biofilm, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof.

[0008a] In one aspect, the present disclosure refers to method for inhibiting the stability of a biofilm, comprising contacting the biofilm with an effective amount of at least one agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is selected from a tRNA, a polyamine analog, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof~~one or more of the following: (a) an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof; (b) an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof; (c) an HMGB1 protein or a biologically active fragment thereof and anti-B-DNA antibody or fragment or derivative thereof, wherein the contacting comprises coating a surface ex-vivo with an effective amount of the HMGB1 protein or biologically active fragment thereof and the anti-B-DNA antibody or fragment or derivative thereof; or (d) chloroquine and anti-B-DNA antibody or a fragment or derivative thereof, wherein the contacting comprises coating a surface ex-vivo with an effective amount of chloroquine and anti-B-DNA antibody or a fragment or derivative thereof~~.

[0008b] In another aspect, the present disclosure refers to a composition comprising one, two or three or more of: an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is selected from a tRNA, a polyamine analog, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof, an agent that depletes cations from the biofilm, an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, an agent that interferes with the binding of the eDNA to a DNA binding protein and/or an antibacterial agent.

[0008c] In another aspect, the present disclosure refers to a use of ~~one or more~~an agent~~s~~ that interferes with the binding of a polyamine to the DNA in the biofilm in the manufacture of a medicament for treating an infection caused by a bacterium that produces a biofilm in a subject in need thereof, wherein the agent that interferes with the binding of a polyamine to the DNA in the biofilm is selected from a tRNA, a polyamine analog difluoromethylornithine, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof.

[0008d] In another aspect, the present disclosure refers to a use of at least one agent that interferes with the binding of a polyamine to DNA in a biofilm in the manufacture of a medicament for inhibiting the stability of a biofilm, or for treating a biofilm in a subject, or for preventing the formation of a biofilm in a subject susceptible to developing a biofilm, wherein the biofilm is to be contacted with the medicament, and wherein the agent is selected from a tRNA, a polyamine analog, trans-4-methylcyclohexylamine, sardomozide,

methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof. ~~treating a biofilm in a subject, wherein said agents are to be administered to the subject infected with a biofilm, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof. In another aspect, the present disclosure refers to a use of one or more agents that interfere with the binding of a polyamine to the DNA in the biofilm in the manufacture of a medicament for preventing the formation of a biofilm in a subject susceptible to developing a biofilm, wherein said agents are to be administered to the subject, optionally wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof. In another aspect, the present disclosure refers to a use of one or more agents that interfere with the binding of a polyamine to the DNA in the biofilm and an agent that inhibits the replication of the organism in the manufacture of a medicament for combination therapy to treat an infection caused by a bacterium that produces a biofilm in a subject in need thereof, wherein said agents are to be administered to the subject, optionally wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof. In another aspect, the present disclosure refers to a use of one or more of the following: (a) an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof; (b) one or more agents that interfere with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof; (c) HMGB1 protein or a biologically active fragment thereof and anti-B-DNA antibody or a fragment or derivative thereof; or (d) chloroquine and anti-B-DNA antibody or a fragment or derivative thereof in the manufacture of a medicament for treating a biofilm producing infection incident to administration of a platinum-based chemotherapy in a patient receiving or having received the chemotherapy, wherein said (a)-(d) are to be administered to the patient. In another aspect, the present disclosure refers to a use of one or more of the following: (a) an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof; (b) one or more agents that interfere with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof; (c) HMGB1 protein or a biologically active fragment thereof and anti-B-DNA antibody or a fragment or derivative thereof; or (d) chloroquine and anti-B-DNA antibody or fragment or derivative thereof in the manufacture of a medicament for treating a biofilm in a patient suffering from systemic lupus erythematosus (SLE) or cystic fibrosis (CF), wherein (a)-(d) are to be administered to the patient. In yet another aspect, the present disclosure refers to a composition comprising one, two or three or more of: an agent that interferes with the binding of a polyamine to DNA in the biofilm, an agent that depletes cations from the biofilm, an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, an agent that interferes with the binding of the eDNA to a DNA binding protein or an antibacterial agent.~~

[0008e] In yet another aspect, the present disclosure refers to a kit comprising the composition as disclosed herein and instructions for use, and optionally wherein the agents are combined or separately packaged, optionally wherein the instruction for use provide directions to conduct the method as described herein or the use as described herein.

