DESCRIPTION

METHODS FOR INCREASING THE INFECTIVITY OF VIRUSES

CROSS REFERENCE

[001] This application claims benefit of priority to U.S. Provisional Application serial no. 61/591,047, filed January 26, 2012, which is hereby incorporated by reference in its entirety.

BACKGROUND

[001] Viruses infecting humans, animals, plant and insects are well known. Infection of these hosts by viruses can result in disease unless an appropriate immunological response is available to neutralize the infection. Vaccines capable of elicting the immunological components necessary for an immunological response have been developed to prevent infection by viruses in humans and animals, with notable examples being the flu vaccine and the rabies vaccine, respectively.

[002] Vaccines typically contain an agent that resembles a disease-causing virus. The agent can be a weakened (attenuated) or killed (inactivated) form of the virus. The production of a whole virus vaccine generally begins with the virus being grown either in primary cells (e.g., flu virus) or in continuous cell lines such as cultured human or animal cells (e.g., polio virus). In order to propagate the virus in such cells, the virus must first infect the cells. Accordingly, there is a need for methods of increasing the infectivity of viruses for the making of vaccines.

[003] Viruses also have use in the preparation of viral vectors used by researchers to deliver genetic material into cells and organisms in both a research or gene therapy setting. Such viral vectors are non-naturally occurring viruses. In order to deliver genetic material to a cell, the vectors need to infect a cell. Accordingly, there is a need for viral vectors having increased infectivity to improve the amount of genetic material that can be delivered to target cells or organisims.

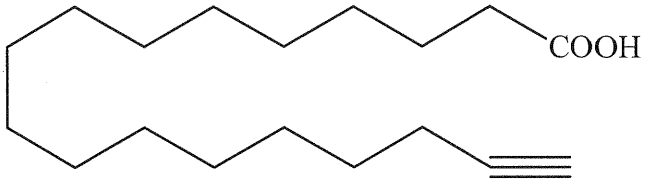
SUMMARY

[004] In ~~One~~one aspect, ~~of the present invention~~ there is provided a method of enhancing the infectivity of a human immunodeficiency virus, the method comprising contacting the

[0013] In certain embodiments comprising contacting the virus with [I], the alkyne-modified fatty acid is 15-ethynylpentadecanoic acid or physiologically acceptable salt thereof.

[0014] In certain embodiments comprising contacting the virus with [I], the alkyne-modified fatty acid is 12-ethynyldodecanoic acid or physiologically acceptable salt thereof.

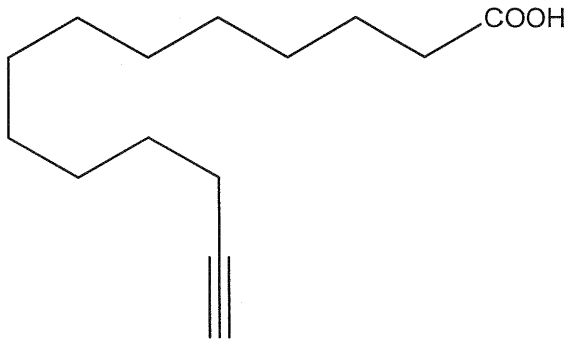
[0015] In certain embodiments comprising contacting the virus with [I], the alkyne-modified fatty acid is



[II]

or physiologically acceptable salt thereof.

[0016] In certain embodiments comprising contacting the virus with [I], the alkyne-modified fatty acid is



[III]

or physiologically acceptable salt thereof.

[0017] In certain embodiments comprising contacting the virus with [I], Y is an ethynyl group, X is a linear carbon chain, and the linear carbon chain comprises 8 to 15 carbons. In some of these, all of the carbons of the carbon chain are carbon, while in others, all of the bonds between the carbons of the carbon chain are single bonds.

[0018] In some embodiments, the contacting is performed in a solution comprising at least one of animal serum, amino acids, buffers, fatty acids, glucose, hormones, inorganic salts, lipids, metal ion chelators, peptides, surfactants, trace metals, and vitamins.

[0019] ~~Another~~ In another aspect, ~~of the present invention~~ there is provided a method of enhancing the infectivity of a human immunodeficiency virus, the method comprising contacting a cell infected with the virus with an alkyne-modified fatty acid, an alkyne-modified

are carbon, while in others, all of the bonds between the carbons of the carbon chain are single bonds.

[0033] In some embodiments, the contacting is performed in a solution comprising at least one of animal serum, amino acids, buffers, fatty acids, glucose, hormones, inorganic salts, lipids, metal ion chelators, peptides, surfactants, trace metals, and vitamins.

