Live-Attenuated West Nile Virus Vaccines with Improved Immune Responses

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Technology description

Summary

West Nile virus (WNV), the etiologic agent of West Nile virus fever and encephalitis, is an emerging human and veterinary pathogen in North America. WNV also periodically poses a serious threat to public health in Africa, Australia, Europe, the Middle East, and Asia. There is no vaccine available. WNV strains are phylogenetically grouped into two distinct lineages based primarily on differences within the envelope (Env) protein gene segment. The highly virulent strains recently emergent on the North American continent are of lineage I. Lineage I viruses are primarily also isolated in the Middle East, Europe, and parts of Africa. Lineage II viruses are mostly isolated in Africa. Both lineages include highly neurovirulent as well as relatively attenuated strains of WNV.
WN vaccine viruses developed by others are chimeric live attenuated WN vaccine viruses. The genomes of these viruses encode the C and NS proteins of dengue or yellow fever virus, respectively, along with the WNV prM and Env proteins, which are the major targets of the humoral immune response to flaviviruses. These chimeric live attenuated WN vaccines have been successful in animal testing and some are currently in clinical trials. However, these vaccines have two potential disadvantages due to their heterogeneous genetic composition: (i) animal host range may be different from that of wild-type WNV, rendering the vaccines less than optimal for immunization of some at-risk species and (ii) the elicited immune response may be suboptimal in duration or quality, due to the absence from these vaccines of homologous WN NS proteins.
FDA□fs technology that is available for licensing comprises live attenuated West Nile viruses that are not chimeric, but instead have one or more mutations in the 3□Œ terminal stem loop secondary structure, resulting in decreased neurovirulence. The related patent application also claims methods of making the viruses claimed in the application and methods for using these viruses to prevent or treat WN infection. More specifically, the inventors modified infectious WN DNA such that all or segments of the wild-type WN 3' stem loop nucleotide sequence was replaced with analogous dengue virus serotype 2 3' stem loop sequences. The inventors also created a number of point mutations in the nucleotide sequence of the WN 3' stem loop sequence.

Application area

Development of live attenuated West Nile Virus vaccines, therapeutics and diagnostics.

Vaccine candidates have been prepared and preclinical (mouse) studies have been performed.

Institution

NIH - National Institutes of Health

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