[0008f] In one example, the methods for inhibiting the stability of a biofilm, comprise, or alternatively consist essentially of, or yet further consist of a contacting the biofilm with an effective amount of one or more agents that interfere with the binding of a polyamine to the DNA in the biofilm. This disclosure also relates to methods for inhibiting the stability of a biofilm, comprising, or alternatively consisting essentially of, or yet further consisting of contacting the biofilm in vitro with an agent that interferes with the binding of a polyamine to the DNA in the biofilm, wherein the contacting comprises, or alternatively consists essentially of, or yet further consists of coating a surface with an effective amount of agent that depletes cations, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof. In one example, the methods for inhibiting the stability of a biofilm, may comprise, or alternatively consist essentially of, or yet further consist of contacting the biofilm in vitro with an effective amount of an agent that interferes with the binding of a polyamine to the DNA in the biofilm, wherein the contacting comprises, or alternatively consists essentially of, or yet further consists of coating a surface with an effective amount of one or more agents that depletes cations. The contacting may be in vitro or in vivo.

[0009] In one example, the agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment. In a second example, the agent comprises, or alternatively consists essentially of, or yet further consists of an anti-B-DNA antibody or fragment or derivative thereof. In a third example, the agent comprises, or alternatively consists essentially of, or yet further consists of riboflavin, ethidium bromide, bis(methidium)spermine, daunorubicin, TMPyP4, a quaternary benzo[*c*]phenanthridine alkaloid, quinacrine, 9-amino acridine, or a derivative thereof. In a fourth example, the agent comprises, or alternatively consists essentially of, or yet further consists of chloroquine or a derivative thereof.

[0010] Further described herein are methods for inhibiting the stability of a biofilm, comprising, or alternatively consisting essentially of, or yet further consisting of contacting the biofilm in vitro with an effective amount of HMGB1 protein or biologically active fragment thereof

WHAT IS CLAIMED IS:

1. An A method for inhibiting the stability of a biofilm, comprising contacting the biofilm *in vitro* with an effective amount of one or more of the following:

(a) anat least one agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof;

(b) an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof;

(c) an HMGB1 protein or a biologically active fragment thereof and anti-B-DNA antibody or fragment or derivative thereof, wherein the contacting comprises coating a surface ex vivo with an effective amount of the HMGB1 protein or biologically active fragment thereof and the anti-B-DNA antibody or fragment or derivative thereof; or

(d) chloroquine and anti-B-DNA antibody or a fragment or derivative thereof, wherein the contacting comprises coating a surface *ex vivo* with an effective amount of chloroquine and anti-B-DNA antibody or a fragment or derivative thereof.

2. Use of one or more agents that interfere with the binding of a polyamine to the DNA in the biofilm in the manufacture of a medicament for treating a biofilm in a subject, wherein said agents are to be administered to the subject infected with a biofilm, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof.

3. Use of one or more agents that interfere with the binding of a polyamine to the DNA in the biofilm in the manufacture of a medicament for preventing the formation of a biofilm in a subject susceptible to developing a biofilm, wherein said agents are to be administered to the subject, optionally wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof.

4. Use of one or more agents that interfere with the binding of a polyamine to the DNA in the biofilm and an agent that inhibits the replication of the organism in the manufacture of a medicament for combination therapy to treat an infection caused by a bacterium that produces a biofilm in a subject in need thereof, wherein said agents are to be administered to the subject, optionally wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof.

~~5. The method of claim 1, wherein one or more of the following applies:~~

~~(i) the agent that interferes with the binding of a polyamine to DNA in the biofilm is a tRNA;~~

~~(ii) the agent is an inhibitor of polyamine synthesis or an agent that inhibits the binding of the polyamine to the DNA, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof;~~

~~(iii) the polyamine is~~ selected from ~~the group of: putrescine, spermine, cadaverine, 1,3-diaminopropane or spermidine;~~

1. ~~(iv) the agent comprises~~a tRNA, a polyamine analog~~-difluoromethylornithine~~, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, ~~cisplatin,~~ dicyclohexylamine, a derivative of any thereof, or a salt thereof~~;~~.

