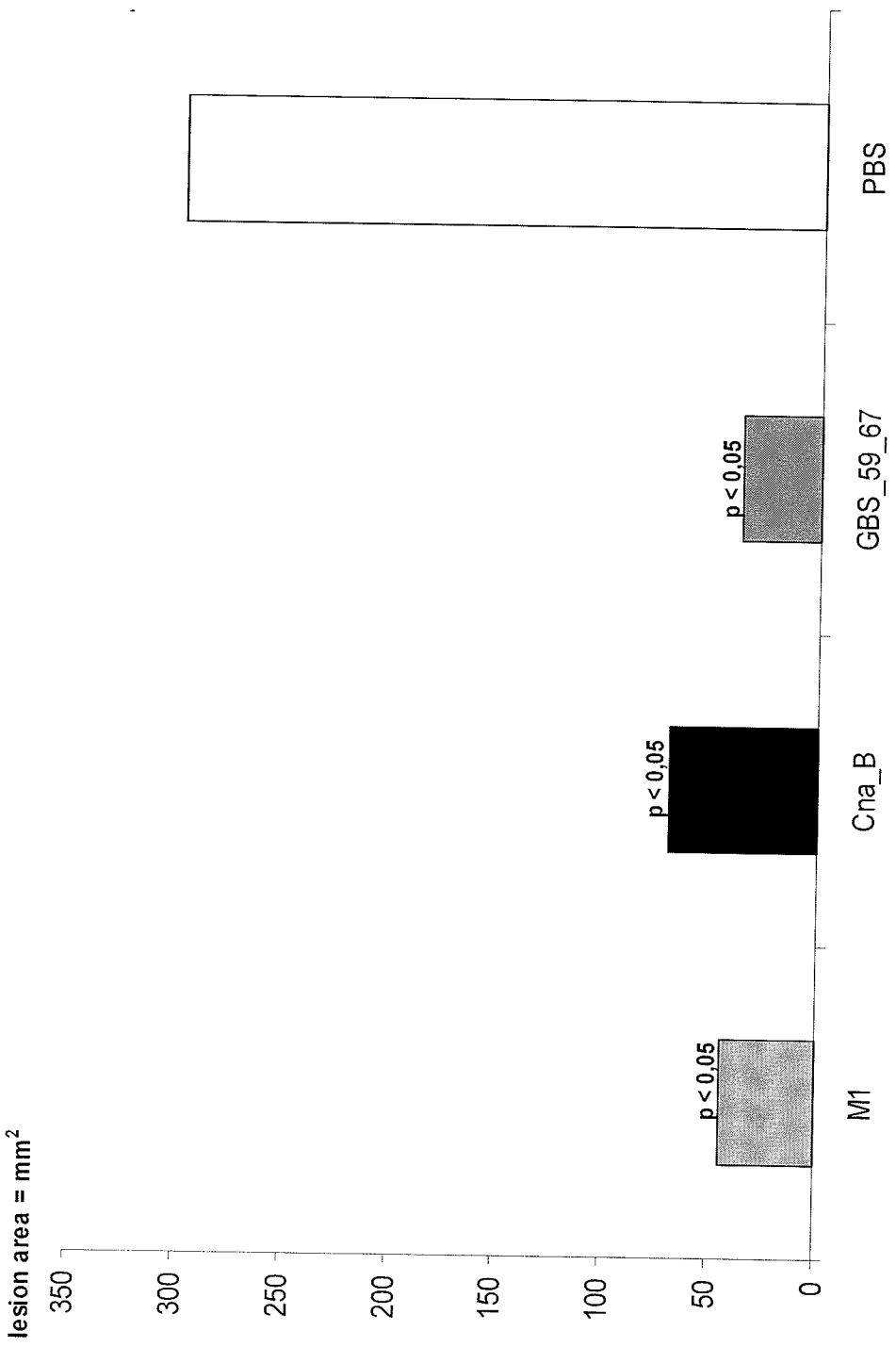
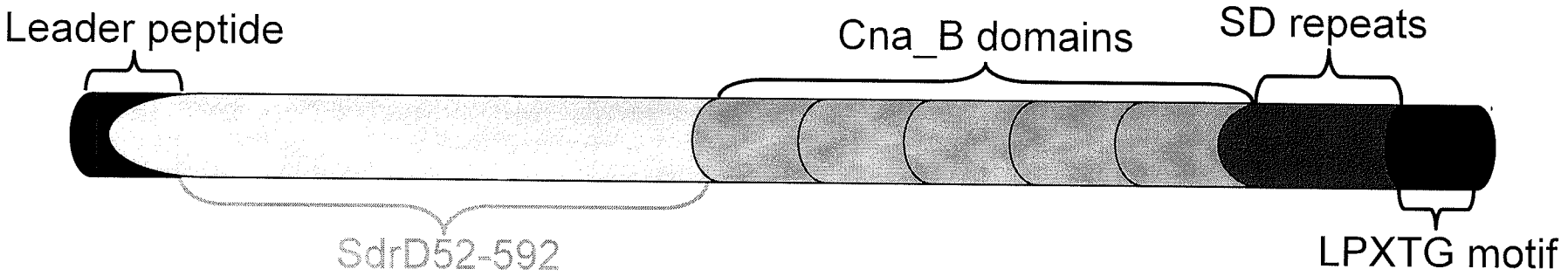

