

CLAIMS

1. **A detoxified Staphylococcal Exotoxin B (SEB) toxin** that is mutated to comprise at least two point mutations at amino acid positions 21 to 25 in the SEB toxin sequence SEQ ID NO:1, wherein said at least two point mutations comprise a deletion of any of aa21-22, aa22-23, aa23-24, aa24-25, aa21-23, aa22-24, or aa23-25, or at corresponding amino acid positions in any other naturally-occurring SEB toxin sequence that has at least 95% sequence identity to SEQ ID NO:1.

2. The detoxified SEB toxin of claim 1, comprising or consisting of SEQ ID NO:3 which differs from SEQ ID NO:1 in the deletion of aa22-24, or a detoxified SEB variant sequence thereof comprising said deletion of aa22-24, and at least 95% sequence identity to SEQ ID NO:3.

3. The detoxified SEB toxin of claim 1 or 2, comprising one or more further point mutations comprising at least one amino acid substitution at a position selected from the group consisting L45, Q43, or F44, preferably L45R, Q43P, F44P, or F44S, preferably wherein the detoxified SEB toxin comprises or consists of any one of SEQ ID NO:5, 7, 9, or 11, or a detoxified SEB variant sequence of any one of the foregoing comprising said at least two point mutations at amino acid positions 21 to 25 and at least 95% sequence identity to of any one of the foregoing.

4. **A protective vaccine antigen** comprising at least one molecule of the detoxified SEB toxin of any one of claims 1 to 3, preferably in combination with a Staphylococcal vaccine antigen that is identical to or different from said detoxified SEB toxin molecule, optionally wherein the combination is provided as a fusion, mixture, or a complex comprising said molecule and antigen bound to each other and/or bound to a carrier, thereby forming the complex.

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5. The vaccine antigen of claim 4, wherein said at least one detoxified SEB toxin molecule is fused to a another detoxified SEB toxin molecule, optionally comprising a linker sequence, preferably comprising or consisting of any one of SEQ ID NO:13, 31, 33, or 35, or a vaccine antigen variant sequence of any one of the foregoing comprising
5 said point mutations at amino acid positions 21 to 25 and at least 95% sequence identity to of any one of the foregoing.

6. **A protective vaccine preparation** comprising the antigen of claim 4 or 5, and a pharmaceutically acceptable carrier, preferably comprising an adjuvant.
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7. The vaccine preparation of claim 6, wherein the adjuvant is selected from the group consisting of an insoluble metal salt, a glucopyranosyl Lipid A adjuvant, adjuvant systems which are stimulants of innate immunity, such as AS01, AS03, or AS04, MF59, a TCR stimulant such as a toll-like receptor agonist or CpG oligonucleotides, preferably
15 alum, aluminum hydroxide, or aluminum phosphate.

8. The vaccine preparation of any one of claims 6 or 7, which is provided in a formulation for intramuscular, subcutaneous, intranasal, mucosal, oral, microneedle skin, transdermal, sublingual, aerosolic or inhaled administration.
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9. The vaccine preparation of any one of claims 6 to 8, which is a multivalent vaccine comprising said vaccine antigen in a combination with one or more Staphylococcal superantigen toxoid antigens, preferably selected from the group consisting of TSST-1, alpha-hemolysin, gamma-hemolysin, beta-hemolysin, and
25 staphylococcal exotoxins or enterotoxins, such as enterotoxin A (SEA), C (SEC), I (SEI), and K (SEK).

10. The vaccine preparation of any one of claims 6 to 9, for use in the prevention or treatment of a Staphylococcal superantigen-expressing bacterial infection, and/or a disease condition directly or indirectly mediated by exposure to Staphylococcal superantigen toxins.

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11. The vaccine preparation for use according to claim 10, wherein a patient is immunized with the vaccine preparation, who is at risk of staphylococcal complications following a surgical intervention or invasive treatment of disease, preferably wherein the disease condition is a sepsis condition induced by microbial mediators of Gram-positive bacterial, viral or fungal pathogens or toxins, preferably wherein the sepsis condition is sepsis, toxic shock syndrome (TSS) or septic shock.

12. Use of the detoxified SEB toxin of any one of claims 1 to 3, or the vaccine antigen of claim 4 or 5, in a method of

- 15 a) producing a vaccine preparation, or
 b) producing antibodies specifically recognizing the SEB toxin.

13. A method of producing the detoxified SEB toxin of any one of claims 1 to 3, or the vaccine antigen of claim 4 or 5, by expressing a nucleic acid sequence encoding the respective toxin or antigen in a recombinant host cell, and isolating and optionally purifying the respective toxin or antigen.

14. A nucleic acid molecule encoding the detoxified SEB toxin of any one of claims 1 to 3, or the vaccine antigen of claim 4 or 5, preferably comprising or consisting of any one of SEQ ID NO:2, 4, 6, 8, 10, 12, 14, 32, 34, or 36, or codon-optimized variants of any of the foregoing.

15. A recombinant host cell comprising the nucleic acid molecule of claim 14 in an expression construct.

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