CHARACTERIZATION OF CHIMERIC JAPANESE ENCEPHALITIS SA14-14-2 VIRUSES AS NOVEL VACCINE CANDIDATES

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Japanese Encephalitis (JE) virus is the leading cause of viral encephalitis in Asia causing significant morbidity and mortality with more than 50,000 cases reported annually. JE virus is a member of the family Flaviviridae genus Flavivirus, which includes other emerging and re-emerging mosquito-borne human pathogens such as dengue (DEN), yellow fever (YF) and West Nile (WN) viruses. Currently there are two live-attenuated flavivirus vaccines in use, YF 17D and JE SA14-14-2 vaccine strains. Although the YF 17D vaccine has been shown to be effective, concerns over serious adverse events plague this vaccine. In comparison, the JE SA14-14-2 vaccine strain has been shown to be highly effective with no reported serious adverse events. The purpose of this research is to generate and characterize chimeric JE vaccine viruses as potential vaccine candidates and compare to DEN/YF17D chimeric viruses. Full length infectious clones have been generated for several chimeric viruses including: DEN2/YF17D, DEN4/YF17D and DEN4DIII/YF17D. These clones have been transfected in Vero cells and infectious virus produced. This virus has been inoculated into mice to determine the antibody response compared to the parental DEN4 and YF17D strains. A full genome cDNA infectious clone for JE SA14-14-2 is underway. A novel vector, termed pBR322M has been engineered specifically for this infectious clone. To prepare for comparative mouse virulence studies of wild-type JE virus, with SA14-14-2 and chimeric SA14-14-2 viruses, the mouse model for wild-type JE virus using strain P3 following peripheral inoculation has been established. Brains of P3 and mock-infected mice were paraffin embedded and tissue slides were prepared. Immunohistochemistry and immunofluorescence assay was utilized to identify JE virus antigen in the brain. Currently, cellular markers are being screened to characterize JE infection in the brain. Confocal microscopy revealed JE infection in the mouse brain is confined to neurons.