filters and orifices. Biofilm and biofilm organisms also cause corrosion of pipeline and petroleum process equipment. These problems can be manifested throughout an oil or gas production facility to the point where fouling and corrosive biofilm organisms have even been found on the surfaces of final product storage tanks.

[0001] In the home, biofilms are found in or on any surface that supports microbial growth, e.g., in drains, on food preparation surfaces, in toilets and in swimming pools and spas.

[0002] Biofilms are implicated in a wide range of water processes, both domestic and industrial. They can grow on the surface of process equipment and impede the performance of the equipment, such as degradation of heat transfer or plugging of filters and membranes. Biofilms growing on cooling tower fill can add enough weight to cause collapse of the fill. Biofilms cause corrosion of even highly specialized stainless steels. Biofilms in a water process can degrade the value of a final product. Biofilms growing in drinking water distribution systems can harbor potential pathogenic organisms, corrosive organisms or bacteria that degrade the aesthetic quality of the water.

[0003] Thus, a need exists to break through the protective barrier of biofilms to treat or kill the associated bacterial infections and clear them from surfaces and in water systems. This disclosure satisfies this need and provides related advantages as well.

SUMMARY

[009a] In one aspect, the present disclosure refers to an isolated B Box polypeptide comprising amino acids 99-133 and 138-164 of SEQ ID NO: 2~~an amino acid mutation at C106 or K114, or an equivalent thereof comprising the amino acid mutation at C106 or K114~~.

~~**[009b]** In another aspect, the present disclosure refers to an isolated A Box polypeptide, or an equivalent thereof comprising an amino acid mutation at an amino acid position selected from K12, C23 or C45.~~

~~**[009c]** In another aspect, the present disclosure refers to an isolated AB Box polypeptide, or an equivalent thereof.~~

[009~~d~~b] In another aspect, the present disclosure refers to an antibody that recognizes and binds an isolated polypeptide as described herein or an antigen binding fragment of the antibody.

[009ce] In another aspect, the present disclosure refers to a composition comprising a carrier and one or more isolated polypeptide as described herein, or an antibody or antigen binding

fragment that recognizes and binds the isolated polypeptide, or an isolated host cell comprising one of more of: the isolated polypeptide, the antibody or antigen binding fragment, a polynucleotide encoding the isolated polypeptide or the antibody or antigen binding fragment, a complement of the polynucleotide, or a vector comprising the polynucleotide.

[009df] In another aspect, the present disclosure refers to a polynucleotide encoding the isolated polypeptide as described herein or the complement of the polynucleotide.

[009eg] In another aspect, the present disclosure refers to a vector comprising the polynucleotide as described herein.

[009hf] In yet another aspect, the present disclosure refers to an isolated host cell comprising one of more of: the polypeptide as described herein, an antibody or antigen binding fragment that recognizes and binds the isolated polypeptide, a polynucleotide encoding the isolated polypeptide or the antibody or antigen binding fragment, a complement of the polynucleotide, or a vector comprising the polynucleotide.

[009gi] In yet another aspect, the present disclosure refers to an *ex vivo* method for inhibiting, competing or titrating the binding of a DNABII polypeptide or protein to a microbial DNA, comprising contacting the DNABII polypeptide or protein or the microbial DNA with the polypeptide as described herein, thereby inhibiting, competing or titrating the binding of the DNABII protein or polypeptide to the microbial DNA.

[009hj] In yet another aspect, the present disclosure refers to an *ex vivo* method for inhibiting, preventing or breaking down a microbial biofilm, comprising contacting the biofilm with the polypeptide as described herein, thereby inhibiting, preventing or breaking down the microbial biofilm.

