

# Optimizing systemic therapies of metastatic and recurrent triple-negative breast cancer using next generation 3D models

## Project Description

<p>Project duration:</p>	<p>Joint PhD Program – Between The University of Queensland and Indian Institute of Technology Delhi.</p> <p>4 years</p> <p>The Academy joint PhD research projects are well defined and developed by a collaborative team of researchers at UQ and IITD. Selected PhD students working on a project will be supervised by a joint supervision team of UQ and IITD academics.</p>
<p>Description:</p>	<p>Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer and is characterized by a lack of estrogen, progesterone and human epidermal growth factor receptor (EGFR) expression. TNBC is more likely to recur than the other two subtypes and one of the primary challenges to treat TNBC is its intra-tumoral heterogeneity (ITH). Recent evidences have shown that these micro-environmental differences led ITH creates hurdles for effective therapy response. In this project, we discuss the evidence of intratumoral heterogeneity and its impact on the disease progression including sensitivity to different treatment options particularly chemotherapy and immunotherapies (PD1/PDL1 based). In this project, we aim to evaluate this Intra-tumoral heterogeneity of TNBC through next-generation patient-derived 3D tumour organoid and explant models, which can effectively expedite preclinical responses towards immune-antibody-directed therapies.</p> <p><u>Aims and Methodology:</u></p> <p>Aim 1. Characterization of genomic, transcriptional, and metabolic signatures identifying intra-tumoral heterogeneity in TNBC patient samples: By examining the spatiotemporal heterogeneity in TNBC, we hope to identify novel targets and biomarkers for personalized therapy. This will be a prospective study where we will collect tumor samples from TNBC patients undergoing biopsy or surgery. The samples will be compartmentalized into vascular-rich and hypoxic niches based on the classical marker gene expression. The genomic, transcriptional, and metabolic profiles of these samples will be analyzed using next-generation sequencing of DNA and RNA (StereoSeq) and LC/MS and metabolomics techniques</p> <p>Aim 2. Next-generation organoids that accurately replicate the intratumoral heterogeneity observed in TNBC tumors can be used to evaluate the response of different tumor subpopulations to therapy</p>

	<p>and to validate new therapeutic targets: In this objective we aim to develop next-generation organoid models.</p> <p>3. Assessment of PD-1/PD-L1 immunological therapy regimen on BC patient-derived explants under different environmental insults. Patient tissue-derived explant culture testing in a biomimetic tissue platform will be performed. The long-term culture of these biopsies will allow us to study how different cell populations interact and respond to therapies over time. The technology has enabled rapid and faithful characterization of perturbations across specific cell types within a tissue on exposure to different cytotoxic agents and immunomodulators. The effect of PD1 (Pembrolizumab, Nivolumab, Cemiplimab; and PD-L1 Atezolizumab, Avelumab, Durvalumab inhibitors) would be assessed ex vivo on breast cancer biopsies, to improve treatment outcomes for individual TNBC patients. Data privacy and confidentiality will be ensured throughout the study.</p> <p>A full comprehensive outline of the project can be found via this <a href="#">link</a>.</p>
Expected outcomes and deliverables:	<p>This is a UQ-Indian Institute of Technology (IIT), Delhi joint PhD project for a highly motivated and talented student to work on a groundbreaking project entitled optimising systemic therapies of metastatic and recurrent triple-negative breast cancer using next-generation 3 D models. Applicant will spend 2 years in IIT Delhi Lab and 2 years in Mater Research Laboratory. This opportunity offer a dual PhD from two world-renowned institutions, access to state-of the art facilities and collaborations with leading researchers in India and Australia.</p>
Suitable for:	<p>Applicant should hold a strong academic background (BSc Honours or Masters) in Biology, Biochemistry or related field. Applicant should be highly motivated and passionate about cancer research and possess excellent communication and teamwork skills.</p>
Primary Supervisor:	<p>Prof Kum Kum Khanna (mater Research Institute)  Assistant Prof Saran Kuma (IIT, Delhi)</p> <p>Call for EOT closes on 3<sup>rd</sup> October, visit the UQ-IITD website to apply <a href="https://uqiitd.org/apply/">https://uqiitd.org/apply/</a></p>
Further info:	<p>Prof Kum Kum Khana  e: <a href="mailto:Kumkum.khanna@mater.uq.edu.au">Kumkum.khanna@mater.uq.edu.au</a></p>