RESULTS

The primary sequence of antibody rFl contained one potential asparagine deamidation site in ~~light~~heavy chain CDR2: NNGNN (SEQ ID NO:24). Stress testing revealed an increase of deamidation in stressed samples at N53 (numbering according to Kabat, 1991). Site-directed mutagenesis was performed to stabilize the rF1 Mab by N (AAC, (SEQ ID NO:25)) to 53S (AGC, (SEQ ID NO:26)) substitution in heavy chain CDR2. Sequencing of the mutagenesis variant confirmed an N53S mutation.

Example 5

Development of Cys variants for antibody-drug conjugate (ADC) applications

The rFl pRK plasmids underwent a series of site-directed mutagenesis with oligos of rFlpRK.LC(205/210)VCF (468075) 5'-GGG CCT GAG CTC GCC CTG CAC AAA GAG CTT CAA CAG-3' (SEQ ID NO:27) and rFlpRK.LC(205/210)VCR (468076) 5'-CTG TTG AAG CTC TTT GTG CAG GGC GAG CTC AGG CCC-3' (SEQ ID NO:28) (Cys mutant is underlined) to generate the light chain linkers of rFl thioMab, and rFlpRK.HCN53S.Al2lCF (468464) 5'-CTG GTC ACA GTC TCG AGT TGC AGC ACC AAG GGC CCA TC-3' (SEQ ID NO:29) and rFlpRK.HCN53S.A12lCR (468465) 5'-GAT GGG CCC TTG GTG CTG CAA CTC GAG ACT GTG ACC AG-3' (SEQ ID NO:30) (Cys mutant is underlined) to make the heavy chain linkers of rFl thioMab via the Stratagene's Site-Directed method. Light chain V205C and heavy chain A114C were confirmed by sequencing of the variants (figure 9).

WHAT IS CLAIMED IS:

1. An isolated antibody or a functional part comprising:

a heavy chain variable domain comprising

(a) a heavy chain CDR1 sequence RFAMS (SEQ ID NO:1), and

(b) a heavy chain CDR2 sequence SINNGNNPYYARSVQY (SEQ ID NO:2) or SINSGNNPYYARSVQY (SEQ ID NO:60), and

(c) a heavy chain CDR3 sequence DHPSSGWPTFDS (SEQ ID NO:3); and

a light chain variable domain comprising

(d) a light chain CDR1 sequence RASENVGDWLA (SEQ ID NO:4), and

(e) a light chain CDR2 sequence KTSILES (SEQ ID NO:5), and

(f) a light chain CDR3 sequence QHYXRFPYT (SEQ ID NO:6), wherein X is I or M.

2. The antibody or functional part of claim 1, wherein the light chain CDR3 sequence is QHYIRFPYT.

3. The antibody or functional part of claim 1, wherein the light chain CDR3 sequence is QHYMRFPYT.

4. The antibody or functional part of claim 1, wherein the heavy chain variable domain comprises:

(a) framework 1 (FW1) which has the sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLS (SEQ ID NO: 38) or EVQLVESGGGLVQPGGSLRLSCAASGFTLS (SEQ ID NO: 61);

(b) framework 2 (FW2) which has the sequence of WVRQAPGRGLEWVA (SEQ ID NO: 40);

(c) framework 3 (FW3) which has the sequence of RFTVSRDVSQNTVSLQMNNLRAEDSATYFCAK (SEQ ID NO: 42); and

(d) framework 4 (FW4) which has the sequence of WGPGTLVTVSS (SEQ ID NO: 44).

5. The antibody or functional part of claim 1 or claim 4, wherein the light chain variable domain comprises:

(a) framework 1 (FW1) which has the sequence of DIQLTQSPSALPASVGDRVSITC (SEQ ID NO: 48);

(b) framework 2 (FW2) which has the sequence of WYRQKPGKAPNLLIY (SEQ ID NO: 50);

(c) framework 3 (FW3) which has the sequence of GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC (SEQ ID NO: 52); and

(d) framework 4 (FW4) which has the sequence of FGQGTKLEIKRTV (SEQ ID NO: 54) or the sequence of FGQGTKVEIKRTV (SEQ ID NO: 59).

