IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	Blood brain barrier (BBB) on chip	
Project Number	**IMURA0689**	
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IITB Department:	Mechanical Engineering	

Research Clusters:

Highlight which of the Academy's CLUSTERS this project will address? 6

*(Please nominate JUST **one.** For more information, see www.iXXXXX.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***

The research problem

Define the problem

An organ-on-a-chip is a microfluidic cell culture device that features continuously perfused channels covered by living cells that are arranged to simulate tissue- and organ-level physiology. One particular organ structure is the blood-brain barrier (BBB). Research efforts are directed at mimicking the BBB on a chip in order to understand roles of brain microenvironment in viral infections and brain tumour progression.

The goal of this proposal is to develop a high-throughput and yet highly predictive experimental platform, base on the use of a brain organoid-on-a-chip with BBB and microfluidics, to enable fast evaluation of new therapeutics performance, and unlock unprecedented insights into the roles of brain microenvironment in viral infections.

This project aims to develop a brain organoid on-a-chip that composes of an in-vitro BBB monolayer and a 3D co-culture of brain cells. The microfluidic chip will have a layer of fractal channels with decreasing diameter and heights. These channels will be coated with extracellular matrix proteins lined with cerebral endothelial cell monolayer representing the BBB. The channels will on one side be separated by a porous membrane from a wide channel which will the house 3D matrix of brain cells (astrocytes and glioma cells).

We envisage that this organoid-on-a-chip will be a versatile brain disease model. Here, we focus on two applications to demonstrate the potential: 1) Testing therapeutics in high-throughput: There are numerous strategies documented for maximising drug delivery to the brain tumour such as chemotherapeutics disguised in transferring-coated nanoparticles. However, the efficacy of nanoparticle delivery has been questioned. Using this platform, we will visualise the BBB transcytosis, tumour cells targeting, cytotoxicity, proliferation, metastasis, and decipher the mode of action. 2) Visualising viral invasion of a developing brain microenvironment: Zika virus, which is believed to cause microcephaly of fetuses, is a pressing issue nowadays. There is a constant debate on how and why fetuses are sometimes vulnerable to viruses, despite BBB is fully functional since it is developed. Using the organoid-on-a-chip, we will recreate features of a developing brain, such as an increase in plasma protein concentration, decreased astrocyte populations and increased hydrostatic pressure. We will use non-replicating adenovirus particle carrying luciferase transgene to represent the virus. Infection rate will be measured by measuring luciferase activity in the brain organoid.

Project aims

Define the aims of the project

The specific aims are:

1. To develop a physiological relevant 3-dimensional BBB/brain/ tumour organoid-on-a-chip brain disease model.
2. To apply this model in high-throughput screening of targeted chemotherapeutics against brain tumour and interrogate their interactions with the brain cells.
3. To apply this platform to decipher the microenvironmental characteristics in a developing brain/ BBB that makes the brain vulnerable to viral infections.

Expected outcomes

Highlight the expected outcomes of the project

A microfluidic device based on lithography-less fabrication, which enables us to assess the integrity of the BBB in biomimetic blood vessels when challenged by drugs, nanoparticles and viruses.

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

Describe how the project will address the goals of one or more of the 6 Themes listed above.

This project will enable us to develop better therapeutics to treat viral infections affecting the brain as well as currently incurable brain tumours.

Capabilities and Degrees Required

List the ideal set of capabilities that a student should have for this project. Feel free to be as specific or as general as you like. These capabilities will be input into the online application form and students who opt for this project will be required to show that they can demonstrate these capabilities.

Bachelors or Masters degree in Materials or Mechanical Engineering, ideally with experience in mammalian cell culture. Strong hands-on expertise with fluidics.

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.

Select up to **(4)** keywords from the Academy's approved keyword list **(available at www.iitbmonash.org)** relating to this project to make it easier for the students to apply.

Bioengineering and biosciences, mechanical engineering,