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RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		The identification of key driver genes in acute kidney transplant rejection
Name		Dr Karen L. Keung
Award Received		2016 Jacquot Research Entry Scholarship
Report Date		10 April 2017
Chief Investigator / Supervisor		Philip O'Connell
Administering Institution		The University of Sydney
Funding Period	Start Date:	1 January 2016
	Finish Date:	1 January 2017

PROJECT SUMMARY

Kidney transplantation remains the best treatment option for patients with end stage kidney disease. Over the last 10-15 years, there have been significant improvement in drug treatment regimens in these patients, but acute rejection of the transplant still occurs in 10-20% of recipients, and remains a risk factor for premature loss of the transplant.

Significant technological advances have allowed for an individual's entire genetic make-up to be profiled, and this has provided opportunities to identify differences in the genetic expression in biological fluids (such as blood and urine) and tissue in different individuals. For example, the kidney transplant biopsy tissue of patients with, and without, acute rejection has been compared in various studies to help identify 'culprit' genes causing acute rejection.

In our study, we combined multiple studies that used microarray (gene chip technology) on kidney transplant biopsies to study the genes that are over-expressed in acute rejection patients. A set of key genes in acute rejection were identified.

Strategies were employed to identify drugs that are already in clinical use for other conditions/diseases, which may target our genes of interest. Currently, a potential drug is being tested in our laboratory to see if it can, by suppressing the key genes, result in suppression of the acute rejection process.

PROJECT AIMS / OBJECTIVES

1. To perform a meta-analysis of microarray datasets of human kidney transplant biopsy tissue

a) To identify differentially expressed genes (DEGs) in acute rejection versus no AR

b) From the DEGs, to derive the 'Key Drivers' (key regulatory genes)

2. Apply a drug repurposing strategy to identify potential novel therapies

3. Experimental validation

SIGNIFICANCE AND OUTCOMES

Preliminary data in an animal model suggests that our chosen agent suppresses the expression of a number of our key driver genes. Currently we are assessing whether there is an impact on allograft survival when used as an additive agent to standard immune suppression.

To the best of our knowledge, computational methods with the aim of identifying key driver/regulatory genes in acute kidney allograft rejection has not been performed. It also shows the potential application of drug repurposing tools/platforms to find new uses for existing drugs.

PUBLICATIONS / PRESENTATIONS

Oral abstract, nomination for President's Prize, Transplantation Society of Australia and New Zealand Annual Scientific Meeting May 2017

Jerry Koutts Young Investigator Award, Westmead Hospital 2016 – for the best post-graduate presentation at the Westmead Precinct.