6. The antibody or functional part of claim 1, wherein the heavy chain variable domain comprises a sequence which has at least 90% sequence identity to the sequence EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7).

7. The antibody or functional part of claim 6, wherein the heavy chain variable domain comprises a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7).

8. The antibody or functional part of claim 6, wherein the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINSGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:62).

9. The antibody or functional part of claim 1, wherein the light chain variable domain comprises a sequence which has at least 90% sequence identity to the sequence DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

10. The antibody or functional part of claim 9, wherein the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

11. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

12. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN

PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9)

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRTV, wherein X is I or M (SEQ ID NO:8).

13. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9)

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRA,wherein X is I or M (SEQ ID NO:10).

14. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

15. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises g a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRTV, wherein X is I or M (SEQ ID NO:8).

16. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRA, wherein X is I or M (SEQ ID NO:10).

17. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINSGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:62); and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is M (SEQ ID NO:11).

18. The antibody or functional part of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP (SEQ ID NO:63); and

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:64).

19. The antibody or functional part of claim 18, wherein the valine at light chain position 205 is replaced by a cysteine, wherein the amino acid position is as shown in Figure 9B.

20. The antibody or functional part of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP (SEQ ID NO:63) and;

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPCTKSFNRGEC (SEQ ID NO:65).

21. The antibody of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: CSTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP (SEQ ID NO:66) and;

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPCTKSFNRGEC (SEQ ID NO:65).

22. The antibody or functional part of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: CSTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP (SEQ ID NO:66) and;

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:64).

23. An isolated antibody or a functional part thereof comprising:

(a) a heavy chain comprising a sequence of SEQ ID NO: 55 and

(b) a light chain comprising a sequence of SEQ ID NO: 57.

24. An isolated antibody or a functional part thereof comprising:

(a) a heavy chain comprising a sequence of SEQ ID NO: 56 and

(b) a light chain comprising a sequence of SEQ ID NO: 58.

25. The antibody or functional part of claim 23, wherein an asparagine at position 53 in the heavy chain has been replaced by another amino acid, wherein the amino acid position is as shown in Figure 9A.

26. The antibody or functional part of claim 25, wherein said asparagine at position 53 is replaced with a serine, wherein an alanine at position 114 of the heavy chain is replaced with a cysteine, and wherein an arginine at position 222 of the heavy chain is replaced with a lysine, wherein the amino acid position is as shown in Figure 9A.

27. The antibody or functional part of claim 23, wherein a valine at a light chain position 205 is replaced with cysteine, an alanine at light chain position 110 is replaced with valine, and a leucine at light chain position 104 is replaced with a valine, wherein the amino acid position is as shown in Figure 9B.

28. The antibody or functional part of claim 1 comprising:

(a) the heavy chain variable domain comprising the sequence of SEQ ID NO:62 and a heavy chain constant domain comprising the sequence of SEQ ID NO:63; and

(b) the light chain comprising a sequence of SEQ ID NO:58.

29. The antibody or functional part of claim 1 comprising:

(a) the heavy chain comprising a sequence of SEQ ID NO: 56; and

(b) the light chain variable domain comprising the sequence of SEQ ID NO:11 and a light chain constant domain comprising the sequence of SEQ ID NO:64;

30. The antibody or functional part of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASIN NGNNPYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTF DSWGPGTLVTVSS (SEQ ID NO:9), wherein the asparagine at position 53 (numbering according to Kabat) is replaced by serine, and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

31. The antibody or the functional part of claim 30, wherein the antibody further comprises a heavy chain constant domain comprising a sequence of SEQ ID NO:66 or SEQ ID NO:63.

32. The antibody or the functional part of claim 30 or 31, wherein the antibody further comprises a light chain constant domain comprising a sequence of SEQ ID NO:65 or SEQ ID NO:64.

33. The antibody of any one of claims 1-32, wherein the antibody is coupled to a cytotoxic agent.

34. The antibody of claim 33, wherein the cytotoxic agent is an antibiotic.

35. The antibody of claim 33 or 34, wherein the cytotoxic agent is conjugated to a cysteine at light chain position 205, wherein the amino acid position is as shown in Figure 9B.

