INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: Molecular characterization of Japanese encephalitis virus (JEV) strain SA14-14-2 and the development of recombinant Newcastle disease virus-based immunogen against JEV

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SHORT ABSTRACT

Japanese encephalitis (JE) – the mosquito-borne zoonosis, is a global public health concern. It is the predominant cause of acute encephalitis syndrome (AES) in Asia, the Western Pacific, and Australia. It is caused by the Japanese encephalitis virus (JEV), which belongs to the genus Flavivirus and is the prototype member of the JE serocomplex. The envelope protein (E) of JEV is a major antigenic determinant and responsible for immunogenic responses as well as receptor binding, membrane fusion and virion assembly. The non-structural protein 1 (NS1) of JEV helps in viral replication, generates an immune response and serves as a diagnostic marker for JEV infections.

Recently, JE/AES cases are reported to occur in areas with an established JE vaccination program that uses the JEV live attenuated vaccine strain SA14-14-2. We characterized the SA14-14-2 strain in baby hamster kidney (BHK-21) cells and observed an enhanced replication following its passage in BHK-21 cells. On sequence analysis and docking studies, the cell-culture adapted vaccine strain showed a relevant point mutation identical to its wild-type parent strain SA14, which suggests the possibility of reversion of SA14-14-2 following its adaptation in permissive host cells.

Newcastle disease virus (NDV) is a notable virus of the poultry industry, but it does not affect humans due to its natural host-range restriction. NDV is used as a broad-spectrum vaccine vector to express several human and animal immunogenic proteins. We generated recombinant NDVs (rNDVs) individually expressing the E and NS1 proteins of JEV (rNDV-Ejev and rNDV-NS1jev). The rNDVs induced immunity against JEV upon intranasal immunization in BALB/c mice. They produced sufficient neutralization antibody titers against both NDV and JEV and also T helper cells (Th1 and Th2) mediated immune responses. On comparison with rNDVs expressing NS1, and a combination of both E and NS1, the results suggested rNDV-Ejev can be a promising live viral-vectored vaccine against JEV.

The differential diagnosis of JEV with the existing diagnostic kits is inefficient because of the immunocrossreactivity between the envelope proteins of JEV and other antigenically similar and co-circulating flaviviruses such as West Nile virus (WNV) and Dengue virus. Based on in-silico analysis, we identified four epitope-based peptides on the JEV E and NS1 proteins, which are conserved, surface-exposed, solvent-accessible, and predicted to have good B- and T-cell epitope binding efficiency. This study will help in the development of a peptide-based enzyme-linked immunosorbent assay (ELISA) against JEV with the least immunocrossreactivity.