[009ik] In yet another aspect, the present disclosure refers to a use of the polypeptide as described herein in the manufacture of a medicament for one or more of the following: (a) inhibiting, preventing or breaking down a bacterial biofilm in a subject, (b) inhibiting, preventing or treating a microbial infection that produces a bacterial biofilm in a subject, (c) disrupting a bacterial biofilm and clearance thereof that does not enhance or induce an

inflammatory response in a subject in need thereof, or (d) treating an infection or disorder incident to the presence of a bacterial biofilm in a subject in need thereof,

wherein the polypeptide comprises an amino acid mutation at C106 and is to be administered into the subject, thereby (a') inhibiting, preventing or breaking down the bacterial~~microbial~~ biofilm, (b') inhibiting, preventing or treating a bacterial~~microbial~~ infection that produces the biofilm in the subject, (c') disrupting the bacterial biofilm and clearance thereof that does not enhance or induce an inflammatory response, or (d') treating the infection or disorder incident to the presence of the~~a~~ bacterial biofilm in the subject, respectively.

[009j~~i~~] In yet another aspect, the present disclosure refers to a kit comprising one or more of: the isolated polypeptide as described herein, an antibody or antigen binding fragment that recognizes and binds the isolated polypeptide, a polynucleotide encoding the isolated polypeptide or the antibody or antigen binding fragment, or a complement of the polynucleotide and instructions for use.

[009k~~m~~] In yet another aspect, the present disclosure refers to the polypeptide as described herein for use as a therapy.

[0004] Bacterial biofilms are notoriously recalcitrant to existing treatment modalities (for example they are >1000 fold more resistant to antimicrobials than their planktonic counterparts). Given the high prevalence and the enormous consequences in terms of attributable mortality and economic burden of biofilm-mediated infections, novel therapeutic approaches are urgently needed. One of the defining characteristics of a biofilm is the extracellular polymeric substance, in which biofilm cells are embedded. Key components of the extracellular polymeric substance are extracellular DNA and bacterial DNABII family of proteins, which are crucial to biofilms' structural integrity. Targeting and sequestration of DNABII proteins can disrupt biofilms. High Mobility Group B1 (HMGB1) protein is a DNA-binding eukaryotic protein that binds to the same DNA structures as the DNABII proteins, causing, disruption of bacterial biofilms. Derivatives of HMGB1 can be engineered to possess the same efficacious anti-biofilm activity but are smaller and do not induce inflammation.

What is claimed is:

1. An isolated B Box polypeptide comprising amino acids 99-133 and 138-164 of SEQ ID NO: 2.

2. The isolated B Box polypeptide of claim 1, comprising amino acids 89 to 162 SEQ ID NO: 2.

3.~~1~~ ~~An~~The isolated B Box polypeptide of claim 1 or 2, comprising an amino acid mutation at C106 or K114~~, or an equivalent thereof comprising the amino acid mutation at C106 or K114~~.

4.~~2~~. The isolated B Box polypeptide of claim ~~1~~3, comprising the amino acid mutation C106S~~, or an equivalent thereof comprising the amino acid mutation C106S.~~

~~3. An isolated A Box polypeptide, or an equivalent thereof comprising an amino acid mutation at an amino acid position selected from K12, C23 or C45.~~

~~4. An isolated AB Box polypeptide, or an equivalent thereof.~~

~~5. The isolated AB Box polypeptide of claim 4, comprising an amino acid mutation at C106, or an equivalent thereof comprising the amino acid mutation at C106.~~

~~6. The isolated AB Box polypeptide of claim 4, comprising the amino acid mutation C106S, or an equivalent thereof comprising the amino acid mutation C106S.~~

5~~7~~. The isolated polypeptide of claim 1 or 2, further comprising a linker polypeptide located at the N- or C-terminus of the polypeptide or a linker polypeptide located at the N- and C-termini.

~~8. The isolated polypeptide of claim 4, further comprising a linker polypeptide linking the A Box polypeptide and the B Box polypeptide.~~

6~~9~~. An antibody that recognizes and binds an isolated polypeptide of any one of claims 1-5~~1~~ or an antigen binding fragment of the antibody.