36. An isolated antibody or a functional part thereof capable of binding a serine-aspartate (SD) repeat-dependent epitope on a SD repeat (SDR) protein expressed by a *Staphylococcus* species, wherein the antibody or the functional part is coupled to a cytotoxic agent to form an antibody-drug conjugate.

37. The antibody or the functional part of claim 36, wherein the SDR protein is located on the cell surface of a *Staphylococcus* species.

38. The antibody or the functional part of claim 36, wherein the SDR protein is anchored to the peptidoglycan cell wall of a *Staphylococcus* species.

39. The antibody or the functional part of any one of claims 36-38, wherein the epitope further comprises a sugar or sugar residues.

40. The antibody or the functional part of any one of claims 36-39, wherein the cytotoxic agent is an antibiotic.

41. The antibody or the functional part of any one of claims 36-40, wherein the antibody or the functional part competes for binding to the SD repeat-dependent epitope with an antibody comprising:

(a) a heavy chain CDR1 sequence RFAMS (SEQ ID NO:1), and
(b) a heavy chain CDR2 sequence SINNGNNPYYARSVQY (SEQ ID NO:2) or SINSGNNPYYARSVQY (SEQ ID NO:60), and
(c) a heavy chain CDR3 sequence DHPSSGWPTFDS (SEQ ID NO:3), and
(d) a light chain CDR1 sequence RASENVGDWLA (SEQ ID NO:4), and
(e) a light chain CDR2 sequence KTSILES (SEQ ID NO:5), and
(f) a light chain CDR3 sequence QHYXRFPYT (SEQ ID NO:6), wherein X is I or M.

42. The antibody or the functional part of any one of claims 36-41, wherein the *Staphylococcus* species is *S. aureus*.

43. The antibody or the functional part of claim 42, wherein the SDR protein is selected from the group consisting of ClfA (SdrA), ClfB (SdrB), SdrC, SdrD and SdrE.

44. The antibody or the functional part of any one of claims 36-41, wherein the *Staphylococcus* species is *S. epidermidis*.

45. The antibody or the functional part of claim 44, wherein the SDR protein is selected from the group consisting of SdrF, SdrG and SdrH.

46. The antibody or the functional part of any one of claims 36-41, wherein the *Staphylococcus* species is *S. saprophyticus*.

47. The antibody or the functional part of claim 46, wherein the SDR protein is SdrI.

48. The antibody or the functional part of any one of claims 36-41, wherein the *Staphylococcus* species is *S. capitis*.

49. The antibody or the functional part of claim 48, wherein the SDR protein is SdrX.

50. The antibody or the functional part of any one of claims 36-41, wherein the *Staphylococcus* species is *S. caprae*.

51. The antibody or the functional part of claim 50, wherein the SDR protein is selected from the group consisting of SdrY and SdrZ.

52. The antibody or the functional part of any one of claims 36-41, wherein the antibody or the functional part binds to cell wall lysates from *S. aureus* and/or *S. epidermidis*.

53. The antibody or the functional part of any one of claims 1-52, wherein the antibody or the functional part binds to a gram positive bacterium.

54. The antibody or the functional part of claim 53, wherein the gram positive bacterium is a *Staphylococcus* species.

55. The antibody or the functional part of claim 54, wherein the *Staphylococcus* species is *S. aureus, S. epidermidis, S. caprae, S. saprophyticus, S. capitis,* or methicillin-resistant *S. aureus* (MRSA).

56. An isolated antibody or a functional part thereof which is capable of competing with the antibody according to any one of claims 1-35, for binding to a *Staphylococcus* species.

57. The antibody or functional part of any one of claims 1-56, wherein the functional part of an antibody is selected from the group consisting of a single domain antibody, a single chain antibody, a nanobody, an unibody, a single chain variable fragment (scFv), a Fab fragment and a $F(ab')_2$ fragment.

58. A composition comprising the antibody or functional part of any one of claims 1-57.

59. An isolated, synthetic or recombinant nucleic acid encoding for any one of the antibodies or the functional part thereof according to claims 1-57.

60. A producer cell comprising the isolated, synthetic or recombinant nucleic acid sequence or a functional equivalent thereof, according to claim 59.

61. A method for producing an antibody or a functional part thereof comprising providing a cell with a nucleic acid according to claim 59 and allowing said cell to translate said nucleic acid thereby producing said antibody.

