neutralizing the endosomal pH. However, its highest selectivity was only ~24 against influenza virus (PR8) and human rhinovirus (HRV14). Ammonium chloride and chloroquine having pH neutralization ability were also reported to prevent viral infections, but they are highly toxic, limiting clinical applications.

[0009] An ongoing need exists for broad spectrum anti-viral agents that are non-hemolytic and that provide general and safe strategies to prevent viral infections. Anti-viral macromolecules with distinctive functional groups are needed to specifically bind to viral surface proteins as well as compete with viruses for immune cell/target cell binding to prevent infection.

SUMMARY

[0010] In one aspect, there is provided a method, comprising:

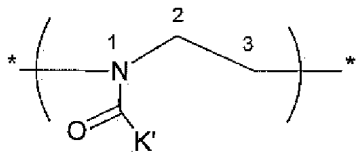
treating a virus with a cationic polyamine, thereby forming a treated virus comprising the cationic polyamine bound by non-covalent interactions to the virus;

wherein:

i) the treated virus is less capable of entering a living mammalian cell and/or undergoing replication within a living mammalian cell compared to the untreated virus,

ii) the cationic polyamine comprises:

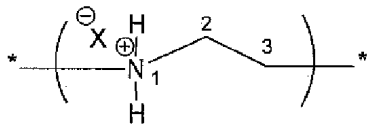
a plurality of non-charged N-acylated ethylenimine units of formula (1):



(1),

wherein each K' comprises at least one carbon and at least one alcohol hydroxyl group, and

a plurality of positive-charged secondary ethylenimine units of formula (3a):



(3a),

wherein the starred bond of the nitrogen is linked to a carbon and $X^{\ominus}$ is a negative-charged counterion bound by non-covalent association with the positive charged nitrogen, and

iii) the cationic polyamine comprises the N-acylated ethylenimine units and the secondary ethylenimine units arranged in a random distribution and linked covalently head-to-tail, wherein nitrogen 1 of a given ethylenimine unit is linked to carbon 3 of a different ethylenimine unit.

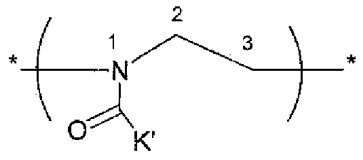
[0011] In another aspect, there is provided an *in vitro* method, comprising:

treating a living mammalian cell with a cationic polyamine, thereby forming a treated cell comprising the cationic polyamine and the cell bound by non-covalent interactions; wherein:

i) the treated cell has more resistance to a virus entering the treated cell and/or replicating within the treated cell compared to the untreated cell,

ii) the cationic polyamine comprises:

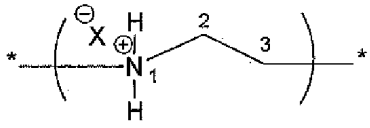
a plurality of non-charged N-acylated ethylenimine units of formula (1):



(1),

wherein each K' comprises at least one carbon and at least one alcohol hydroxyl group, and

a plurality of positive-charged secondary ethylenimine units of formula (3a):



(3a),

wherein the starred bond of the nitrogen is linked to a carbon, and $X^{\ominus}$ is a negative-charged counterion bound by non-covalent association with the positive charged nitrogen, and

iii) the cationic polyamine comprises the N-acylated ethylenimine units and the secondary ethylenimine units arranged in a random distribution and linked covalently head-

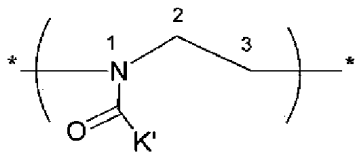
to-tail, wherein nitrogen 1 of a given ethylenimine unit is linked to carbon 3 of a different ethylenimine unit.

[0012]

In a further aspect, there is provided use of a therapeutically effective amount of a cationic polyamine in the manufacture of a medicament for inhibiting and/or preventing replication of a virus in a patient infected with the virus, wherein:

i) the cationic polyamine comprises:

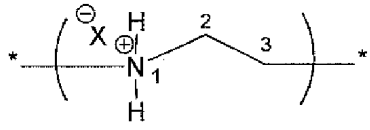
a plurality of non-charged N-acylated ethylenimine units of formula (1):



(1),

wherein each K' comprises at least one carbon and at least one alcohol hydroxyl group, and

a plurality of positive-charged secondary ethylenimine units of formula (3a):



(3a),

wherein the starred bond of the nitrogen is linked to a carbon, and $X^{\ominus}$ is a negative-charged counterion bound by non-covalent association with the positive charged nitrogen, and

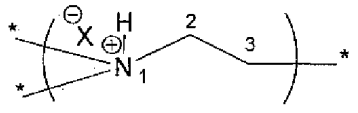
ii) the cationic polyamine comprises the N-acylated ethylenimine units and the secondary ethylenimine units arranged in a random distribution and linked covalently head-to-tail, wherein nitrogen 1 of a given ethylenimine unit is linked to carbon 3 of a different ethylenimine unit.

