effects in *in vitro* and animal studies, clinical data have been conflicting. In addition, adverse effects have been reported such as nephrotoxicity and ototoxicity, potentially leading to drug interactions and further toxicities in patients receiving multiple medications. Besides, use of combinatorial anti-microbial therapies to treat multidrug resistant (MDR) strains leads to increased anti-microbial resistance (AMR) in pathogens and additional cost burden to the patients. Alternative methods such as skin grafting are considered as gold standards in chronic wound management. However, skin grafting is limited by the quality and quantity of donor skin, which does not solve the problem of bacterial clearance either. Similarly, other new procedures such as delivery of angiogenesis-inducing growth factors and cytokines and hyperbaric oxygen therapy do not tackle with the fundamental issue of infections.

[0005] Therefore, what is needed is novel anti-microbial agent effective in treating chronic infections, and method of treating chronic infections using the anti-microbial agent. Furthermore, other desirable features and characteristics will become apparent from the subsequent detailed description and the appended claims, taken in conjunction with the accompanying drawings and this background of the disclosure.

SUMMARY

[0005a] In one aspect, the present disclosure relates to an anti-bacterial peptide consisting of the sequence of HHKAEKSSVLKSKEESH (SEQ ID NO: 4).

[0005b] In another aspect, the present disclosure relates to an anti-bacterial peptide consisting of the sequence of KQRNKVKKIYLDEKR (SEQ ID NO: 5).

[0005c] In another aspect, the present disclosure relates to an anti-bacterial peptide comprising a partial sequence of SPARCL1, wherein the peptide comprises at least a sequence of HHKAEKSSVLKSKEESH (SEQ ID NO: 4).

[0005d] In another aspect, the present disclosure relates to an anti-bacterial peptide comprising a partial sequence of SPARCL1, wherein the peptide comprises at least a sequence of KQRNKVKKIYLDEKR (SEQ ID NO: 5).

[0005e] In another aspect, the present disclosure relates to a conditioned cell culture media (CM) comprising anti-bacterial peptides as disclosed herein, or a full length SPARCL1 peptide.

[0005f] In another aspect, the present disclosure relates to a composition comprising one or more of the anti-bacterial peptides as disclosed herein, or a full length SPARCL1 peptide.

[0005g] In another aspect, the present disclosure relates to a pharmaceutical composition comprising the peptide, the conditioned cell culture media or the composition as disclosed herein.

[0005h] In another aspect, the present disclosure relates to a wound dressing comprising the peptide, the conditioned cell culture media (CM), the composition, or the pharmaceutical composition as disclosed herein.

[0005i] In another aspect, the present disclosure relates to use of the peptide, the conditioned cell culture media (CM), the composition, or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for (a) treating an infection, (b) promoting wound healing and tissue regeneration or (c) reducing/preventing formation of biofilm in a subject.

[0005j] In another aspect, the present disclosure relates to a nucleic acid composition encoding the peptide as disclosed herein. In yet another aspect, the present disclosure relates to an expression vector comprising the nucleic acid composition as disclosed herein. In another aspect, the present disclosure relates to a host cell comprising one or more of the nucleic compositions as disclosed herein or one or more of the expression vectors as disclosed herein.

[0006] In one example, the present disclosure provides an anti-bacterial peptide consisting of the sequence of KVNQIGSVTESIQACKLAQSN (SEQ ID NO: 3).

[0007] In one example, the present disclosure provides an anti-bacterial peptide consisting of the sequence of HHKAEKSSVLKSKEESH (SEQ ID NO: 4).

[0008] In one example, the present disclosure provides an anti-bacterial peptide consisting of the sequence of KQRNKVKKIYLDEKR (SEQ ID NO: 5).

[0009] In one example, the present disclosure provides an anti-bacterial peptide comprising a partial sequence of ENO3, wherein the peptide comprises at least the sequence of KVNQIGSVTESIQACKLAQSN (SEQ ID NO: 3).

[00010] In one example, the present disclosure provides an anti-bacterial peptide comprising a partial sequence of SPARCL1, wherein the peptide comprises at least a sequence of HHKAEKSSVLKSKEESH (SEQ ID NO: 4).

