SUMMARY

In one aspect of the present disclosure, there is provided the use of an effective amount of an agent that increases the intracellular pH of a host cell and/or of an intracellular compartment of a host cell and an effective amount of a bactericidal agent in the manufacture of a medicament for the treatment of a bacterial infection in a subject in need thereof.

In another aspect, there provided a chimeric bactericidal polypeptide comprising a functional enzymatic domain from a cell wall lytic enzyme selected from the group consisting of SEQ ID NO: 1 - 7, or a variant thereof and a protein transduction domain selected from the group consisting of SEQ ID NO: 12 - 25, or a variant thereof and optionally comprising a cell wall binding domain is selected from the group consisting of SEQ ID NO: 8 - 11, or a variant thereof and/or an antimicrobial peptide selected from the group consisting of SEQ ID NO: 70 - 90, or a variant thereof.

In another aspect, there is provided a polynucleotide encoding the chimeric bactericidal polypeptide as disclosed above.

CLAIMS

1. Use of an effective amount of an agent that increases the intracellular pH of a host cell and/or of an intracellular compartment of a host cell and an effective amount of a bactericidal agent in the manufacture of a medicament for the treatment of a bacterial infection in a subject in need thereof.

2. The use according to claim 1, wherein the bacterial infection is an intracellular and/or persistent bacterial infection and/or is a *Staphylococcus* infection, preferably an *S. aureus* infection.

3. The use according to claim 1 or 2, wherein the host cell is a eukaryotic host cell within the subject in need of treatment and/or wherein the intracellular compartment is a phagolysosome.

4. The use according to any of the preceding claims, wherein the agent that increases the intracellular pH and/or the pH of the intracellular compartment is an alkalizing agent, preferably a lysosomotropic alkalizing agent, preferably selected from the group of chloroquine, bafilomycin A1, ammonium chloride.

5. The use according to any of the preceding claims, wherein the bactericidal agent is a bactericidal agent capable of entering the host cell and/or the intracellular compartment of the host cell.

6. The use according to any of the preceding claims, wherein the bactericidal agent is selected from the group consisting of a bacteriocin or a functional part thereof, a bacterial autolysin or a functional part thereof, a bacteriophage lysin or a functional part thereof, an antimicrobial peptide and an antibiotic.

7. The use according to any of the preceding claims wherein the antibiotic is selected from the group consisting of beta-lactam antibiotics such as penicillin derivatives, cephalosporins, monobactams, carbapenems, vancomycins, daptomycin,

fluoroquinolones, metronidazole, nitrofurantoin, co-trimoxazole, telithromycin, aminoglycosidic antibiotics, more preferably flucloxacillin.

8. The use according to claim 1 to 7, wherein the bactericidal agent comprises a functional enzymatic domain from a cell wall lytic enzyme and preferably further comprises a protein transduction domain.

9. The use according to claim 8, wherein the bactericidal agent further comprises an antimicrobial peptide.

10. The use according to claim 8 or 9, wherein the bactericidal agent further comprises a cell wall binding domain.

11. The use according to claim 8 - 10, wherein the protein transduction domain is selected from the group consisting of SEQ ID NO: 12 - 25, or a variant thereof.

12. The use according to claim 8 - 11, wherein the functional enzymatic domain from a cell wall lytic enzyme is selected from the group consisting of SEQ ID NO: 1 - 7, or a variant thereof.

13. The use according to claim 8 - 12, wherein the cell wall binding domain is selected from the group consisting of SEQ ID NO: 8 - 11, or a variant thereof.

14. The use according to claim 8 - 13, wherein the antimicrobial peptide is selected from the group consisting of SEQ ID NO: 70 - 90, or a variant thereof.

15. A chimeric bactericidal polypeptide comprising a functional enzymatic domain from a cell wall lytic enzyme selected from the group consisting of SEQ ID NO: 1 - 7, or a variant thereof and a protein transduction domain selected from the group consisting of SEQ ID NO: 12 - 25, or a variant thereof and optionally comprising a cell wall binding domain is selected from the group consisting of SEQ ID NO: 8 - 11, or a variant thereof and/or an antimicrobial peptide selected from the group consisting of SEQ ID NO: 70 - 90, or a variant thereof.