THE UNIVERSITY OF WESTERN AUSTRALIA

Targeted Epigenetic modification to improve Mesothelioma responses to immunotherapy

Outstanding candidates are encouraged to apply for a PhD project at the National Centre of Asbestos Related Diseases (NCARD), The University of Western Australia. NCARD is a national cooperative research centre that leads innovation and discovery to improve the lives of people affected by asbestos-related diseases. This is an exciting joint project with the Harry Perkins Institute of Medical Research (Perth, Australia) and University of Texas at Greehey Children's Cancer Research Institute (San Antonio, Texas).

National Centre for Asbestos Related Diseases

institute for RESPIRATORY HEALTH

Perkins
HARRY PERKINS INSTITUTE OF MEDICAL RESEARCH

Project description:

Mesothelioma is an aggressive and incurable cancer caused primarily by asbestos exposure. The prognosis is very poor, with five-year survival rates of only 3% for men and 12% for women.
Immunotherapy is an exciting treatment for mesothelioma because it can cause long-term tumour shrinkage. However, it only works exceptionally well for approximately 20% of cancer patients. The goal is to improve the number of mesothelioma patients who benefit from immunotherapy.

Expression of genes are regulated by changes made to the DNA without altering the underlying nucleotide sequence. Some modifications can switch a gene on while others switch genes off. In mesothelioma tumours, important immune genes are often switched off, which may explain why immunotherapy does not work well in some patients. Current epigenetic modifying drugs do not work well in mesothelioma because they lack gene-specificity, and potentially cause high toxicity. Our lab has developed a new, targeted technology called Epi-CRISPR that allows us to manipulate the epigenetic state of cancer-causing genes that will improve immunotherapy responses in patients.

This project will test Epi-CRISPR technology in mesothelioma tumours. We will switch on important immune genes, and use mouse models to test if immunotherapy will work better against these modified tumours.

The long-term application of our research is to use this technology with immunotherapy for mesothelioma patients, with the goal of turning a non-responding patient to a responding one.

Goals:

1. Develop an Epi-CRISPR platform able to activate genes involved in antigen processing and presentation in a panel of murine mesothelioma cell lines.
2. Assess the specificity and longevity of changes in the transcriptome in murine cell lines expressing Epi-CRISPR using next generation sequencing.
3. Validate in vitro and in vivo immunogenicity of Epi-CRISPR modified mesothelioma cell lines using immunoassays and murine models.

Applicant qualifications:

- Successful completion of an honours/master's in immunology, molecular biology or a closely related field, and must have completed a written research thesis
- Possess excellent molecular and protein biology skills, including experience with RT-qPCR, DNA/RNA extractions
- Proficient in cell culture
- Experience with flow cytometry
- Experience working with murine models, including performing tumour inoculations, blood collection, clinical symptom monitoring, euthanasia and analysis of organs
- Substantial experience independently organising and conducting complex procedures and experiments with minimal supervision
- Should be enthusiastic, driven and dedicated, have the ability and interest in learning new techniques; must be able to follow instructions; be observant, attentive to detail, organised, efficient, and work well with others

Preferred qualifications:

- Prior experience with next generation sequencing data analysis, including RNAseq and ChIPseq
- Prior experience in plasmid prep and cloning, transfections and chromatin immunoprecipitation assays
- Proficient in coding (R, Python)

Benefits:

- Be part of a dynamic research team that offers training and mentorship
- Potential pre-PhD vacation scholarship
- Potential travel to Texas, US

Project contact details:

If interested, please send a curriculum vitae and cover letter to:

Dr Jonathan Chee

Email: jonathan.chee@uwa.edu.au

Dr Charlene Waryah

Email: charlene.waryah@perkins.org.au

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