ANNEX W

LKCMedicine PhD Research Project Submission Form

<table>
<thead>
<tr>
<th>Research Theme (Please indicate as appropriate)</th>
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</thead>
<tbody>
<tr>
<td>☐ Dermatology &amp; Skin Biology</td>
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<tr>
<td>☐ Family Medicine &amp; Primary Care</td>
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<tr>
<td>☐ Health Systems &amp; Population Health</td>
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<td>☐ Infection &amp; Immunity</td>
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<td>☐ Metabolic Disorders</td>
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<td>☐ Neuroscience &amp; Mental Health</td>
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<tr>
<td>☐ Others (Please specify): Cross</td>
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<tr>
<td>☒ Medical Education</td>
</tr>
<tr>
<td>☒ Cutting Research</td>
</tr>
</tbody>
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Research Project Title:

An Integrated Multiplatform Analysis of the Role of Exosomes in Therapy Resistance In Cancers

Project Description:

Paclitaxel is the number 1 selling chemotherapy drug of all time and it acts by targeting microtubules during mitosis. Unfortunately, although the most successful of all chemotherapeutics, disease relapse and therapy resistance can still set in. The lab has identified a novel pathway to chemoresistance following treatment with anti-mitotic drugs. Extracellular vesicles known as exosomes mediate intercellular communication and the study of exosomes is an emerging field in cancer. These exosomes contain DNA, RNA including microRNA, that can be transferred from one cell to another. The role of exosomes, tumour cell intrinsic signaling pathways affected and the impact on the tumour environment will be studied. Insights from this research are expected to identify novel cellular targets that could be of relevance to the development of combination therapies to improve sensitization of tumour cells (enhancing efficacy and sensitivity of existing anti-mitotic drugs), or to overcome chemoresistance.

Brief summary of main Methodologies and/or Techniques to be learned during the proposed PhD (experimental or analytical):

Student will investigate whether exosomes play a role in a novel route of chemoresistance pathway identified in the lab. He/she will learn how generate therapy resistance through cell cycle experiments, isolate and quantify exosomes, and to conduct exosome transfer, flow-cytometry and time-lapse microscopy. Specific pro-tumourigenic assays will be utilized to assay for metastasis, angiogenesis and
inflammation. Inflammatory techniques related to cytokine profiling and tumour-associated macrophages. A combination of iterative mathematical/computational modelling and wet-lab experimentation is required for a systemic analysis of the interactions and cross-talks between genomics, transcriptomics, epigenetics, metabolomics, and inflammation-related signaling pathways for better understanding of the role of exosomes in therapy resistance. Student will meet and learn to work with scientists across various disciplines.

Keywords:
Cancer, Paclitaxel, therapy resistance, exosomes
### Supervisor(s)

#### Primary Supervisor
- **Name of Supervisor:** Karen Crasta
- **Designation:** Associate Professor
- **Email:** kccrasta@ntu.edu.sg

#### Co-Supervisor *(need not be determined at this time)*
- **Name of Supervisor:**
- **Designation:**
- **Email:**

### Main Location of Research Work *(Please indicate as appropriate)*
- ☒ LKCMedicine Experimental Medicine Building @ Yunnan Campus
- ☐ LKCMedicine Clinical Sciences Building @ Novena Campus
- Others *(Please specify)*: 

### Other Information

1. Does the proposal need IRB’s approval? ☐ Yes ☒ No
   - If “Yes”, is the IRB’s approval in place? ☐ Yes ☐ No
2. Does the project involve contact with patients? ☐ Yes ☒ No
3. Is there a potential for overseas academic exchange as part of this research project? ☒ Yes ☐ No
   - If “Yes”, please specify: Imperial College