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| Project Title: | Advanced microgels for delivery and penetration of CAR-T cells into solid tumors | |
| Project Number | IMURA1032 | |
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Research Clusters:

Research Themes:

| Highlight which of the Academy's CLUSTERS this project will address? <i>(Please nominate JUST one. For more information, see www.iitbmonash.org)</i> | | Highlight which of the Academy's Theme(s) this project will address? <i>(Feel free to nominate more than one. For more information, see www.iitbmonash.org)</i> | |
|--|---|--|--|
| 1 | Material Science/Engineering (including Nano, Metallurgy) | 1 | Artificial Intelligence and Advanced Computational Modelling |
| 2 | Energy, Green Chem, Chemistry, Catalysis, Reaction Eng | 2 | Circular Economy |
| 3 | Math, CFD, Modelling, Manufacturing | 3 | Clean Energy |
| 4 | CSE, IT, Optimisation, Data, Sensors, Systems, Signal Processing, Control | 4 | Health Sciences |
| 5 | Earth Sciences and Civil Engineering (Geo, Water, Climate) | 5 | Smart Materials |
| 6 | Bio, Stem Cells, Bio Chem, Pharma, Food | 6 | Sustainable Societies |
| 7 | Semi-Conductors, Optics, Photonics, Networks, Telecomm, Power Eng | | |
| 8 | HSS, Design, Management | | |

The research problem

CAR-T cells are genetically modified T cells that express cell surface receptors that specifically target antigens on cancer cells. Despite clinical success for the treatment of blood cancers, the therapy is largely ineffective for the treatment of solid tumors. This is due to poor site retention of CAR-T cells and the inability of the cells to penetrate the extracellular matrix of the tumor.

There are several other challenges that hinder the success of cell-based immunotherapy, or CAR-T cells, in solid tumors. These include the heterogeneity of tumor antigens and the 'cold'/immunosuppressive

tumor microenvironment. There are several ongoing clinical studies to test cell-based immunotherapies solid tumors. In this project, we will focus on ovarian and pancreatic cancer and their 'cold'/immunosuppressive tumor microenvironment.

Project aims

The overall aim of this project is to develop a biomaterial/CAR-T cell therapy for the treatment of solid tumors. This will be achieved by

1. Generating CAR-T cells and encapsulating them within microgels using a microfluidic technique
2. Identifying factors to help CAR-T cells infiltrate the tumor microenvironment
3. Determine the efficacy of this approach using static and microfluidic multicellular 3D tumor models.

How skills/experience of the IITB and the Monash supervisor(s) support the proposed project

Prof. Tayalia's lab is already working on genetically modifying immune cells (T cells, DCs, macrophages) using viral and non-viral methods for cancer immunotherapy. Her lab has developed material platforms for studying tumor immune cell interactions using spheroid models.

What is expected of the student when at IITB and when at Monash?

The project brings together a multi-disciplinary team of experts in biomaterials for cancer treatment (Tayalia, Loessner), cancer biology (Loessner) and hydrogels/microfluidics (Forsythe). Together, this group will train a PhD student in the rapidly growing field of immunotherapy for cancer treatment.

Expected outcomes

The PhD project will determine the efficacy of using a biomaterials approach to treat solid tumors. Specifically:

- i) CAR-T cells can be encapsulated within microgels and delivered directly at the site of tumor via a minimally invasive injection.
- ii) Microgels will be able to deliver additional cargo that will weaken the tumor ECM allowing penetration of the CAR-T cells.
- iii) Develop a deeper understanding of the factors that will yield increased on-target function of CAR-T immunotherapy.

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

CAR-T cell immunotherapy holds significant promise for the treatment of many cancer with multiple companies in Melbourne and Mumbai now manufacturing cells for this personalised medicine, e.g. Cartherics. This project directly addresses the Theme of "Biotechnology" and will help train a PhD student across multiple disciplines, e.g. med tech, biomaterials, biology and immunotherapy.

Potential RPCs from IITB and Monash

Prof Gail Risbridger, Dept Anatomy and Developmental Biology, Monash University. World expert in prostate cancer.

Prof. Rahul Purwar, Department of Biosciences & Bioengineering, IIT Bombay. CAR-T cell expert in hematological malignancies.

Capabilities and Degrees Required

The student should ideally have a background in one or more of the following: cell biology, biomaterials or biomedical engineering.

Necessary Courses

Name three tentative courses relevant to the project that the student should complete during his/her coursework at IITB (the student will require to secure 8 point in these courses)

BB 616-Cellular and Tissue Engineering
BB 706-Fundamental and Practical Aspects of Microscopy
BB 612-Cell Mechanics and Mechanobiology
BB 408-Immunology

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.

Prof Forsythe has an existing collaboration with the CAR-T cell manufacturer, Cartherics, who will be approached to supply cells.

Select up to **(4)** keywords from the Academy's approved keyword list (**available at <http://www.iitbmonash.org/becoming-a-research-supervisor/>**) relating to this project to make it easier for the students to apply.

BioScience, Bio Medical Engineering, Novel Functional Materials