lesion area = mm2
350
300
250
200
150
100
50
0
p < 0,05
p < 0,05
p < 0,05
M1
Cna_B
GBS_59_67
PBS

FIG. 26A

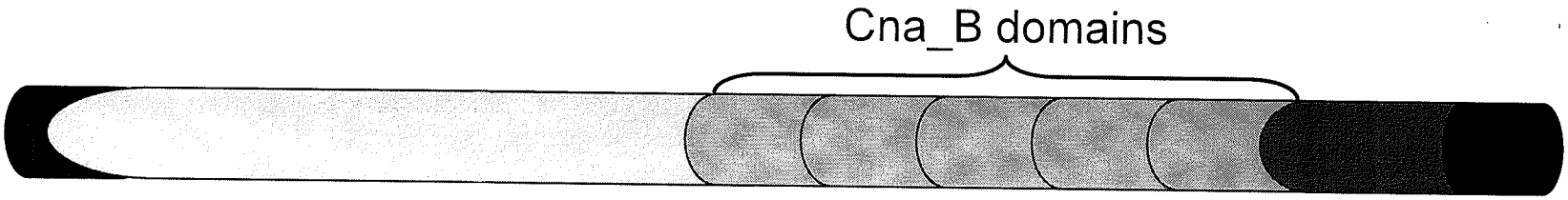


>SAOUHSC_00545 - SdrD (1363 aa)
MLNRENKTAITRKGMVSNRLNKFSIRKYTVGTASILVGTTLIFGLGNQEAKAAESTNKEL
NEATTSASDNQSSDKVDMQQLNQEDNTKNDNQKEMVSSQGNETTSNGNKLIEKESVQSTT
GNKVEVSTAKSDEQASPKSTNEDLNTKQTISNQEALQPDLQENKSVVNVQPTNEENKKVD
AKTESTTLNVKSDAIKSNDETLVDNNSNSNNENNADIILPKSTAPKRLNTRMRIAAVQPS
STEAKNVNDLITSNTTLTVVDADKNNKIVPAQDYLSLKSQITVDDKVKSGDYFTIKYSDT
VQVYGLNPEDIKNIGDIKDPNNGETIATAKHDTANNLITYTFTDYVDRFNSVQMGINYSI
YMDADTIPVSKNDVEFNVTIGNTTTKTTANIQYPDYVVNEKNSIGSAFTETVSHVGNKEN
PGYYKQTIYVNPSENSLTNAKLKVQAYHSSYPNNIGQINKDVTDIKIYQVPKGYTLNKGY
DVNTKELTDVTNQYLQKITYGDNNSAVIDFGNADSAYVVMVNTKFQYTNSESPTLVQMAT
LSSTGNKSVSTGNALGFTNNQSGGAGQEVYKIGNYVWEDTNKNGVQELGEKGVGNVTVTV
FDNNTNTKVGEAVTKEDGSYLIPNLPNGDYRVEFSNLPKGYEVTPSKQGNNEELDSNGLS
SVITVNGKDNLSADLGIYKPKYNLGDYVWEDTNKNGIQDQDEKGISGVTVTLKDENGNVL
KTVTTDADGKYKFTDLDNGNYKVEFTTPEGYTPTTVTSGSDIEKDSNGLTTTGVINGADN
MTLDSGFYKTPKYNLGNYVWEDTNKDGKQDSTEKGISGVTVTLKNENGEVLQTTKTDKDG
KYQFTGLENGTYKVEFETPSGYTPTQVGSGTDEGIDSNGTSTTGVIKDKDNDTIDSGFYK
PTYNLGDYVWEDTNKNGVQDKDEKGISGVTVTLKDENDKVLKTVTTDENGKYQFTDLNNG
TYKVEFETPSGYTPTSVTSGNDTEKDSNGLTTTGVIKDADNMTLDSGFYKTPKYSLGDYV
WYDSNKDGKQDSTEKGIKDVKVTLLNEKGEVIGTTKTDENGKYCFDNLDSGKYKVIFEKP
AGLTQTVTNTTEDDKDADGGEVDVTITDHDDFTLDNGYFEEDT*SDSDSDSDSDSDSDSDS*
DSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDS
DSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDS
*DSDSDSDSDSDSDSDSDSDSDSDSDSDAGKHTPVKPMSTTKDHHNKAKA*LPETGSENN
GSNNATLFGGLFAALGSLLLFGRRKKQNK