62. The method according to claim 61, further comprising harvesting, purifying and/or isolating said antibody or functional part thereof.

63. An antibody or a functional part thereof according to any one of claims 1-57 or a nucleic acid according to claim 59, for use as a medicament and/or prophylactic agent.

64. An antibody or a functional part thereof according to any one of claims 1-57 or a nucleic acid according to claim 59, for use as a medicament and/or prophylactic agent for treating and/or preventing a Gram-positive bacterium-related disorder.

65. Use of an antibody or functional part thereof according to any one of claims 1-57 or a nucleic acid according to claim 59, for the preparation of a medicament and/or prophylactic agent for treating and/or preventing a Gram-positive bacterium-related disorder.

66. Use of an antibody or functional part thereof according to any one of claims 1-57 or a nucleic acid according to claim 59 for in vitro diagnosis of a *Staphylococcus* infection.

67. The use of claim 66, wherein the *Staphylococcus* infection is a *S. aureus* infection.

68. The use of claim 67, wherein the *S. aureus* infection is a MRSA infection.

69. Use of an antibody or functional part thereof according to any one of claims 1-57 or a nucleic acid according to claim 59 for detecting *S. aureus* and/or *S. epidermidis* in a sample obtained from an individual or from any other source suspected to be infected with a *Staphylococcus* bacteria.

70. An antibody or functional part thereof according to any one of claims 1-57, for use in the diagnosis of a *Staphylococcus* infection.

71. A method for isolating *S. aureus* and/or *S. epidermidis* bacteria from a solution using an antibody or functional part thereof according to any one of claims 1-57.

WHAT IS CLAIMED IS:

1. An isolated antibody or a functional part thereof that binds to a *Staphylococcus* species, wherein the antibody or functional part thereof comprises:

a heavy chain variable domain comprising

(a) a heavy chain CDR1 sequence RFAMS (SEQ ID NO:1), and

(b) a heavy chain CDR2 sequence SINNGNNPYYARSVQY (SEQ ID NO:2) or SINSGNNPYYARSVQY (SEQ ID NO:60), and

(c) a heavy chain CDR3 sequence DHPSSGWPTFDS (SEQ ID NO:3); and

a light chain variable domain comprising

(d) a light chain CDR1 sequence RASENVGDWLA (SEQ ID NO:4), and

(e) a light chain CDR2 sequence KTSILES (SEQ ID NO:5), and

(f) a light chain CDR3 sequence QHYXRFPYT (SEQ ID NO:6), wherein X is I or M.

2. The antibody or functional part thereof of claim 1, wherein the light chain CDR3 sequence is QHYIRFPYT.

3. The antibody or functional part thereof of claim 1, wherein the light chain CDR3 sequence is QHYMRFPYT.

4. The antibody or functional part thereof of claim 1, wherein the heavy chain variable domain comprises:

(a) framework 1 (FW1) which has the sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLS (SEQ ID NO: 38) or EVQLVESGGGLVQPGGSLRLSCAASGFTLS (SEQ ID NO: 61);

(b) framework 2 (FW2) which has the sequence of WVRQAPGRGLEWVA (SEQ ID NO: 40);

(c) framework 3 (FW3) which has the sequence of RFTVSRDVSQNTVSLQMNNLRAEDSATYFCAK (SEQ ID NO: 42); and

(d) framework 4 (FW4) which has the sequence of WGPGTLVTVSS (SEQ ID NO: 44).

5. The antibody or functional part thereof of claim 1 or claim 4, wherein the light chain variable domain comprises:

(a) framework 1 (FW1) which has the sequence of DIQLTQSPSALPASVGDRVSITC (SEQ ID NO: 48);

(b) framework 2 (FW2) which has the sequence of WYRQKPGKAPNLLIY (SEQ ID NO: 50);

(c) framework 3 (FW3) which has the sequence of GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC (SEQ ID NO: 52); and

(d) framework 4 (FW4) which has the sequence of FGQGTKLEIKRTV (SEQ ID NO: 54) or the sequence of FGQGTKVEIKRTV (SEQ ID NO: 59).

6. The antibody or functional part thereof of claim 1, wherein the heavy chain variable domain comprises a sequence which has at least 90% sequence identity to the sequence EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7).

