Project Title: Development of broad spectrum, non-genotoxic cancer treatments for acute myeloid leukaemias and multiple myeloma.
Grant Awarded: $340,000 over 3 years: $113,334 in 2015-16
Principal Investigators: Prof Ross Hannan and A/Prof Anneke Blackburn, John Curtin School of Medical Research, The Australian National University.

February - June 2016

New therapeutic approaches for cancer are urgently needed. Our team has developed two novel approaches, targeting processes fundamental to cancer cell growth – the making of proteins and controlling metabolism. This proposal will initiate new studies combining these two approaches in models of blood cancers (multiple myeloma (MM) and acute myeloid leukaemia(AML)). The aims of the full proposal were to:

1. Identify metabolism modifying therapies that improve the effectiveness of CX-5461 in human cell lines and mouse models of AML and MM.
2. Identify metabolic signatures that associate with (i) sensitivity to, and (ii) acquired resistance to CX-5461 in AML and MM.
3. Validate new combination therapies and sensitivity/resistance mechanisms identified in Aims 1 and 2 in pa tient-derived primary xenografts of human AML.

With CCACT support, we will focus our efforts on Aims 1 and 2. We have employed a Research Assistant, Melissa Rooke, and are supervising two PhD students to contribute to this project, Laura Ferguson focusing on AML and Dan Tian contributing to MM studies.

To date, in Aim 1 we have initiated testing of drug combinations against blood cancer cells in the laboratory. A novel drug, CX-5461, which inhibits the making of proteins and is currently in clinical trials against cancer, is being combined with drugs already in use for metabolic problems such as high cholesterol, diabetes, or which can inhibit the uptake of glucose by cancer cells. We have identified several promising combinations that are undergoing further testing in vitro, and the best combinations will be tested in a mouse model of leukaemia. We are also making progress on aims 2 and 3, with the proposed metabolic studies to be initiated towards the end of 2016, and we have completed all the ethics requirements for aim 3.

We expect this combination approach will lead to highly effective cancer therapies with minimal additional toxicity to normal cells, relevant to many cancer types.

Conference Abstract:
D. Tian and A. C. Blackburn. Targeting the Glycolytic Phenotype of Multiple Myeloma with Dichloroacetate. In Lorne Cancer Conference. VIC, Australia. Feb., 2016.