Project Title: Targeting cancer metabolism to reduce metastases
Grant Awarded: $65,000 over one year (2018-19)
Principal Investigator: A/Prof Anneke Blackburn, John Curtin School of Medical Research, The Australian National University.

Interim report July 2019-June 2020
New therapeutic approaches for cancer are urgently needed, especially for drugs that can target metastatic cancer cells, or cancer cells that are resilient to chemotherapy. Our laboratory has been conducting a research program investigating the drug dichloroacetate (DCA) for over 10 years now. With regular support from the CCACT, we have performed laboratory studies on the effect of DCA on the growth and survival of several cancers, particularly breast cancer and the blood cancers, multiple myeloma and acute myeloid leukaemia, which have complemented our clinical trial research (1).

As part of our journey towards improving patient outcomes, we need to confirm that changes we observe in cells in the laboratory are also occurring in patients taking the drug. Our most recent work has demonstrated in normal white blood cells from myeloma patients in our clinical trial that the effect of DCA on its target protein could be observed at clinically relevant doses. Additional samples from patients are now needed to show this occurs in cancer cells as well as normal cells from patients taking DCA.

In breast cancers in mice, we are examining the differences between those that respond or don't respond to DCA treatment, focusing on features of the cancers that enable them to spread around the body (metastasize). Our first set of mouse tumours has been processed for gene expression, and the data is currently undergoing analysis for evidence of signatures or patterns indicating DCA can reduce the metastatic ability of these cancers. Once the analysis is optimized, additional archived tumour samples will be processed with this grant support, to strengthen and refine the signature.

Determining the correct effective dose, and being able to identify cancers most likely to respond to DCA are important steps in our ongoing program, paving the way for clinical trials in patients who will receive the most benefit from this drug.

Manuscript in preparation:
Markers for the effectiveness of dichloroacetate in multiple myeloma.
Dan Dan Tian, Melissa Rooke, James D'Rozario, and Anneke C. Blackburn.

(1) Tian DD, Bennett SK, Coupland LA, Forwood K, Lwin Y, Pooryousef N, Tea I, Truong TT, Neeman T, Crispin P, D'Rozario J, Blackburn AC. GSTZ1 genotypes correlate with dichloroacetate pharmacokinetics and chronic side effects in multiple myeloma patients in a pilot phase 2 clinical trial. *Pharmacology Research & Perspectives (2019). Oct 8;7(6):e00526. doi: 10.1002/prp2.526*