

## **Abstract**

Powassan virus (POWV) is recognized as an emerging Tick-Borne virus entering Long Island and the Northeastern US that causes severe neuronal damage which substantially impacts human health. Both the NIH and DOD have announced funded programs for research on Tick-Borne pathogens including POWV. POWV is a neurovirulent flavivirus that spreads across endothelial cells that comprise the blood brain barrier to protected neuronal compartments. Based on our current pathogenesis studies of Zika virus, a related mosquito-borne flavivirus, we are well suited to develop a research program that defines determinants of POWV pathogenesis and therapeutic approaches to resolving POWV infection, spread and neurovirulence.

Proposed seed funding is needed to generate data for Grant submissions on POWV. Seed funding will permit my lab to acquire preliminary data on the pathogenesis of Powassan virus in primary human brain microvascular endothelial cells (hBMECs) and resolve potential targets for therapeutic intervention. Our approach is to reveal mechanisms by which POWV regulates normal hBMEC functions that permit POWV to bypass innate immune responses, regulate POWV transcriptional responses and spread across hBMECs to protected neuronal compartments. Our studies are aimed at defining determinants of POWV pathogenesis that have the potential to be therapeutically targeted to reduce or prevent severe neurologic consequences.

Seed funding will permit us to successfully compete for NIH and DOD grant support recently announced through an NIH Notice of Special Interest for Advancing Research for Tick-borne Diseases; and a Congressionally Directed Medical Research Program (CDMRP) of the DOD Entitled "Defense Health Program: Tick-Borne Disease Research Program. Both of these announcements have targeted funding for Tick-Borne POWV research and defining determinants of POWV pathogenesis.