7. The antibody or functional part thereof of claim 6, wherein the heavy chain variable domain comprises a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7).

8. The antibody or functional part thereof of claim 6, wherein the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINSGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:62).

9. The antibody or functional part thereof of claim 1, wherein the light chain variable domain comprises a sequence which has at least 90% sequence identity to the sequence DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

10. The antibody or functional part thereof of claim 9, wherein the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

11. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

12. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN

PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9)

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRTV, wherein X is I or M (SEQ ID NO:8).

13. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9)

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRA,wherein X is I or M (SEQ ID NO:10).

14. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

15. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises g a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRTV, wherein X is I or M (SEQ ID NO:8).

16. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLLESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:7) and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKLEIKRA, wherein X is I or M (SEQ ID NO:10).

17. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINSGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:62); and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is M (SEQ ID NO:11).

18. The antibody or functional part thereof of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP (SEQ ID NO:63); and

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:64).

19. The antibody or functional part thereof of claim 18, wherein the valine at light chain position 205 is replaced by a cysteine, wherein the amino acid position is as shown in Figure 9B.

20. The antibody or functional part thereof of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCP (SEQ ID NO:63) and;

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPCTKSFNRGEC (SEQ ID NO:65).

21. The antibody or functional part thereof of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: CSTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP (SEQ ID NO:66) and;

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPCTKSFNRGEC (SEQ ID NO:65).

22. The antibody or functional part thereof of claim 17, further comprising

(a) a heavy chain constant domain comprising the sequence of: CSTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP (SEQ ID NO:66) and;

(b) a light chain constant domain comprising the sequence of: AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:64).

23. An isolated antibody that binds to a *Staphylococcus* species, wherein the antibody comprises:

(a) a heavy chain comprising a sequence of SEQ ID NO: 55 and

(b) a light chain comprising a sequence of SEQ ID NO: 57.

24. An isolated antibody that binds to a *Staphylococcus* species, wherein the antibody comprises:

(a) a heavy chain comprising a sequence of SEQ ID NO: 56 and

(b) a light chain comprising a sequence of SEQ ID NO: 58.

25. An isolated antibody that binds to a *Staphylococcus* species comprising a heavy chain comprising a sequence of SEQ ID NO:55, wherein the asparagine at position 53 in the heavy chain variable domain has been replaced by another amino acid, wherein the amino acid numbering is according to Kabat numbering, and a light chain comprising a sequence of SEQ ID NO:57.

26. An isolated antibody that binds to a *Staphylococcus* species comprising a heavy chain comprising a sequence of SEQ ID NO:55, wherein the asparagine at position 53 is replaced with a serine, wherein the alanine at position 114 of the heavy chain is replaced with a cysteine, and wherein the arginine at position 222 of the heavy chain is replaced with a lysine, wherein the amino acid numbering is according to Kabat numbering, and a light chain comprising a sequence of SEQ ID NO:57.

27. An antibody that binds to a *Staphylococcus* species comprising a light chain comprising a sequence of SEQ ID NO:57, wherein the valine at the light chain variable domain position 205 is replaced with cysteine, the alanine at the light chain variable domain position 110 is replaced with valine, and the leucine at the light chain variable domain position 104 is replaced with a valine, wherein the amino acid numbering is according to Kabat numbering, and a heavy chain comprising a sequence of SEQ ID NO:55.

28. The antibody or functional part thereof of claim 1 comprising:

(a) the heavy chain variable domain comprising the sequence of SEQ ID NO:62 and a heavy chain constant domain comprising the sequence of SEQ ID NO:63; and

(b) the light chain comprising a sequence of SEQ ID NO:58.

29. The antibody or functional part thereof of claim 1 comprising:

(a) the heavy chain comprising a sequence of SEQ ID NO: 56; and

(b) the light chain variable domain comprising the sequence of SEQ ID NO:11 and a light chain constant domain comprising the sequence of SEQ ID NO:64;

30. The antibody or functional part thereof of claim 1, wherein

(a) the heavy chain variable domain comprises a sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTLSRFAMSWVRQAPGRGLEWVASINNGNN PYYARSVQYRFTVSRDVSQNTVSLQMNNLRAEDSATYFCAKDHPSSGWPTFDSWGP GTLVTVSS (SEQ ID NO:9), wherein the asparagine at position 53 (numbering according to Kabat) is replaced by serine, and

(b) the light chain variable domain comprises a sequence of DIQLTQSPSALPASVGDRVSITCRASENVGDWLAWYRQKPGKAPNLLIYKTSILESGV PSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYXRFPYTFGQGTKVEIKRTV, wherein X is I or M (SEQ ID NO:11).

