RACP
Specialists. Together
EDUCATE ADVOCATE INNOVATE

RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		Whole body analysis of human immune cells
Name		Dr Claire Gordon
Award Received		2020 RACP Research Establishment Fellowship
Report Date		19/05/2021
Administering Institution		Austin Health
Funding Period	Start Date:	01/08/2019
	Finish Date:	31/12/2020

PROJECT SUMMARY

T cells provide critical immune protection against infection and cancer, and dysfunctional T cells cause autoimmune disease. Much of our understanding of human T cells comes from studies of blood and how T cells work in organs like the gut and lung is not fully understood. In a unique collaboration between DonateLife and Austin Health transplant surgeons, we studied immune responses in samples gifted from organ donors.

PROJECT AIMS / OBJECTIVES

This project aimed to determine how human T cells survive and function using a rare organ donor tissue resource. We have successfully obtained tissue samples 50 organ donors and analysed T cell populations in blood, multiple lymphoid sites (spleen, bone marrow, lymph nodes), visceral (liver) and mucosal sites (lung, skin, gut). So far, the data has provided insights into the identification, function and developmental requirements of T cells around the human body. We are still in the process of analysing the data and expect publication in the next 1 year.

SIGNIFICANCE AND OUTCOMES

Tissues that reside in tissues (TRM) have a defensive role in infection and cancer yet can mediate destructive immune processes in autoimmune diseases. This project will provide several new fundamental insights into tissue T cell immunology. Firstly, we expect to develop an unbiased map of tissue T cells around the human body which will provide a framework for future studies of tissue-resident T cells. Secondly, we expect to identify new targets for TRM identification or a combination of markers that cluster on T cells from a particular organ. This would represent a breakthrough in the study of human TRM given the current lack of consensus on human TRM identification. Thirdly, we expect to identify distinct transcriptional profiles of TRM subsets throughout the body and

further, tracking of T cell receptor usage would provide insight into TCR clonotype usage between circulating T cells and TRM subsets in different tissues. Fourthly, we expect to develop new insights regarding the phenotype, functional and TCR sensitivity characteristics of TRM subsets in diverse human tissue, providing a baseline of TRM subsets in health, which will assist future studies investigating the role of TRM in infections, cancer and autoimmune diseases. Finally, we expect to define the cytokine responsiveness of human TRM, which will provide the first step in investigating key molecular targets for the manipulation of TRM development, survival and function. Taken together, this project is likely to yield results which challenge the paradigms developed from TRM mouse models and potentially lead to breakthroughs in the development of therapies that manipulate human TRM.

PUBLICATIONS / PRESENTATIONS
We are still in the process of analysing the data and expect publication in the next 1 year.