[00011] In one example, the present disclosure provides an anti-bacterial peptide comprising a partial sequence of SPARCL1, wherein the peptide comprises at least a sequence of KQRNKVKKIYLDEKR (SEQ ID NO: 5).

[00012] In one example, the present disclosure provides a conditioned cell culture media (CM) comprising anti-bacterial peptides of claims 1-8, a full length ENO3 peptide, or a full length SPARCL1 peptide.

[00013] In one example, the present disclosure provides a composition comprising one or more of the anti-bacterial peptides as disclosed herein, a full length ENO3 peptide, or a full length SPARCL1 peptide.

[00014] In one example, the present disclosure provides a pharmaceutical composition comprising the peptide as disclosed herein, the conditioned cell culture media as disclosed herein, or the composition as disclosed herein.

[00015] In one example, the present disclosure provides a wound dressing comprising the peptide as disclosed herein, the conditioned cell culture media (CM) as disclosed herein, the composition as disclosed herein, or the pharmaceutical composition as disclosed herein.

[00016] In one example, the present disclosure provides an in vitro method of inducing anti-bacterial responses in tissue-derived stem cells, wherein the method comprises: (a) obtaining a tissue sample from a subject; (b) isolating tissue-derived stem cells from the tissue sample of (a) in a cell culture; (c) culturing the tissue-derived stem cells in differentiation media to obtain intermediately differentiating cells; and (d) incubating the intermediately differentiating cells with a bacteria culture or a bacterial surface antigen to induce an anti-bacterial response of the intermediately differentiating cells.

[00017] In one example, the present disclosure provides an in vitro method of inducing anti-bacterial responses in adipose-derived mesenchymal stem cells (ASCs), comprising: (a) obtaining an adipose tissue sample from a subject; (b) isolating adipose-derived mesenchymal stem cells (ASCs) from the adipose tissue sample of (a) in a cell culture; (c) culturing the adipose-derived mesenchymal stem cells (ASCs) in adipogenic differentiation media to obtain intermediately differentiating ASCs; and (d) incubating the intermediately differentiating ASCs with a bacteria culture or a bacterial surface antigen to induce an anti-bacterial response by the intermediately differentiating ASCs.

[00018] In one example, the present disclosure provides an in vitro method of producing the conditioned cell culture media (CM) as disclosed herein, comprising: (a) obtaining a tissue sample from a subject; (b) isolating tissue-derived stem cells from the tissue sample of (a); (c) culturing the tissue-derived stem cells in a differentiation media to obtain intermediately differentiating stem cells; (d) incubating the intermediately differentiating cells in a cell culture media with a bacteria culture or a bacterial surface antigen; and (e) collecting the conditioned cell culture media (CM) by removing the bacteria and the intermediately differentiating cells.

[00019] In one example, the present disclosure provides a method of making the conditioned cell culture media (CM) as disclosed herein, comprising: (a) obtaining an adipose tissue sample from a subject; (b) isolating adipose-derived mesenchymal stem cells (ASCs) from the adipose tissue of (a) in a cell culture; (c) culturing the adipose-derived mesenchymal stem cells (ASCs) in adipogenic differentiation media to obtain intermediately differentiating ASCs; (d) incubating the intermediately differentiating ASCs in a cell culture media with a bacteria culture or a bacterial surface antigen; and (e) collecting the conditioned cell culture media (CM) by removing the bacteria and the intermediately differentiating ASCs.

[00020] In one example, the present disclosure provides a method of treating an infection in a subject, or a method of promoting wound healing and tissue regeneration in a subject, or a method of reducing/preventing formation of biofilm in a subject, comprises administering to the subject a pharmaceutically effective amount of the peptide as disclosed herein, the conditioned cell culture media (CM) as disclosed herein, the composition as disclosed herein, or the pharmaceutical composition as disclosed herein.

[00021] In one example, the present disclosure provides a nucleic acid composition encoding the peptide as disclosed herein.

[00022] In one example, the present disclosure provides an expression vector comprising the nucleic acid composition as disclosed herein.