Sequences cut in SdrD52-592:

- Leader peptide and LPXTG motif (underlined and bold)
- SD repeats (italics)
- Cna_B domains (bold)

FIG. 26B



>SAOUHSC_00545 - SdrD (1363 aa)
MLNRENKTAITRKGMVSNRLNKFSIRKYTVGTASILVGTTLIFGLGNQEAKAAESTNKEL
NEATTSASDNQSSDKVDMQQLNQEDNTKNDNQKEMVSSQGNETTSNGNKLIEKESVQSTT
GNKVEVSTAKSDEQASPKSTNEDLNTKQTISNQEALQPDLQENKSVVNVQPTNEENKKVD
AKTESTTLNVKSDAIKSNDETLVDNNSNSNNENNADIILPKSTAPKRLNTRMRIAAVQPS
STEAKNVNDLITSNTTLTVVDADKNNKIVPAQDYLSLKSQITVDDKVKSGDYFTIKYSDT
VQVYGLNPEDIKNIGDIKDPNNGETIATAKHDTANNLITYTFTDYVDRFNSVQMGINYSI
YMDADTIPVSKNDVEFNVTIGNTTTKTTANIQYPDYVVNEKNSIGSAFTETVSHVGNKEN
PGYYKQTIYVNPSENSLTNAKLKVQAYHSSYPNNIGQINKDVTDIKIYQVPKGYTLNKGY
DVNTKELTDVTNQYLQKITYGDNNSAVIDFGNADSAYVVMVNTKFQYTNSESPTLVQMAT
LSSTGNKSVSTGNALGFTNNQSGGAGQEVYKIGNYVWEDTNKNGVQELGEKG
VGNVTVTVFDNNTNTKVGEAVTKEDGSYLIPNLPNGDYRVEFSNLPKGYEVTPSKQGNNEELDSNGLSSVITVN ←
GKDNLSADLGIYKPKYNLGDYVWEDTNKNGIQDQDEKG
ISGVTVTLKDENGNVLKTVTTDADGKYKFTDLDNGNYKVEFTTPEGYTPTTVTSGSDIEKDSNGLTTTGVIN ← Cna_B domains ~70 aa
GADNMTLDSGFYKTPKYNLGNYVWEDTNKDGKQDSTEKG
ISGVTVTLKNENGEVLQTTKTDKDGKYQFTGLENGTYKVEFETPSGYTPTQVGSGTDEGIDSNGTSTTGVIK ←
DKDNDTIDSGFYKPTYNLGDYVWEDTNKNGVQDKDEKG
ISGVTVTLKDENDKVLKTVTTDENGKYQFTDLNNGTYKVEFETPSGYTPTSVTSGNDTEKDSNGLTTTGVIK ←
DADNMTLDSGFYKTPKYSLGDYVWYDSNKDGKQDSTEKG
IKDVKVTLLNEKGEVIGTTKTDENGKYCFDNLDSGKYKVIFEKPAGLTQTVTNTTEDDKDADGGEVDVTIT ←
DHDDFTLDNGYFEEDT
SDSDSDSDSDSDSDS
DSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDS
DSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDSDS
DSDSDSDSDSDSDSDSDSDSDSDSDSDSDAGKHTPVKPMSTTKDHHNKAKALPETGSENN
GSNNATLFGGLFAALGSLLLFGRRKKQNK

