Developing novel immune-oncology combination therapies for high-grade serous ovarian cancers

Project Description

Project duration:	PhD – 3.5 years
Description:	Epithelial ovarian cancer remains the deadliest form of gynaecological malignancy. Each year approximately 225,500 cases of ovarian cancer are diagnosed, and 140,200 patients succumb to this disease. It is the 5th most common cause for cancer-related death in women with overall survival time of <5-years. Epithelial ovarian cancer is sub-classified into different histotypes including high-grade serous (HGSCs), low-grade serous (LGSCs), and clear cell ovarian cancers. HGSCs accounts for approximately 70% of epithelial ovarian cancer. High-grade serous type ovarian cancer (HGSOC) accounts from most (>80%) cancer death from ovarian cancers and overall survival has not changed over several decades. To date, platinum-based chemotherapy remains a front-line treatment option for these patients. However, about 50% of HGSC patients either develop resistance to platinum-based chemotherapy or are inherently resistant to these chemotherapies. Moreover, high-dose platinum-based chemotherapies are often associated with severe side effects. To date, there are no targeted therapies available for these patients and hence, there is an unmet clinical need to develop safe and more effective targeted treatments for HGSC patients. Using high-throughput drug library screens, we have identified candidate targeted therapies for HGSCs. The aim of this project is to evaluate the anti-cancer activity of our candidate targeted therapies using a panel of HGSC cell lines and patient-derived tumour xenografts *in vivo*. We also aim to elucidate the underlying molecular mechanism for their anti-cancer activity using multi-omics approach (transcriptomics, proteomics, and metabolomics). Moreover, we will use CRISPR library screening to identify the biomarkers of response to our candidate targeted therapies, which will help to identify which tumour may or may not respond to our drugs and will also help to identify novel combination therapies. Furthermore, we will also assess the effect of our drugs on tumour immune microenvironment and identify potential novel immune-oncology combination therapies using syngeneic mouse models of HGSCs.
Expected outcomes and deliverables:	PhD student will acquire hands-on experience of multiple cell and molecular biology techniques and multi-omics techniques. Applicants

	acquire expertise in developing in vivo mouse models including patient-derived tumour xenografts and syngeneic mouse models to study the anti-cancer activity of drugs, effect of drugs on tumour immune-microenvironment, and underlying molecular mechanism for their efficacy. In addition, student will acquire excellent presentation, communication, and scientific writing skills. During the project, a PhD student will be expected to acquire a thorough background knowledge on the subject area, acquire training on multiple sophisticated scientific techniques, and develop skills in generating hypothesis, planning and executing experiments, analysing and interpreting the results, presenting their findings in lab meetings and conferences, and write scientific research articles.
Suitable for:	The successful candidate should have prior experience of working in a research lab and have honours degree completed. Candidate should be motivated and enthusiastic to establish a career in oncology research.
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