~~(v) the agent comprises an agent that depletes cations from the biofilm, optionally a cation exchange resin, an aminopolycarboxylic acid, a crown ether, an azacrown, or a cryptand, and optionally wherein the agent that depletes cations from the biofilm are from the group of: sulfonate, sulfopropyl, phosphocellulose, P11 phosphocellulose, heparin sulfate, or a derivative or analog thereof;~~

~~(vi) the agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment; or (vii) the method is performed in the absence of administration of a DNAse enzyme.~~

~~6. The use of claim 2, wherein one or more of the following applies:~~

~~(i) the agent is an inhibitor of polyamine synthesis or an agent that inhibits the binding of the polyamine to the DNA, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof;~~

~~(ii) the polyamine is selected from the group of: putrescine, spermine, cadaverine, 1,3-diaminopropane or spermidine;~~

~~(iii) the agent comprises a polyamine analog difluoromethylornithine, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, cisplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof;~~

~~(iv) the agent comprises an agent that depletes cations from the biofilm, optionally a cation exchange resin, an aminopolycarboxylic acid, a crown ether, an azacrown, or a cryptand and optionally wherein the agent that depletes cations from the biofilm are~~

from the group of: sulfonate, sulfopropyl, phosphocellulose, P11 phosphocellulose, heparin sulfate, or a derivative or analog thereof;

(v) the agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment; or

(vi) the method is performed in the absence of administration of a DNAse enzyme.

7. The use of claim 3 wherein one or more of the following applies:

(i) the agent is an inhibitor of polyamine synthesis or an agent that inhibits the binding of the polyamine to the DNA, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof;

(ii) the polyamine is selected from the group of: putrescine, spermine, cadaverine, 1,3-diaminopropane or spermidine;

(iii) the agent comprises a polyamine analog difluoromethylornithine, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, cisplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof;

(iv) the agent comprises an agent that depletes cations from the biofilm, optionally a cation exchange resin, an aminopolycarboxylic acid, a crown ether, an azacrown, or a cryptand and optionally wherein the agent that depletes cations from the biofilm are from the group of: sulfonate, sulfopropyl, phosphocellulose, P11 phosphocellulose, heparin sulfate, or a derivative or analog thereof;

(v) the agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment; or

(vi) the method is performed in the absence of administration of a DNAse enzyme.

8. The use of claim 4, wherein one or more of the following applies:

(i) the agent is an inhibitor of polyamine synthesis or an agent that inhibits the binding of the polyamine to the DNA, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof;

(ii) the polyamine is selected from the group of: putrescine, spermine, cadaverine, 1,3-diaminopropane or spermidine;

(iii) the agent comprises a polyamine analog difluoromethylornithine, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, cisplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof;

(iv) the agent comprises an agent that depletes cations from the biofilm, optionally a cation exchange resin, an aminopolycarboxylic acid, a crown ether, an azacrown, or a cryptand and optionally wherein the agent that depletes cations from the biofilm are from the group of: sulfonate, sulfopropyl, phosphocellulose, P11 phosphocellulose, heparin sulfate, or a derivative or analog thereof;

(v) the agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment; or

(vi) the method is performed in the absence of administration of a DNAse enzyme.

9. The method of claim 1, wherein the contacting is *ex vivo* and comprises coating a surface with an effective amount of one or more agents that deplete cations, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof.

10. The method of claim 9, wherein one or more of the following applies:

(a) the agent comprises an anti-B-DNA antibody or a fragment thereof or derivative thereof;

(b) the agent comprises riboflavin, ethidium bromide, bis(methidium)spermine, daunorubicin, TMPyP4, a quaternary benzo[c]phenanthridine alkaloid, quinacrine, 9-amino acridine, or a derivative thereof; or

(c) the agent comprises chloroquine or a derivative thereof.

11. Use of one or more of the following:

(a) an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof;

(b) one or more agents that interfere with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof;

(c) HMGB1 protein or a biologically active fragment thereof and anti-B-DNA antibody or a fragment or derivative thereof; or

(d) chloroquine and anti-B-DNA antibody or fragment or derivative thereof in the manufacture of a medicament for treating a biofilm in a patient suffering from systemic lupus erythematosus (SLE) or cystic fibrosis (CF),

wherein (a)-(d) are to be administered to the patient.