[00023] In one example, the present disclosure provides a host cell comprising one or more of the nucleic acid compositions as disclosed herein, or one or more of the expression vectors as disclosed herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[00024] **Figure 1A** provides a summary of the optimization of the conditioned media culturing conditions for triggering anti-bacterial response, in particular antibacterial response in adipose-derived mesenchymal stem cells (ASCs) based on the parameters of: (i) priming of adipose-derived mesenchymal stem cells (ASCs) with either heat-inactivated bacteria or live bacteria at the multiplicity of infection (MOI) ratios of 1:2, 1:20, 1: 200, or 1: 2000 (Bacteria: ASC) as indicated in Figure 1A; (ii) priming period of 3, 6, 12 or 24 hours; (iii) stages of adipose-derived mesenchymal stem cells (ASCs) undergoing adipogenic differentiation as indicated based on the number of dates after differentiation (0 day, 6 days, or 12 days); (iv) culturing conditions in presence of either high or low glucose and in the presence or absence of 10% FBS. Conditions showing >50% bacterial killing compared to media control are circled. As shown in the summary, an exemplary condition for inducing anti-bacterial response in mesenchymal stem cells comprises using live bacterial of a multiplicity of infection (MOI) ratio of 1: 200 (bacteria: ASC, for example), under either high or low glucose levels, or in the presence or absence of FBS. The condition further comprises co-culturing the bacterial and the mesenchymal stem cells are co-cultured for about 24 hours, wherein the mesenchymal stem cells are intermediately differentiating stem cells.

[00025] **Figure 1B** summaries the various combinations of the conditions tested in Figure 1A.

[00026] **Figure 1C** shows the viability of exemplary bacterium *Salmonella typhimurium* (ST) treated with the conditioned media obtained from culturing adipose derived mesenchymal stem cell line from healthy donors (ATCC SCRC 4000) under the conditions summarized in Figure 1A. The percentage of Colony Forming Units (CFU) counts of the treated bacteria are shown for each conditions stratified based on the stem cell differentiation stages, and the strain of priming bacteria used. As demonstrated in Figure 1C, intermediately differentiating stem cells (D6: 6 days) primed with *S. typhimurium* (ST)

CLAIMS

What is claimed is:

1. An anti-bacterial peptide consisting of the sequence of HHKAEKSSVLKSKEESH (SEQ ID NO: 4).

2. An anti-bacterial peptide consisting of the sequence of KQRNKVKKIYLDEKR (SEQ ID NO: 5).

3. An anti-bacterial peptide comprising a partial sequence of SPARCL1, wherein the peptide comprises at least a sequence of HHKAEKSSVLKSKEESH (SEQ ID NO: 4).

4. An anti-bacterial peptide comprising a partial sequence of SPARCL1, wherein the peptide comprises at least a sequence of KQRNKVKKIYLDEKR (SEQ ID NO: 5).

5. The peptide of claims 3 or 4, wherein the SPARCL1 has an amino acid sequence of SEQ ID NO: 2.

6. A conditioned cell culture media (CM) comprising anti-bacterial peptides of claims 1-5, or a full length SPARCL1 peptide.

7. A composition comprising one or more of the anti-bacterial peptides of any one of the claims 1-5, or a full length SPARCL1 peptide.

8. The composition of claim 7, further comprising an antibiotic agent; optionally
wherein the antibiotic agent is selected from the group consisting of gentamycin, colistin, piperacillin, kanamycin, nalidixic acid, ampicillin, vancomycin and linezolid and ciprofloxacin.

9. A pharmaceutical composition comprising the peptide of any one of the claims 1-5, the conditioned cell culture media of claim 6, or the composition of claim 7 or 8.

10. A wound dressing comprising the peptide of any one of the claims 1-5, the conditioned cell culture media (CM) of claim 6, the composition of claim 7 or 8, or the pharmaceutical composition of claim 9.

11. Use of the peptide of any one of claims 1-5, the conditioned cell culture media (CM) of claim 6, the composition of claim 7 or 8, or the pharmaceutical composition of claim 9 in the manufacture of a medicament for (a) treating an infection, (b) promoting wound healing and tissue regeneration or (c) reducing/preventing formation of biofilm in a subject.

12. The use of claim 11, wherein the infection comprises a bacterial infection; optionally
wherein the infection is resistant to one or more anti-bacterial agents.

13. A nucleic acid composition encoding the peptide of any one of the claims 1-5.

14. An expression vector comprising the nucleic acid composition of claim 13.

15. A host cell comprising one or more of the nucleic acid compositions of claim 13, or one or more of the expression vectors of claim 14.