31. The antibody or the functional part thereof of claim 30, wherein the antibody further comprises a heavy chain constant domain comprising a sequence of SEQ ID NO:66 or SEQ ID NO:63.

32. The antibody or the functional part thereof of claim 30 or 31, wherein the antibody further comprises a light chain constant domain comprising a sequence of SEQ ID NO:65 or SEQ ID NO:64.

33. The antibody or functional part thereof of any one of claims 1-32, wherein the antibody or functional part thereof is coupled to a cytotoxic agent.

34. The antibody or functional part thereof of claim 33, wherein the cytotoxic agent is an antibiotic.

35. The antibody or functional part thereof of claim 33 or 34, wherein the cytotoxic agent is conjugated to a cysteine at light chain position 205, wherein the amino acid numbering is according to Kabat numbering.

36. The antibody or the functional part thereof of any one of claims 1-35, wherein the antibody or the functional part binds to a gram positive bacterium.

37. The antibody or the functional part thereof of claim 36, wherein the gram positive bacterium is a *Staphylococcus* species.

38. The antibody or the functional part thereof of claim 37, wherein the *Staphylococcus* species is *S. aureus, S. epidermidis, S. caprae, S. saprophyticus, S. capitis,* or methicillin-resistant *S. aureus* (MRSA).

39. The antibody or functional part thereof of any one of claims 1-38, wherein the functional part of an antibody is selected from the group consisting of a single domain antibody, a single chain antibody, a nanobody, an unibody, a single chain variable fragment (scFv), a Fab fragment and a $F(ab')_2$ fragment.

40. A composition comprising the antibody or functional part thereof of any one of claims 1-39.

41. An isolated, synthetic or recombinant nucleic acid encoding for any one of the antibodies or the functional part thereof according to claims 1-39.

42. A producer cell comprising the isolated, synthetic or recombinant nucleic acid sequence or a functional equivalent thereof, according to claim 41.

43. A method for producing an antibody or a functional part thereof comprising providing a cell with a nucleic acid according to claim 41 and allowing said cell to translate said nucleic acid thereby producing said antibody or functional part thereof.

44. The method according to claim 43, further comprising harvesting, purifying and/or isolating said antibody or functional part thereof.

45. An antibody or a functional part thereof according to any one of claims 1-39 or a nucleic acid according to claim 41, for use as a medicament and/or prophylactic agent.

46. An antibody or a functional part thereof according to any one of claims 1-39 or a nucleic acid according to claim 41, for use as a medicament and/or prophylactic agent for treating and/or preventing a Gram-positive bacterium-related disorder.

47. Use of an antibody or functional part thereof according to any one of claims 1-39 or a nucleic acid according to claim 41, for the preparation of a medicament and/or prophylactic agent for treating and/or preventing a Gram-positive bacterium-related disorder.

48. Use of an antibody or functional part thereof according to any one of claims 1-39 or a nucleic acid according to claim 41 for diagnosis of a *Staphylococcus* infection.

49. The use of claim 48, wherein the *Staphylococcus* infection is a *S. aureus* infection.

50. The use of claim 49, wherein the *S. aureus* infection is a MRSA infection.

51. Use of an antibody or functional part thereof according to any one of claims 1-39 or a nucleic acid according to claim 41 for detecting *S. aureus* and/or *S. epidermidis* in a sample obtained from an individual or from any other source suspected to be infected with a *Staphylococcus* bacteria.

52. An antibody or functional part thereof according to any one of claims 1-39, for use in the diagnosis of a *Staphylococcus* infection.

53. A method for isolating *S. aureus* and/or *S. epidermidis* bacteria from a solution using an antibody or functional part thereof according to any one of claims 1-39.

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Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50   55   60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65   70   75   80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys