SCPA/D 3231037 : MAJOR: PATHOBIOLOGY ; Ph.D. (PATHOBIOLOGY)
KEYWORD : JAPANESE ENCEPHALITIS VIRUS / ENVELOPE PROTEIN / DENGUE VIRUS TYPE 2 / MUTATION

SIRITORN BUTRAPET : MOLECULAR CHANGE OF FLAVIVIRUS WHICH INVOLVES IN ITS PATHOGENESIS. THESIS ADVISORS : VINA CHURDBOONCHART Ph.D., NATH BRAMARAPRAVATI Ph.D., SOMPHONG SAHAPHONG Ph.D., SUDA RIENGROJPITAK Ph.D. 176 p. ISBN 974-588-912-1

Conformational changes of the envelope protein (E) of Japanese encephalitis virus (JEV) and mutations in the genome of Dengue type 2 virus (DEN2) are examples of molecular changes which effect flavivirus pathogenesis. Entry of JEV into the cells was studied using JEV-specific neutralizing monoclonal antibody (MAb) 503, radiolabeled-JEV, and observations with microscope. Treatment with MAb503 strongly inhibited internalization of JEV into the cells but not binding of the JEV to the cell surface, and also resulted in enhanced release of JEV-RNA from the cells in the form of intact virus particles. Binding of the MAb503 induced the formation of protease resistance E protein. Because of the fusion inhibition activity of the MAb503, the binding of MAb503 to JEV probably interferes with the structural rearrangement of the E protein, which further resultes in the failure of viral internalization into the cells.

The genome of the attenuated DEN2-16681-PDK53 virus differs from that of DEN2-16681 virus by 9 nucleotide mutations. Recombinant infectious cDNA clones 16681/PDK53 viruses were constructed to investigate the affects of these mutations. Neurovirulence in mice and biological markers of the recombinant viruses were also studied. A mutation that occurred in prM did not effect virus virulence. Recombinant viruses containing mutation at position 57 in the 5'-noncoding region of PDK53 virus were significantly reduced in their virulence. A mutation of amino acid 250 in NS3 gene contributed a major part to temperature sensitivity phenotype. Small plaque size correlated well with a less virulence property of the recombinant viruses. Therefore, attenuation phenotype of the PDK53 virus is clearly defined by multiple genetic loci.