FIG. 27A

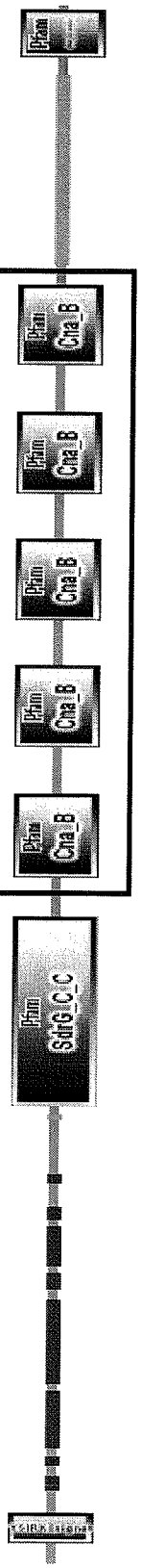


FIG. 27B

MKNKHHHHHHVGNVTVTVFDNNTNTKVGEAVTKEDGSYLIPNLPNGDYRVEFS
NLPKGYEVTPSKQGNNEELDSNGLSSVITVNGKDNLSADLGIYKPKYNLG
DYVWEDTNKNGIQDQDEKGISGVTVTLKDENGNVLKTVTTDADGKYKFTD
LDNGNYKVEFTTPEGYTPTTVTSGSDIEKDSNGLTTTGVINGADNMTLDS
GFYKTPKYNLGNYVWEDTNKDGKQDSTEKGISGVTVTLKNENGEVLQTTK
TDKDGKYQFTGLENGTYKVEFETPSGYTPTQVGSGTDEGIDSNGTSTTGV
IKDKDNDTIDSGFYKPTYNLGDYVWEDTNKNGVQDKDEKGISGVTVTLKD
ENDKVLKTVTTDENGKYQFTDLNNGTYKVEFETPSGYTPTSVTSGNDTEK
DSNGLTTTGVIKDADNMTLDSGFYKTPKYSLGDYVWYDSNKDGKQDSTEK
GIKDVKVTLLNEKGEVIGTTKTDENGKYCFDNLDSGKYKVIFEKPAGLTQ
TVTNTTEDDKDADGGEVDVTITDHDDFTLDNGYFEEDT

