IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	**Identification of human host factors required for human influenza virus assembly and budding**	
Project Number	**IMURA0684**	
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Research Academy Themes:

Highlight which of the Academy's Theme(s) this project will address?
(*Feel free to nominate more than one. For more information, see www.iitbmonash.org)*

1. Advanced computational engineering, simulation and manufacture
2. Infrastructure Engineering
3. Clean Energy
4. Water
5. Nanotechnology
6. **Biotechnology** and Stem Cell Research **(Basic biology, Molecular Biology/Virology)**
7. Humanities and Social Sciences

The research problem

Influenza infections affect more than 60 million people every year worldwide. Of the three known types of influenza virus (A, B and C), type A influenza virus is the most

harmful and is usually responsible for large flu epidemics. Because of their ability to evolve rapidly, influenza A viruses that infect birds and other animals have the ability to cross the species barrier and could cause fatal infections in humans. This rapid evolvability and error prone RNA replication also resulted in resistance to commercially available drugs such as Zanamivir and Osletamavir (tamiflu). Hence, it is essential to understand the virus cycle, how viral proteins interact with host factors and hijack certain pathways for its replication. Influenza A virus (IAV) code for up to 13 proteins and many of them have to interact with multiple host factors in order to establish a successful replication cycle. Previous genome-wide RNAi based studies have identified around 1400 human genes as potential host factors involved in influenza virus replication. However, host factors responsible for virus assembly and budding, nature of their interactions, have not been conclusively established from these studies yet. The aim of this study is to map the human host cellular proteins that interact with viral matrix proteins matrix proteins M1 (a bifunctional protein that binds to both membrane and RNA) and M2 (a small proton channel forming protein that plays an important role in both early and later stages of virus replication) of IAV strain H3N2 (laboratory strain X31) of influenza virus on infecting A549 cell lines (alveolar basal epithelial cells) and identify the drugs that disrupt the virus-host interactions significantly. This study will provide insights into the identification of new possible therapeutic targets to stymie the infection.

Project aims

1. To identify new host partners of IAV matrix proteins, M1 and M2, infecting A549 cell line in the purified complex by liquid chromatography-tandem mass spectrometry (LC-MS/MS) and generate an interactome map of the host interacting proteins.
2. Study the effect of overexpression of IAV M1 and M2 proteins on the host proteome.
3. Effect of silencing of selected host factors on the virus assembly and replication processes.
4. Identification of putative drugs/inhibitors for disruption of host viral interaction as potential antiviral targets.

Expected outcomes

The findings from this study will help in understanding how the host factors/pathways are utilized by IAV for its assembly and budding. Identification of these interactors will further help in devising novel anti-viral strategies to combat IAV infection.

How will the project address the Goals of the above Themes?

Although a large number of studies have been carried out on understanding the influenza virus infection biology and epidemiology, the host factors that are essential for virus assembly and budding are poorly understood. Hence, this study has the potential for aiding novel intervention strategies by providing insights into the fundamentals of IAV assembly and budding. In addition, it will help in translating our basic understanding of Influenza virus infection cycle into developing novel anti-viral therapeutics.

Capabilities and Degrees Required

MSc in Microbiology, Virology, Biochemistry, Life Sciences, Immunology, Molecular Biology, Biotechnology or BTech/BE or MTech/ME in Biotechnology and related subject areas

Capabilities highly desired:

1. Mammalian cell culture
2. Cloning
3. Protein purification
4. Microscopy (fluorescence/confocal)

Potential Collaborators

Please visit the IITB website www.iitb.ac.in OR Monash Website www.monash.edu to highlight some potential collaborators that would be best suited for the area of research you are intending to float.

Please provide a few key words relating to this project to make it easier for the students to apply.

Influenza virus, interactome, virus budding, assembly, antiviral