

# Development of Dengue Virus Type 3 Vaccine Candidates Containing Either 1) Nucleotide Deletions in the 3'-UTR of the Genome Consisting of More Than 30 Contiguous Nucleotides in One or Multiple Regions, or 2) a 3'-UTR Derived From DEN4 and Containing the d

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## Technology description

### Summary

The disease burden associated with dengue virus infection has increased over the past several decades in the tropical and semi-tropical regions of the world, where over 2 billion people live at risk of dengue infection. Annually, there are an estimated fifty (50) to one hundred (100) million cases of dengue fever, making development of an effective vaccine a priority. In addition, there is a need for a "travelers vaccine" to protect those visiting dengue virus endemic areas, similar in scope to other currently available "travelers vaccines", such as hepatitis A vaccine.

The previously identified delta30 attenuating mutation, created in each dengue virus serotype by the removal of 30 homologous nucleotides from the 3'-UTR, is capable of attenuating wild-type strains of dengue virus type 1 (DEN1), type 4 (DEN4) and to a limited extent type 2 (DEN2). These DEN1delta30 and DEN4delta30 viruses have been shown to be both safe and immunogenic in humans. However, the delta30 mutation failed to have an attenuating effect on dengue virus type 3 (DEN3). To generate DEN3 vaccine candidates with a clearly attenuated phenotype, viruses were produced containing 3'-UTR deletions consisting of extensions of the original delta30 mutation or additional mutations which remove stem-loop structures similar to those removed by delta30. In addition, the entire 3'-UTR of DEN3 was replaced with the 3'-UTR derived from DEN4 and containing the delta30 mutation. Studies in monkeys demonstrated that these newly developed viruses are highly attenuated, yet sufficiently immunogenic to warrant their further development for use as live attenuated vaccine candidates. Such viruses are anticipated to become the DEN3 component of a tetravalent vaccine formulation designed to immunize against all four dengue virus serotypes.

### Application area

Immunization against all four serotypes of Dengue Virus.

Institution

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