7~~10~~. A composition comprising a carrier and one or more isolated polypeptide of any one of claims 1-5~~1~~ or an antibody or antigen binding fragment that recognizes and binds the isolated polypeptide, or an isolated host cell comprising one of more of: the isolated polypeptide, the antibody or antigen binding fragment, a polynucleotide encoding the isolated polypeptide or the

antibody or antigen binding fragment, a complement of the polynucleotide, or a vector comprising the polynucleotide.

8~~11~~. A polynucleotide encoding the isolated polypeptide of any one of claims 1-5~~1~~ or the complement of the polynucleotide.

9~~12~~. A vector comprising the polynucleotide of claim ~~11~~8.

10~~13~~. An isolated host cell comprising one of more of: the polypeptide of any one of claims 1-5~~1~~, an antibody or antigen binding fragment that recognizes and binds the isolated polypeptide, a polynucleotide encoding the isolated polypeptide or the antibody or antigen binding fragment, a complement of the polynucleotide, or a vector comprising the polynucleotide.

11~~14~~. An *ex vivo*~~A~~ method for inhibiting, competing or titrating the binding of a DNABII polypeptide or protein to a microbial DNA, comprising contacting the DNABII polypeptide or protein or the microbial DNA with the polypeptide of any one of claims 1-5~~1~~, thereby *inhibiting*, competing or titrating the binding of the DNABII protein or polypeptide to the microbial DNA.

12~~15~~. An *ex vivo*~~A~~ method for inhibiting, preventing or breaking down a microbial biofilm, comprising contacting the biofilm with the polypeptide of any one of claims 1-5~~1~~, thereby inhibiting, preventing or breaking down the microbial biofilm.

13~~16~~. Use of the polypeptide of any one of claims 1-5,~~1~~ in the manufacture of a medicament for one or more of the following: (a) inhibiting, preventing or breaking down a bacterial biofilm in a subject, (b) inhibiting, preventing or treating a microbial infection that produces a bacterial biofilm in a subject, (c) disrupting a bacterial biofilm and clearance thereof that does not enhance or induce an inflammatory response in a subject in need thereof, or (d) treating an infection or disorder incident to the presence of a bacterial biofilm in a subject in need thereof,

wherein the polypeptide comprises an amino acid mutation at C106 and is to be administered into the subject, thereby (a') inhibiting, preventing or breaking down the bacterial~~microbial~~ biofilm, (b') inhibiting, preventing or treating a microbial infection that produces the bacterial biofilm in the subject, (c') disrupting the bacterial biofilm and clearance thereof that does not enhance or induce an inflammatory response, or (d') treating the infection or disorder incident to the presence of ~~a~~the bacterial biofilm in the subject, respectively.

1417. The *ex vivo* method of claim 1512, wherein the biofilm is produced by an organism selected from the group of uropathogenic *Escherichia coli* (UPEC), *Klebsiella pneumonia, Burkholderia cenocepacia, S. epidermidis, Streptococcus agalactiae, Neisseria meningitidis, Treponemes, denticola, pallidum), Burkholderia cepacia, Burkholderia pseudomallei, Haemophilus influenzae* (nontypeable)(NTHI), *Moraxella catarrhalis, Streptococcus pneumoniae, Streptococcus pyogenes, Pseudomonas aeruginosa, Mycobacterium tuberculosis* or an ESKAPE pathogen.

1518. The use of claim 1614, wherein an antimicrobial is to be further administered.

1619. A kit comprising one or more of: the isolated polypeptide of any one of claims 1-51, an antibody or antigen binding fragment that recognizes and binds the isolated polypeptide, a polynucleotide encoding the isolated polypeptide or the antibody or antigen binding fragment, or a complement of the polynucleotide and instructions for use.

~~20. The isolated AB Box polypeptide of claim 4, comprising one or more amino acid mutations at an amino acid position selected from K12, C23, C45, K114 or C106, or an equivalent thereof comprising an amino acid mutation at a position selected from K12, C23, C45, K114, or C106.~~

1721. The polypeptide of any one of claims 1-51 for use as a therapy.