SUMMARY OF NCARD PROJECTS 2017

Project: Characterising neo-antigen T cell responses in mesothelioma immunity
Chief investigator: Dr Jonathan Chee

Brief description: Neo-antigens are mutated proteins which arise from DNA mutations caused by carcinogens, like asbestos. Neo-antigens are unique for every tumour, and some recent advances in whole tumour gene sequencing suggest the possibility of tailoring treatments that are specific to patients. This project focusses on neo-antigen CD8 T cells (otherwise known as CTL) to determine whether immunotherapy or chemotherapy can increase their frequency or change the effect they have on a tumour.

Funding source: US Department of Defense

Project: Improving treatment outcomes for malignant mesothelioma patients using biomarkers
Chief investigator: Professor Jenette Creaney

Brief description: Tumour biomarkers specific to malignant mesothelioma potentially offer an inexpensive, sensitive means of diagnosis. Findings from our group and others have identified biomarkers such as mesothelin-SMRP, fibulin-3 and calretinin. This study will perform a robust clinical evaluation of a panel of biomarkers for malignant mesothelioma diagnosis, monitoring and early detection.

Funding source: National Health & Medical Research Council (NHMRC) Project Grant 1063067

Project: Establishing the biological activity of malignant effusions in malignant pleural mesothelioma
Chief investigator: Professor Jenette Creaney

Brief description: Fluid accumulates between the lung and chest wall in many cancers, causing pain and difficulty in breathing. This is called a malignant pleural effusion. Malignant pleural effusions occur in over 90% of patients with malignant pleural mesothelioma. Conventionally this fluid is considered to be a by-product of the disease process. However, in preliminary studies we have found that this fluid is biologically active, that it may speed tumour growth and protect the tumour from the action of chemotherapeutics. We plan to study this phenomenon and explore its clinical impact.

Funding source: Dust Diseases Board of NSW (now iCare)

Project: Cancer chemo-immunotherapy: Exploiting the immunogenic momentum of cytotoxic chemotherapy
Chief investigator: Professor Richard Lake

Brief description: We recently found that chemotherapy has beneficial effects on the immune response against cancer rather than ill effects. Here we want to exploit this positive effect by combining different chemotherapeutics with immune-stimulating treatments in laboratory models. These studies will result in a better understanding of how chemotherapy influences the immune system, and may also result in new combinations that improve the effectiveness of cancer therapy.

Funding source: National Health & Medical Research Council (NHMRC) Project Grant 1067113

Project: Resetting the tipping point: converting immune checkpoint non-responders into responders
Chief investigator: Dr Willem Lesterhuis

Brief description: We want to characterise the events that occur during the decrease of the size of a tumour through successful immunotherapy, known as regression. We will do this by using animal models, and techniques developed in network science that allow us to pinpoint the key molecules that govern the response to treatment. We thus aim to tip the balance towards a response to immunotherapy, and increase the cure rate to thoracic cancer.

Funding source: National Health & Medical Research Council (NHMRC) Project Grant 1103980

Project: Identification of the molecular networks that drive mesothelioma invasion
Chief investigator: Dr Willem Lesterhuis

Brief description: Mesothelioma, a cancer of the pleural lining of the lungs, rapidly invades surrounding tissues such as the heart and ribcage, causing severe, treatment-resistant pain and shortness of breath. It is not known why mesothelioma is so invasive. We have developed animal models which faithfully demonstrate the invasive and rapid growth of mesothelioma. We will use these to investigate the mechanisms underlying this behaviour, to find novel treatments that inhibit this process.

Funding source: Cancer Council of Western Australia

Project: Comparing the immune response to cancer antigens in blood, lymph nodes and pleural effusion in lung and mesothelioma patients.
Chief investigator: Professor Bruce Robinson

Brief description: To improve immunotherapy for cancer we have to be able to determine how mutated cancer proteins are “seen”. Blood is the easiest and most useful source of immune “killer” cells, but the lymph node that drains the tumour, and the fluid that bathes a tumour probably contain a much higher number of these killer cells than blood. In this study we will obtain lung cancer tissue, draining lymph nodes and pleural fluid from patients who give their consent, examine and compare the samples and identify the killer cell responses.

Funding source: Cancer Council of WA 1125163

Project: Reactivities of CD8 T cells to mutated neo-antigens in lung malignancies
Chief investigator: Professor Bruce Robinson

Brief description: Tumours express mutated proteins (called neo-antigens) which can be targets of powerful killer T cells capable of destroying cancer cells. To understand why these T cells fail to cure most cancers, we will study and analyse neo-antigens identified by modern DNA sequencing methods, and the responses to them. The eventual aim is to design personalised vaccines for individual patients to “force” the immune system to attack cells bearing these neo-antigens.

Funding source: National Health & Medical Research Council (NHMRC) Project Grant 1107091

Project: The impact of therapy on T-cell recognition of mutated tumour neo-antigens
Chief investigator: Professor Bruce Robinson

Cancer is caused by mutations which should be detected by the patient's killer cells, in the same way that killer cells protect us from viruses. And yet this doesn't happen. This project will look at how current cancer treatments help the killer cells detect these mutations. Crucially, it will look at whether a vaccine consisting of mutated cancer proteins can stimulate anti-cancer killer cells in lung cancer and mesothelioma.

Funding source: National Health & Medical Research Council (NHMRC) Project Grant 1130737

Website: ncard.uwa.edu.au