IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	**Finding cues for metabolism inside giant virus particles – Are giant viruses 'alive'?**	
Project Number	**IMURA0787**	
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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

The study of giant viruses began only a decade ago when the first virus (mimivirus) with a megabase genome was isolated, successfully cultured in the lab, and sequenced.
The discovery of mimivirus was entirely unexpected and redefined our understanding of 'what a virus is'. Mimivirus is bigger than many bacteria and its discovery caught everyone off guard as the dogma of what a virus is and what a virus should be had taken firm grips in the minds of researchers as filterable non-

living “particles”. From the discovery arose many fundamental questions, pertinent not only to the nature of viruses, but to ‘life’ more generally, including: What is the origin and evolution of mimivirus? How and why is this virus so big and complex? Where does it belong in the tree of life? Indeed, whether giant viruses belong in the tree of life at all, are matters of continued debate. Analysis of some of the unique genes indicate that mimivirus could have emerged well before the cellular organisms, so representing a critical progenitor to cellular life. Recent discoveries have further shown that mimivirus is not just a freak of nature, and its close relatives exist in large numbers everywhere -- from a lake in India to a pond in La Trobe University, Melbourne to permafrost of Siberia. Pandoravirus with 2.5 Mb genome and Pithovirus sibercum with a particle size of 1.5 μm are the current record holders.

Normally, virions house a small genome and sometimes a few proteins tightly associated with the genome, and so have no intrinsic metabolic/biological activity outside of a host cell, essentially representing inert ‘particles’; this is a key defining property of viruses. However, some giant viruses appear to have broken this ‘rule’ by having large amounts of proteins and RNA packaged independently of the genome. In essence, these viruses have a distinct genomic compartment and a surrounding proteinaceous/RNA-containing compartment, and so look very much like cells. In cells, such protein/RNA material would be intricately arranged into functional domains, and such organization would be a precursor to life, but ‘sub-virion’ organization of the packaged material in not known. Such organization could enable activity independent of host cell, a possible precursor to cellular metabolism. We plan to investigate these possibilities with the following aims.

Project aims

1. To perform quantitative proteomic, transcriptomic and bioinformatics analysis of giant virions to make predictions on potential functional proteins
   This will enable us to identify candidate proteins/RNA for further analysis of potential functions within the virion
2. To use confocal and super-resolution imaging of virions to define the localization of these proteins and RNA, and compaction of genome.
   This will enable us to determine whether giant viruses form intra-virion complexes/domains indicative of a cell-like architecture, as well as indicating whether such complexes might be active in the virion, including within the genome.
3. Metabolic analysis of virions, including use of energy sources and synthesis of biomolecules such as mRNA.
   This will determine whether virions have the capacity to mediate biological processes independently of host cells – indicative of a primordial form of ‘life’

Expected outcomes

Findings from this study will help in understanding potential way that giant viruses fit into the tree of life, possibly as key links in the evolution of cellular life.

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

The aim of the project is to explore whether virions of giant viruses are metabolically inert or active. Expertise and facilities available at IIT Bombay and Monash University will help in devising experiments to tease out the details.

Capabilities and Degrees Required

MSc in Microbiology, Virology, Biochemistry, Life Sciences, Immunology, Molecular Biology, Biotechnology or BTech or MTech in Biotechnology

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.

Dr Toby Bell (Monash, School of Chemistry)– physical chemist with expertise in super-resolution microscopy analysis of biological systems; already a collaborator of Moseley, with whom he has produced novel insights into viral infectious processes using single molecule imaging techniques.

Dr. Darren Creek (Monash Institute of Pharmacological Sciences) – Biochemist expert in metabolomics analysis, who will enable analysis of potential metabolic activity in giant virus virions.

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

Giant viruses, live cell & super-resolution microscopy, proteomics, functional genomics, metabolomics