[0034] ~~Another~~ In another aspect, there is provided ~~of the present invention is~~ a human immunodeficiency virus comprising an alkyne-modified fatty acid moiety, an alkyne-modified carbohydrate moiety, or an alkyne-modified isoprenoid lipid moiety; wherein the moiety is non-naturally occurring.

[0035] In some embodiments, the virus is HIV-1.

[0036] In some embodiments, the virus is inactivated.

[0037] In some embodiments, the virus is attenuated.

[0038] In some embodiments, the alkyne-modified fatty acid moiety has the formula:

$$Y\text{-}CH_2\text{-}X\text{-}CO\text{-} \qquad [IV]$$

wherein, Y is H or an ethynyl group; and when Y is an ethynyl group, X is a linear or branched carbon chain comprising 6 to 28 carbons, wherein one or more of said carbons may be independently replaced by an oxygen, selenium, silicon, sulfur, SO, SO_2 or NR_1, or wherein one or more pairs of said carbons adjacent to one another may be attached to one another by a double or triple bond; or when Y is H, X is a linear or branched carbon chain comprising 6 to 28 carbons, wherein at least one hydrogen on one of said carbons is replaced with an ethynyl group and wherein one or more of said carbons not having an the ethynyl group attached thereto may be independently replaced by an oxygen, selenium, silicon, sulfur, SO, SO_2 or NR_1, or wherein one or more pairs of said carbons adjacent to one another and not having an ethynyl group attached thereto may be attached to one another by a double or triple bond; wherein, R_1 is H or an alkyl comprising 1 to 6 carbons.

[0039] In certain embodiments comprising [IV], Y is an ethynyl group.

[0040] In certain embodiments comprising [IV], X is a linear carbon chain.

[0041] In certain embodiments comprising [IV], X is a carbon chain comprising 8 to 15 carbons.

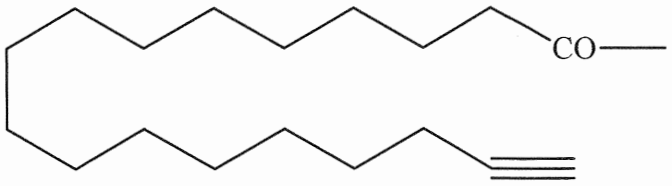
[0042] In certain embodiments comprising [IV], X is a carbon chain in which all of the carbons of the carbon chain are carbon.

[0043] In certain embodiments comprising [IV], X is a carbon chain in which all of the bonds between the carbons of the carbon chain are single bonds.

[0044] In certain embodiments comprising [IV], the alkyne-modified fatty acid moiety is 15-ethynylpentadecanyl.

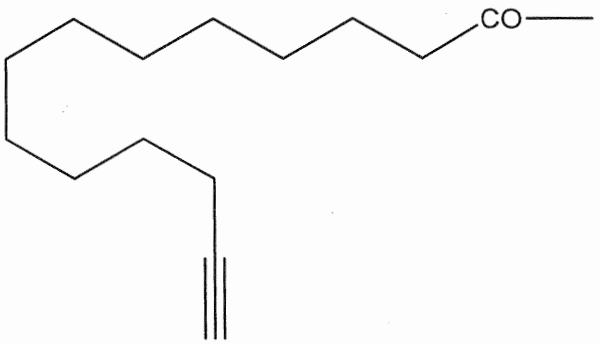
[0045] In certain embodiments comprising [IV], the alkyne-modified fatty acid moiety is 12-ethynyldodecanyl.

[0046] In certain embodiments comprising [IV], the alkyne-modified fatty acid moiety is



. [V]

[0047] In certain embodiments comprising [IV], the alkyne-modified fatty acid moiety is



. [VI]

[0048] In certain embodiments comprising [IV], Y is an ethynyl group, X is a linear carbon chain, and the linear carbon chain comprises 8 to 15 carbons. In some of these, all of the carbons of the carbon chain are carbon, while in others, all of the bonds between the carbons of the carbon chain are single bonds.

[0049] In certain embodiments comprising [IV], the alkyne-modified fatty acid moiety is attached to the virus by an amide or a thioester bond.

[0050] Another ~~aspect~~ embodiment of the present ~~invention~~disclosure is a composition comprising a human immunodeficiency virus comprising an alkyne-modified fatty acid moiety, an alkyne-modified carbohydrate moiety, or an alkyne-modified isoprenoid lipid moiety; wherein the moiety is non-naturally occurring.

[0050a] In one aspect, there is provided a composition comprising the virus as defined above.

[0051] In some embodiments, the virus is HIV-1.