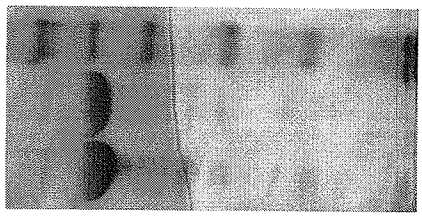
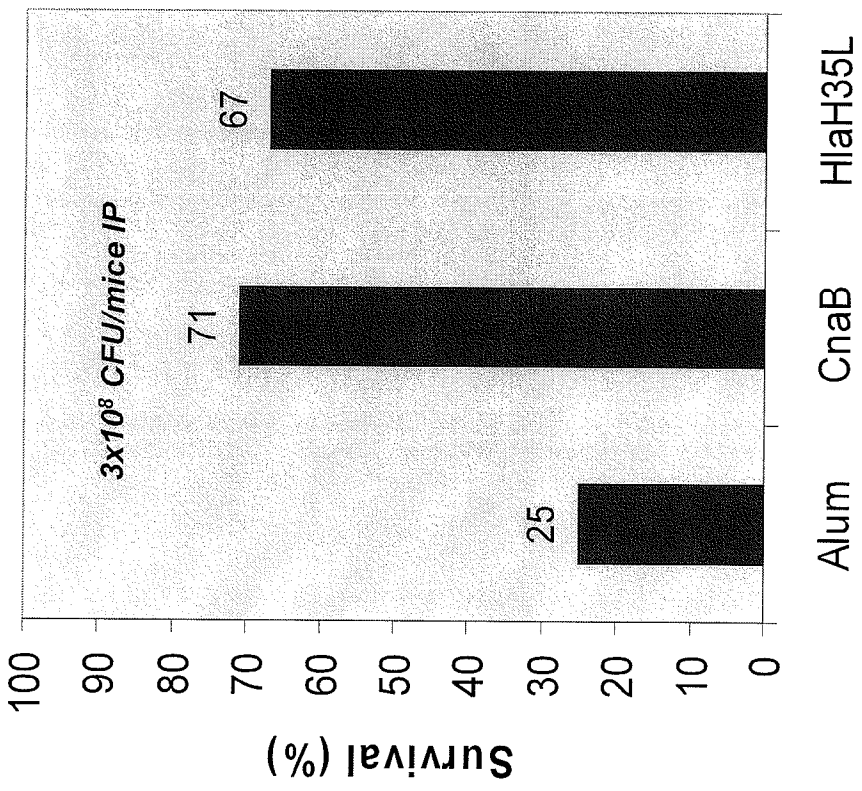


FIG. 27C

FIG. 28


Survival (%)
100
90
80
70
60
50
40
30
20
10
0
3x10^8 CFU/mice IP
25
71
67
Alum
CnaB
HlaH35L

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2010/050110

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/02 A61K39/085 C07K14/31 C07K14/315 A61K39/09
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/088822 A1 (UNIV COLUMBIA [US]; ARRECUBIETA CARLOS [US]; LEE MEI-HO [US]; LOWY FRA) 24 July 2008 (2008-07-24) sequences 3,4 page 11, line 30 - page 13, line 18 page 14, line 25 - page 15, line 6 page 24, line 1 - page 32, line 33 page 33, line 1 - page 34, line 2 table 1 page 46, lines 3-5 page 49, line 17 - page 54, line 19 ----- -/--	15,20, 22, 24-27, 32-34, 36,38

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 April 2010	17/05/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Irion, Andrea

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2010/050110

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DEIVANAYAGAM CHAMPION C S ET AL: "NOVEL FOLD AND ASSEMBLY OF THE REPETITIVE B REGION OF THE STAPHYLOCOCCUS AUREUS COLLAGEN-BINDING SURFACE PROTEIN" STRUCTURE, CURRENT BIOLOGY LTD., PHILADELPHIA, PA, US LNKD- DOI:10.1016/S0969-2126(00)00081-2, vol. 8, no. 1, 15 January 2000 (2000-01-15), pages 67-78, XP008073113 ISSN: 0969-2126 page 71, right-hand column, paragraph 3 - page 72, left-hand column page 74, left-hand column, paragraph 2 - right-hand column, paragraph 1	15,20, 22, 24-27, 32-34, 36,38
X	JOSEFSSON ELISABET ET AL: "Three new members of the serine-aspartate repeat protein multigene family of Staphylococcus aureus" MICROBIOLOGY (READING), vol. 144, no. 12, December 1998 (1998-12), pages 3387-3395, XP002578752 ISSN: 1350-0872 abstract page 3389, right-hand column, paragraph 4 - page 3390, left-hand column, paragraph 1 table 2 figure 3	15,20, 22, 24-27, 32-34, 36,38
X	JOSEFSSON ELISABET ET AL: "The binding of calcium to the B-repeat segment of SdrD, a cell surface protein of Staphylococcus aureus" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 47, 20 November 1998 (1998-11-20), pages 31145-31152, XP002578753 ISSN: 0021-9258 abstract page 31145, left-hand column, paragraph 1 page 31152, left-hand column	15,20, 22, 24-27, 32-34, 36,38