[0013] The above-described and other features and advantages of the present invention will be appreciated and understood by those skilled in the art from the following detailed description, drawings, and appended claims.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

9. The method of claim 1, wherein the virus is a dengue virus.

10. The method of claim 1, wherein the cationic polyamine has a plurality of polymer branches comprising the N-acylated ethylenimine units, the secondary ethylenimine units, and tertiary ethylenimine unit having the structure



(4),

wherein $X^{\ominus}$ is a negative-charged counterion bound by non-covalent association with the positive charged nitrogen.

11. The method of claim 10, wherein the cationic polyamine is formed in a process comprising treating a branched polyethylenimine with an acylating agent comprising K' and/or a protected form of K'.

12. The method of claim 11, wherein the branched polyethylenimine has a number average molecular weight (Mn) greater than 1000.

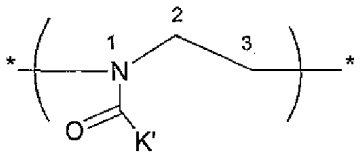
13. An *in vitro* method, comprising:

treating a living mammalian cell with a cationic polyamine, thereby forming a treated cell comprising the cationic polyamine and the cell bound by non-covalent interactions; wherein:

i) the treated cell has more resistance to a virus entering the treated cell and/or replicating within the treated cell compared to the untreated cell,

ii) the cationic polyamine comprises:

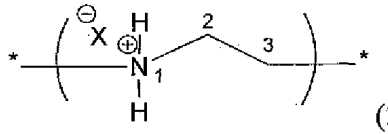
a plurality of non-charged N-acylated ethylenimine units of formula (1):



(1),

wherein each K' comprises at least one carbon and at least one alcohol hydroxyl group, and

a plurality of positive-charged secondary ethylenimine units of formula (3a):



(3a),

wherein the starred bond of the nitrogen is linked to a carbon, and $X^{\ominus}$ is a negative-charged counterion bound by non-covalent association with the positive charged nitrogen, and

iii) the cationic polyamine comprises the N-acylated ethylenimine units and the secondary ethylenimine units arranged in a random distribution and linked covalently head-to-tail, wherein nitrogen 1 of a given ethylenimine unit is linked to carbon 3 of a different ethylenimine unit.

14. The method of claim 13, wherein the virus is selected from the group consisting of dengue fever viruses, SARS corona viruses, Chikungunya viruses, enteroviruses, influenza viruses, herpes simplex viruses, and combinations thereof.

15. The method of claim 13, wherein the cationic polyamine inhibits entry of the virus into the mammalian cell by disrupting endosomal release of the virus.

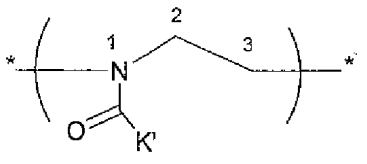
16. The method of claim 13, wherein the mammalian cell is selected from the group consisting of blood cells, liver cells, nasal cells, lung cells, and cervical cells.

17. Use of a therapeutically effective amount of a cationic polyamine in the manufacture of a medicament for inhibiting and/or preventing replication of a virus in a patient infected with the virus,

wherein:

i) the cationic polyamine comprises:

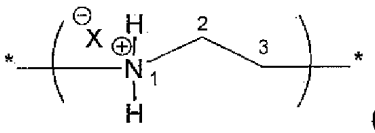
a plurality of non-charged N-acylated ethylenimine units of formula (1):



(1),

wherein each K' comprises at least one carbon and at least one alcohol hydroxyl group, and

a plurality of positive-charged secondary ethylenimine units of formula (3a):



(3a),

wherein the starred bond of the nitrogen is linked to a carbon, and $X^{\ominus}$ is a negative-charged counterion bound by non-covalent association with the positive charged nitrogen, and

ii) the cationic polyamine comprises the N-acylated ethylenimine units and the secondary ethylenimine units arranged in a random distribution and linked covalently head-to-tail, wherein nitrogen 1 of a given ethylenimine unit is linked to carbon 3 of a different ethylenimine unit.

18. The use of claim 17, wherein the cationic polyamine is to be administered as an aqueous mixture.

19. The use of claim 18, wherein the aqueous mixture is to be administered by injection.

20. The use of claim 17, wherein the cationic polyamine binds non-covalently to the virus, thereby impeding entry of the virus into cells of the patient.

21. The use of claim 17, wherein the cationic polyamine binds non-covalently to cells of the patient, thereby impeding entry of the virus into the cells of the patient.

22. The use of claim 17, wherein the cationic polyamine is non-cytotoxic at the therapeutically effect dose.