1. Introduction and Exposition of Problem

Rapid globalization has paved the road for re-emergence of arthropod borne infection, which were once exotic and confined to particular endemic regions. Entities of major global concern include Japanese encephalitis virus (JEV) and other arboviruses (such as West Nile virus (WNV), dengue virus, yellow fever virus (YFV), etc) belonging to Flaviviridae family. In India, JEV is one of the major causative agents associated with outbreaks of viral encephalitis in pediatric population. JEV infection in humans can range from mild febrile illness to a full-blown meningoencephalomyelitis, with the ratio of clinical encephalitis to sub clinical infection in the range of 1:300. Severe JEV infection results in permanent impairment of neurological functions of the host. Consequently, JEV not only causes immediate disease burden, but it leaves a socio-economical burden on the society in the long run.

During an infection, interplay between the host immune response and the virus (virulence factors, capacity to evade the host immune response) plays an essential role in influencing the outcome of an infection. Innate immune response represents the first line of defense; on activation, it establishes a cascade of anti-viral immune responses as well as act as the scaffold for establishment of adaptive response. Several studies have shown immunoprotection and/or immunopathologic role of peripheral innate immune response during viral infection (such as HIV, HCV, HBV, and dengue virus).

In spite of several efforts to understand JEV-pathogenesis, the exact mechanism remains unclear. Until recently, most of the studies on JEV immunology are primarily focused on the adaptive immune response and are based on mouse or in-vitro models. Immune response studies to JEV infection in humans involve comparison of cytokine responses between JEV infected survivors and non-survivors, or humoral responses in vaccinated and non-vaccinated individuals. However, role of innate immune response during JEV infection in humans remains elusive.

Therefore, we studied the interaction between JEV (pathogenic wild-type / attenuated vaccine strains), peripheral antigen presenting cells (i.e. macrophages, DCs) and innate anti-viral response (type-I interferon, nitric-oxide, and CD56\(^+\) NK/NKT cells) to
understand the ability of JE-viral virulence in modulating the innate immune response. We hypothesized that pathogenic (i.e. wild-type / clinical isolate) JEV strain might hamper innate immune response activation or might be less-sensitive to innate anti-viral response as compared to the vaccine JEV strain. Studying JEV pathogenesis / immunology would enable us not only to comprehend the pathophysiology of the disease, but also in devising therapeutic and/or vaccination strategies that would minimize the neurological deficits of the host.