~~12. The use of claim 11, wherein the agent comprises one or more of the following: chloroquine or a derivative thereof; an anti-B-DNA antibody or fragment or derivative thereof; riboflavin, ethidium bromide, bis(methidium)spermine, daunorubicin, TMPyP4, a quaternary benzo[c]phenanthridine alkaloid, quinacrine, 9-amino acridine, or a derivative thereof.~~

~~13. Use of one or more of the following:~~

~~(a) an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, fragment or an equivalent of each thereof;~~

~~(b) one or more agents that interfere with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, wherein the agent is not an HMGB1 protein, a fragment thereof or an equivalent of each thereof;~~

~~(c) HMGB1 protein or a biologically active fragment thereof and anti-B-DNA antibody or a fragment or derivative thereof; or~~

~~(d) chloroquine and anti-B-DNA antibody or a fragment or derivative thereof in the manufacture of a medicament for treating a biofilm producing infection incident to administration of a platinum-based chemotherapy in a patient receiving or having received the chemotherapy,~~

~~wherein said (a)-(d) are to be administered to the patient.~~

~~14. The use of claim 13, wherein the agent comprises one or more of the following: chloroquine or a derivative thereof; an anti-B-DNA antibody or a fragment or derivative thereof; riboflavin, ethidium bromide, bis(methidium)spermine, daunorubicin, TMPyP4, a quaternary benzo[c]phenanthridine alkaloid, quinacrine, 9-amino acridine, or a derivative thereof.~~

~~15. The method of claim 1,~~The method of claim 1 further comprising contacting the biofilm with an effective amount of ~~either or both of~~ an agent that interferes with the binding of the eDNA to a DNA binding protein and/or an antibacterial agent~~.~~

~~16.~~2. ~~The method of claim 15,~~, optionally wherein the agent that interferes with the binding of the eDNA to the DNA binding protein comprises one or more of an anti-DNABII antibody, an anti-IHF antibody and/or an anti-HU antibody, or fragments of each thereof~~.~~

~~17. The use of claim 8, wherein the agent that depletes cations from the biofilm has a net negative charge or a net neutral charge.~~

~~18.~~3. The method of claim ~~15,~~2, wherein the agent that interferes with the binding of the eDNA to a DNA binding protein has a net negative charge or ~~net neutral or~~a net positive charge.

4. The method of any one of the preceding claims, wherein the methods are performed in the absence of administration of a DNAse enzyme.

~~19.~~5. A composition comprising one, two or three or more of: an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is selected from a tRNA, a polyamine analog, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof, an agent that depletes cations from the biofilm, an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment, an agent that interferes with the binding of the eDNA to a DNA binding protein and/or an antibacterial agent.

6. Use of an agent that interferes with the binding of a polyamine to the DNA in the biofilm and an agent that inhibits the replication of the bacterium in the manufacture of a medicament for treating an infection caused by a bacterium that produces a biofilm in a subject in need thereof, wherein the agent that interferes with the binding of a polyamine to the DNA in the biofilm is selected from a tRNA, a polyamine analog difluoromethylornithine, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof.

7. Use of at least one agent that interferes with the binding of a polyamine to DNA in a biofilm in the manufacture of a medicament for inhibiting the stability of a biofilm, or for treating a biofilm in a subject, or for preventing the formation of a biofilm in a subject susceptible to developing a biofilm, wherein the biofilm is to be contacted with the medicament, and wherein the agent is selected from a tRNA, a polyamine analog, trans-4-methylcyclohexylamine, sardomozide, methylglyoxal-bis[guanylhydrazone] (MGBG), 1-aminooxy-3-aminopropane, oxaliplatin, dicyclohexylamine, a derivative of any thereof, or a salt thereof.

8. The use of claim 6 or 7, wherein the biofilm is to be further contacted with an effective amount of an agent that interferes with the binding of the eDNA to a DNA binding protein and/or an antibacterial agent, optionally wherein the agent that

interferes with the binding of the eDNA to the DNA binding protein comprises one or more of an anti-DNABII antibody, an anti-IHF antibody and/or an anti-HU antibody, or fragments of each thereof

9. The use of claim 8, wherein the agent that interferes with the binding of the eDNA to a DNA binding protein has a net negative charge or a net positive charge.

10. The use of any one of claims 6-9, wherein administration of a DNAse enzyme is absent.

11. A kit comprising the composition of claim ~~19~~5 and instructions for use, and optionally wherein the agents are combined or separately packaged~~.~~, optionally wherein the instruction for use provide directions to conduct the method of any one of claims 1 to 5 or the use according to any one of claims 6-10.

~~20.~~