Project Proposal for Ph.D.

**Project Details**

**Project Title**
Repurposing drugs for anti-Chikungunya therapeutics: combining *in silico*, *ex vivo* and *in vivo* approaches

**Project Summary**
Chikungunya Virus (CHIKV) is a mosquito-borne alphavirus of the family *Togaviridae* which causes major outbreaks globally. There are no licensed therapeutics or vaccines against CHIKV. We aim to design effective drugs to prevent the propagation of CHIKV in host cells, by targeting an ion channel protein called 6K, which is crucial for virus assembly and budding. We have shown that an anti-influenza drug, amantadine, can be repurposed to prevent CHIKV infections in cell culture. The interaction of amantadine and its derivatives, as well as other FDA approved drugs, with recombinant 6K will be tested *in silico*. The effect of selected drugs to prevent the ion-channel activity of recombinant 6K will be tested using biochemical assays standardized in IIT-Delhi.

We will then test these selected drugs in cultured cells for their anti-viral properties. CHIKV is known to infect synovial fibroblasts leading to joint inflammation in human subjects. We will use primary mouse embryonic fibroblasts, which provide for genetically tractable and biochemically amenable ex vivo cell system. We will determine if these drugs prevented entry and replication of CHIKV in cultured mouse embryonic fibroblasts and curtailed the viral yield. We will perform some of the key *ex vivo* experiments in human-derived SW982 synovial fibroblast cell line. In addition, we plan to examine if some of these drugs reinforce anti-viral cell signaling. Finally, we will examine the efficacy of these drugs in the mouse infection model for CHIKV. We hope that this comprehensive set of analyses will improve therapeutic options against the Chikungunya menace.

**Ph.D. Supervisors**

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<tr>
<th>Role</th>
<th>Name of Faculty</th>
<th>Academic Unit in IITD/Institute/University</th>
<th>Email ID (Official)</th>
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<tbody>
<tr>
<td>Supervisor 1</td>
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**Project requirements (Student qualifications, experience required, etc)**

*The candidate will be shortlisted based on common shortlisting criteria decided by ScRC (SIRe)*

- The student must have M.Sc. or M. Tech. degree in any branch of biological sciences, with excellent academic record throughout.
- The student must have CSIR/DBT-A/ICMR/INSPIRE JRF qualification and must be eligible for receiving research fellowships from these agencies.
- The student must have some experience in molecular biology and cell culture techniques

**Source of fellowship/funding**

( Allowable options: CSIR/UGC/DBT/ICMR/ICAR/NEET-PG/DST-INSPIRE/IRD/FITT Project details, if any)

Own Fellowship

**Role of Faculty Members involved:**
**Supervisor-1**

Prof. Manidipa Banerjee’s laboratory at the Kusuma School of Biological Sciences works at the interface of computational and experimental biology with the goal of understanding host-virus interactions and to identify effective antivirals. Prof. Banerjee will guide the student for computational screening of potential inhibitors of CHIKV 6K. Purification of recombinant 6K, and the effect of selected inhibitors on the membrane activity of 6K will be carried out in Prof. Banerjee’s laboratory.

**Supervisor-2**

Dr. Basak possesses close to fifteen years of research experience in experimental animal models. In particular, his laboratory has optimized the mouse infection model for Chikungunya virus. In addition, the PI has a deep interest in understanding fully the anti-viral host signaling pathways. Dr. Basak will provide training in ex vivo cell signaling studies and in vivo mouse infection research. The training will include technical modalities as well as data analyses.