COMPOSITIONS AND METHODS FOR ADMINISTRATION OF VACCINES AGAINST DENGUE VIRUS

PRIORITY

[001] This application claims the benefit under 35 USC § 119(e) of provisional U.S. patent application Serial No. 61/183,020 filed on June 01, 2009, which is incorporated herein by reference in its entirety.

FIELD

[002] Embodiments of the present invention report compositions and methods for administering a vaccine to a subject against dengue viruses. In some embodiments, vaccine compositions may be administered by intradermal injection. In certain embodiments, intradermal injection in a subject of a vaccine against dengue virus may include one or more intradermal boosts after initial vaccination. Other embodiments include intradermal injection of a vaccine composition against dengue virus wherein the composition provides protection against more than one serotype of dengue virus, such as DEN-1, DEN-2, DEN-3 and DEN-4.

BACKGROUND

[003] Vaccines for protection against viral infections have been effectively used to reduce the incidence of human disease. One of the most successful technologies for viral vaccines is to immunize animals or humans with a weakened or attenuated strain of the virus (a "live, attenuated virus"). Due to limited replication after immunization, the attenuated strain does not cause disease. However, the limited viral replication is sufficient to express the full repertoire of viral antigens and can generate potent and long-lasting immune responses to the virus. Thus, upon subsequent exposure to a pathogenic strain of the virus, the immunized individual is protected from disease. These live, attenuated viral vaccines are among the most successful vaccines used in public health.

SUMMARY

[003a] In a first aspect, there is provided a single vaccine composition against dengue virus for use in a method for inducing protection in a subject against three or four dengue virus serotypes, wherein the single vaccine composition against dengue virus is a mixture of live attenuated dengue viruses against three or four dengue virus serotypes to be administered to a subject by intradermal introduction to thereby induce protection in the subject against three or four dengue virus serotypes.

[003b] In a second aspect, there is provided a composition for protecting a subject against a dengue virus serotype comprising, an intradermally (ID) administered single vaccine composition of predetermined ratio of three or four dengue virus serotypes made up of live attenuated dengue viruses.

[003c] In a third aspect, there is provided a system for administering a dengue vaccine composition to a subject comprising, a single vaccine composition against three or four dengue virus serotypes wherein the single vaccine composition comprises three or four dengue virus serotypes and an apparatus capable of introducing the vaccine composition intradermally by needle-free administration to a subject.

[003d] In a fourth aspect, there is provided a vaccine kit comprising;

a vaccine composition against dengue virus comprising the composition as defined above; and

an apparatus capable of administering the composition intradermally to a subject.

[003e] In a fifth aspect, there is provided the use of a single vaccine composition against dengue virus in the manufacture of a medicament for inducing protection in a subject against three or four dengue virus serotypes, wherein the single vaccine composition against dengue virus is to be administered to the subject by intradermal introduction to thereby induce protection in the subject against multiple dengue virus serotypes.

[004] Embodiments of the present ~~invention~~disclosure generally relate to methods and compositions for inducing protection in a subject against dengue virus by, for example, administering a vaccine to a subject against dengue viruses. Some embodiments can include introducing a vaccine composition to a subject via intradermal (ID) injection. In accordance with these embodiments,

the vaccine composition can be introduced to a subject intradermally to, for example, protect against one or more than one dengue serotype (*e.g.* cross protection). In certain embodiments, a vaccine composition can include, but is not limited to, a single dose of one serotype of dengue virus (*e.g.* DENVax 4) administered to a subject. In other embodiments, a vaccine composition may include, but is not limited to; an initial dose of one serotype of dengue virus (*e.g.* DENVax 4 or other serotype) and then one or more boosts of the same, a combination or a different serotype can be administered to a subject.

[005] Other ~~aspects~~embodiments herein can concern inducing a cellular immune response in a subject by, for example, introducing a vaccine composition to a subject via intradermal introduction wherein the vaccine composition includes, but is not limited to, a dengue virus vaccine. In accordance with these embodiments, compositions disclosed can be administered intradermally to a subject for modulating neutralizing antibody production in the subject against dengue virus serotypes. Some ~~aspects~~embodiments concern predetermined composition ratios (*e.g.* 1:1, 1:2, 1:4, any ratio of two or more serotypes is contemplated) of the various serotypes of dengue virus or fragments thereof or attenuated compositions thereof in a single vaccine composition in order to increase cross protection in a subject against some or all dengue virus serotypes when the subject is administered the single vaccine composition intradermally.

[006] In certain embodiments, some advantages of using intradermal introduction of a vaccine against dengue virus can include, but are not limited to, multiple protection against some or all dengue virus serotypes in a subject, reduced cost by using small doses compared to subcutaneous injection, modulation of antibodies produced against some or all dengue virus serotypes in a subject and reduced pain at a site of administration in a subject administered a composition of vaccine against dengue virus.

[007] In some embodiments, a single dose vaccine against dengue virus can include one or more dengue virus serotype(s). In accordance with these embodiments, a subject may be treated with at least one additional intradermal injection(s) administered at a separate site from the first injection, for example, next to or in a separate anatomical site on the subject. In addition, at least one additional intradermal injection(s) may be performed less than 30 days after the first administration to the subject. Vaccine compositions of these and other embodiments disclosed herein may include two or more dengue virus serotypes at a predetermined ratio.