IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	**Hybrid Lipid-Protein Based Nano Drug Delivery Systems**	
Project Number	**IMURA0944**	
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Research Clusters:

Highlight which of the Academy's CLUSTERS this project will address? *(Please nominate JUST **one**. For more information, see www.iitbmonash.org)*	
1	*Material Science/Engineering (including Nano, Metallurgy)*
2	*Energy, Green Chem, Chemistry, Catalysis, Reaction Eng*
3	*Math, CFD, Modelling, Manufacturing*
4	*CSE, IT, Optimisation, Data, Sensors, Systems, Signal Processing, Control*
5	*Earth Sciences and Civil Engineering (Geo, Water, Climate)*
6	*Bio, Stem Cells, Bio Chem, Pharma, Food*
7	*Semi-Conductors, Optics, Photonics, Networks, Telecomm, Power Eng*
8	*HSS, Design, Management*

Research 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*
7	*Humanities and social sciences*
8	Design

The research problem

In the drug discovery process, new molecular entities (synthesized or modified) are usually hydrophobic affecting their bioavailability and clinical exploitation. Functionalization of drugs to improve solubility in the aqueous phase can compromise with their potencies thus posing a serious problem in pharmaceutical industry, and hence get dropped from development in the preclinical stage itself. Therefore, there is a need to develop drug delivery systems which can solubilize these compounds, are non-toxic, and are able to penetrate cell membrane to release drug at specific target sites.Amphiphilic lipid based bicontinuous cubic phases can offer robust, versatile and relatively inexpensive matrix for encapsulation of a variety of drug molecules including peptides and protein. Further, a hybrid lipid-protein based nano drug delivery system can offer improved drug delivery due to properties of both the lipid and protein in the carrier system. A quantitative understanding of drug affinity towards such formulations in terms of partitioning, release and correlation with the properties of the drug delivery systems and the drugs are important in deriving guidelines for rational drug design and drug delivery vehicles.

Project aims

The project aims to develop lipid based (vesicles in comparison with bicontinuous cubic phases) drug delivery systems which are capable of encapsulating a variety of drugs including those based on peptides and proteins. The proteins and additive lipids forming such cubic phases of amphiphilic nature, can phase separate locally and adopt a preferred location, and thus provide an environment which can effectively encapsulate drugs with varying degree of hydrophobicity, peptides and proteins including membrane proteins. Specifically, the aims of the proposal are following:

- develop lipid based bicontinuous cubic phases drug delivery systems (DDSs) which are capable of encapsulating a variety of drugs including those based on peptides and proteins.
- Study the partitioning of drugs (including peptides and proteins) in such DDSs both qualitatively and quantitatively by using a variety of techniques such as isothermal titration calorimetry, differential scanning calorimetry, fluorescence, uv-visible, NMR and Mass Spectrometry.
- Size-shape analysis of thus developed hybrid protein-lipid cubic phases nanosystemsby SAXS, SANS, DLS, Imaging
- Solubility/encapsulation of drugs with varying extent of hydrophobicity, peptides, and proteins in the DDSs under investigation
- Interaction of molecular entities (drugs/peptides) to be incorporated with lipids and additive proteins forming the cubic phases to understand role of their association in DDS
- the exact location of drugs, transmembrane proteins, and peptides within the bicontinuous cubic phase unit cell will also be focused at.
- Cell studies to address cytotoxicity and cancer cell affinity / cell viability
- Develop structure-property-energetics relationship correlations and identify functionalities responsible for improved DDS.
- Special focus will be on anticancer peptides with an aim of developing DDS which have ability to penetrate cell walls and deliver drug without toxic effects of the components of the DDS.

Expected outcomes

Target oriented drug delivery systems with specific focus on tumor cells are expected to be major outcomes of the proposed work. The deliverables will not just be a qualitative understanding of the

incorporation of proteins in lipid cubic spaces, but also a quantitative understanding of such lipid-protein interactions, and interactions of the encapsulated drugs with these components. These interactions will decide the ease of delivery of the encapsulated drugs at the target site with an advantage of cell membrane penetration via these developed nanosystems. A structure-property-energetics correlation is expected to contribute to recognition of cancer cell markers. The developed drug delivery systems will also provide a multi-component platform for drug delivery capable of targeting multiple features of cancer cells and tumour environment. Further, the work will lead to development of biocompatible drug delivery systems withlow or no healthy cell toxicity, and helpful in recognizing significant markers in tumour cells.Overall the proposed work will contribute to the ongoing efforts in cancer treatment.

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

The developed drug delivery systems will be nano-sized vehicles which will have the ability of encapsulating a variety of drugs and have ability of penetrating cell membranes and delivering drugs at target sites. Thus the proposed work is a direct application of nanotechnology in biotechnology.

Capabilities and Degrees Required

The students should have the following capabilities:
The student should be capable of working at the interface of Chemistry/Chemical Engineering/Biochemistry. The candidate should have major degree in Chemistry/Chemical Engineering/Biotechnology/Biochemistry/Physical Chemistry

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.