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RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		Case discovery and genotyping of C3 glomerulopathy
Name		Dr Thomas Barbour
Award Received		2016 Jacquot Research Establishment Award
Report Date		13 June 2017
Chief Investigator / Supervisor		Dr Thomas D Barbour
Administering Institution		The Royal Melbourne Hospital
Funding Period	Start Date:	1 February 2016
	Finish Date:	30 January 2017

PROJECT SUMMARY

C3 glomerulopathy (C3G) refers to a rare group of kidney disorders in which the 'complement' system is the cause of kidney injury. Complement plays a key part in every person's defence (or 'immunity') against infection. However, in patients with C3G, complement becomes mis-targeted, and attacks a person's own kidneys. Specifically, a complement particle called 'C3' lodges within the tiny filtration units of the kidney, leading to inflammation and injury (the medical term for this is 'glomerulonephritis').

Unfortunately, there is no proven treatment for C3G, which in most patients results in the need for longterm dialysis or transplantation. This project attempts to identify the processes by which C3 inflicts damage in the kidneys. Some of these processes may be preventable using new drugs that have been developed specifically to inhibit complement, offering the prospect of a cure for C3G.

PROJECT AIMS / OBJECTIVES

The aims of this project are:

(1) Case discovery: to identify individuals and families with C3G using the clinical and biopsy databases of the nephrology and anatomical pathology departments at Royal Melbourne Hospital (RMH).

(2) Genotyping: to screen patients with C3G for DNA mutations using sequencing and cytogenetics-based approaches.

(3) Research collaborations: to elucidate novel disease mechanisms and treatments in C3G.

SIGNIFICANCE AND OUTCOMES

The major outcome of this case discovery project has been the development of a Phase 1 b prospective, open-label, uncontrolled trial of a novel therapeutic complement inhibitor in patients with C3G. The trial is sponsored by a complement pharmaceutical company, and is being undertaken at RMH as a single centre international study. Ethics approval of an amendment is currently awaited before the expected commencement of screening in June 2017. It is hoped that the trial will lead to Phase 2 and 3 trials, also to be conducted at RMH. A second outcome is my ongoing laboratory research using patient samples as part of my second year (2017) Jacquot project. I intend to apply for a third and final year's Jacquot funding for this laboratory work.

PUBLICATIONS / PRESENTATIONS

Ruderman I, Finlay M, Barbour T. The perfect storm. Kidney International 2017

Lioufas N, Finlay M, Barbour T. Durable remission of C3 glomerulonephritis with mycophenolate mofetil. Nephrology 22 (S1) 2017: 36-9

http:llonlinelibrary.wiley.com/doi/10.1111 /nep.12939/full

A paper describing the RMH C3G cohort is in preparation but I am awaiting completion of some of the key laboratory work (as part of my 2017 Jacquot project) for publication. An ethics amendment at RMH will enable the incorporation of select data into an international 'C3 Glomerulopathy Natural History Study' through my collaboration with Imperial College, London.