Title: Entry and Assembly of Pathogenic Viruses

Abstract: Engineering of virus-like particles (VLPs) is a viable strategy for development of vaccines and for identification of therapeutic targets without using live virus. The present work is focused on the generation and characterization of quadruple-antigen SARS-CoV-2 VLPs as virus surrogate and analysis of chikungunya virus 6K structural protein anticipated to play an important role in viral egress. VLPs were generated by transient transfection of two expression cassettes in adherent HEK293T cells – one cassette containing M^{pro} for processing of three structural proteins (M, E and N), and the second cassette expressing the Spike protein. Further characterization revealed that the VLPs retain close morphological and antigenic similarity with the native virus, and also bind strongly to the SARS-CoV-2 receptor hACE-2 in an *in vitro* binding assay. Interestingly, the VLPs was found to internalize into U87-MG cells through cholesterol rich domains in a dynamin dependent process. Finally, our results showed that mice immunized with VLPs induce robust humoral and cellular immune response mediated by enhanced levels of IL-4, IL-17 and IFNγ. Taken together, our results demonstrate that VLPs mimic the native virus and induce strong immune response indicating possible use of these particles as an alternative vaccine candidate against SARS-CoV-2. VLPs can also be effective in mapping the initial stages of virus entry and screening of inhibitors. In the second part of this work, we have made an effort to structurally analyze the chikungunya virus 6K hydrophobic peptide by utilizing electron microscopy, biochemical and *in silico* studies.