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2010/050110

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HARTFORD ORLA ET AL: "Matrix-binding proteins of Staphylococcus aureus: Functional analysis of mutant and hybrid molecules" MICROBIOLOGY (READING), vol. 145, no. 9, September 1999 (1999-09), pages 2497-2505, XP002578754 ISSN: 1350-0872 abstract figure 1g page 2502, left-hand column, paragraph 2 - right-hand column, paragraph 1 page 2503, left-hand column, paragraph 3	15,20, 22, 24-27, 32-34, 36,38
X	DEIVANAYAGAM CHAMPION C S ET AL: "Crystallization and preliminary X-ray analysis of B-domain fragments of a Staphylococcus aureus collagen-binding protein" ACTA CRYSTALLOGRAPHICA SECTION D: BIOLOGICAL CRYSTALLOGRAPHY, MUNKSGAARD PUBLISHERS LTD. COPENHAGEN, DK LNKD- DOI:10.1107/S0907444998010051, vol. 55, no. 2, 1 February 1999 (1999-02-01), pages 525-527, XP009132307 ISSN: 0907-4449 abstract page 526, middle column, paragraph 2	15,20, 22, 24-27, 32-34, 36,38
Y	SNODGRASS JAMES L ET AL: "Functional analysis of the Staphylococcus aureus collagen adhesin B domain" INFECTION AND IMMUNITY, vol. 67, no. 8, August 1999 (1999-08), pages 3952-3959, XP002578755 ISSN: 0019-9567 page 3958, left-hand column, paragraph 4 - right-hand column, paragraph 1	1-14, 16-19, 21,23, 28-31, 35,37
Y	WO 97/43314 A2 (TEXAS A & M UNIV SYS [US]; UAB RESEARCH FOUNDATION [US]; HOEOEK MAGNUS) 20 November 1997 (1997-11-20) the whole document	1-14, 16-19, 21,23, 28-31, 35,37
A	WO 01/70267 A1 (INHIBITEX INC [US]; TEXAS A & M UNIV SYS [US]; UNIV PAVIA [IT]) 27 September 2001 (2001-09-27) the whole document	1-38

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2010/050110

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MICHAEL OTTO: "Targeted immunotherapy for staphylococcal infections: Focus on anti-MSCRAMM antibodies" BIODRUGS: CLINICAL IMMUNOTHERAPEUTICS, BIOPHARMACEUTICALS AND GENE THERAPY, ADIS INTERNATIONAL, FR, vol. 22, no. 1, 1 January 2008 (2008-01-01), pages 27-36, XP009132068 ISSN: 1173-8804 the whole document	1-38
A	SMELTZER M S ET AL: "Molecular pathogenesis of staphylococcal osteomyelitis" POULTRY SCIENCE, CHAMPAIGN, IL, US, vol. 79, no. 7, 1 July 2000 (2000-07-01), pages 1042-1049, XP009132065 ISSN: 0032-5791 the whole document	1-38
A	ZHOU H ET AL: "An immunogenicity study of a newly fusion protein Cna-FnBP vaccinated against Staphylococcus aureus infections in a mice model" VACCINE, ELSEVIER LTD, GB LNKD-DOI:10.1016/J.VACCINE.2006.03.020, vol. 24, no. 22, 29 May 2006 (2006-05-29), pages 4830-4837, XP025151352 ISSN: 0264-410X [retrieved on 2006-05-29] the whole document	1-38

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2010/050110

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		DE 69734601 T2	03-08-2006
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