### Project / Program Title
Genetic Diagnostics in Genetic Renal Disease - Methods, Applications and Therapeutics

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<tr>
<th>Name</th>
<th>Dr Andrew John Mallett</th>
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<tr>
<td>Award Received</td>
<td>2015 Jacquot Research Entry Scholarships in Nephrology</td>
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<td>Report Date</td>
<td>1 May 2017</td>
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<tr>
<td>Chief Investigator / Supervisor</td>
<td>Dr Helen Healy</td>
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<td>Administering Institution</td>
<td>The University of Queensland</td>
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<td>Funding Period</td>
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<td>Start Date: 1 December 2015</td>
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<td>Finish Date: 1 December 2016</td>
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### PROJECT SUMMARY
This PhD program of work seeks to translate advances in genetic technologies into healthcare for those affected by inherited kidney disease.

Firstly, this involves undertaking epidemiological analyses of cohorts of patients in Australia affected by inherited kidney diseases individually and collectively.

Secondly, a clinical and multidisciplinary service model has been proposed and commenced with short-term evaluation of effectiveness to be undertaken.

Thirdly, a collaborative diagnostic genomic service is being established, validated and assessed to identify causative variants in known genes implicated in inherited kidney disease for affected Australian families.

Lastly, a research genomic and functional genomic project has been assessed in order to identify and validate new or novel genetic causes of inherited kidney disease for those in whom current diagnostic genomics has been unable to secure a genetic diagnosis.

Together this pipeline of activities is a patient-centric attempt to understand and explain inherited kidney disease in Australia whilst investigating ways in which to optimise clinical care and to thus attempt to improve future outcomes.

### PROJECT AIMS / OBJECTIVES

The hypothesis of this study is that modern genetic sequencing and interpretation in GRD can contribute to personalised care by

Aim 1 Systematic Reviews of
• Clarifying clinical diagnosis
• Improving options for clinical management

Aim 1.1 Therapeutics in GRD
Aim 1.2 GRD Clinical Services

Aim 2 Profiling GRD populations
Aim 2.1 Registry-based analysis of existing GRD cohorts
Aim 2.2 Identify cohort with Phenotypically Indeterminate GRD
Aim 2.3 Describe phenotypes/pedigrees

Aim 3 Genetic Sequencing of GRD populations
Aim 3.1 DNA extraction/banking
Aim 3.2 Perform Whole Exome Sequencing (WES)
Aim 3.3 Describe and interpret gene mutations of affected patients and families

Aim 4 Translation into Personalised Healthcare
Aim 4.1 Validate GRD genotype-phenotype relationships against clinical outcomes
Aim 4.2 Implement Collaborative GRD Service
Aim 4.3 Identify candidates for targeted therapeutics

SIGNIFICANCE AND OUTCOMES

This PhD program has this year resulted in several significant outcomes:

1. Commencement and growth of RBWH Renal Genetics Clinic (commenced 1/7/13) - a national first
2. First Description of the Epidemiology of Genetic Renal Disease in QLD - publication OJRD
3. Report of the Epidemiology of RRT treated AI port Syndrome related ESKD in Australia and New Zealand – publication NDT
4. Dissemination of a proposed Australian Renal Genetic Clinic Model - abstracts ANZSN, HGSA, RBWH Symposium
5. Commencement of Diagnostic Renal Gene Panels - abstracts ANZSN, ASN, RBWH Symposium (Award – Best Clinical Science Oral)
6. Commencement of a national Research & Functional Genomics Project for cases of genetically unresolved inherited kidney disease

PUBLICATIONS / PRESENTATIONS

Publications during candidature

Published Peer-Reviewed Articles


Manuscripts Under Review

Conference Abstracts - Oral Presentations
1. Mallett A (oral presenter), Maier B, Er P, Takasato, M, Sun J, Wolvetang E, Alexander S, Simons C, Little M. Patient-Derived Induced Pluripotent Stem Cell (iPSC) Modeling of Genetic Renal Disease (GRD).
   a. 2015 American Society of Nephrology Kidney Week, San Diego (USA), November 2015. Published as JASN; 26(S1):1 2a.
   b. 2015 Royal Brisbane and Women's Hospital Healthcare Symposium.
   a. 2015 American Society of Nephrology Kidney Week, San Diego (USA), November 2015. Published as JASN; 26(S1):46a.
   a. 2015 American Society of Nephrology Kidney Week - Early Program: Advances in Research Conference "Engineering Genomes to Model Disease, Target Mutations and Personalise Therapy", San Diego (USA), November 2015.

a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra, September 2015. Published as Nephrology; 20(S3):41.


a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra, September 2015. Published as Nephrology; 20(S3):42.

b. 2015 Royal Brisbane and Women's Hospital Healthcare Symposium, October 2015, Prize: "2015 RBWH Foundation Award for Best Overall Research"


a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra, September 2015. Published as Nephrology; 20(S3):51.


a. 2015 International Workshop on Development Nephrology, Snowbird (USA), July 2015.


a. 2014 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Melbourne, August 2014. Published as Nephrology; 19(S1):37.


a. 2014 Royal Brisbane and Women's Hospital Symposium, October 2014, Prize: "Best Clinical Science Oral Presentation"


a. 2013 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Brisbane, September 2013. Published as Nephrology; 18(S1):47.


a. 2013 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Brisbane, September 2013. Published as Nephrology; 18(S1):23.

b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.

   a. 2013 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Brisbane, September 2013. Published as Nephrology; 18(S 1 )42.

   b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.


   a. 2013 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Brisbane, September 2013. Published as Nephrology; 18(S1 )33.


   a. 2013 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Brisbane, September 2013. Published as Nephrology; 18(S 1 )32.

Conference Abstracts - Poster Presentations

1. Mallett A, Healy H, McGaughran J, Little M, Patel C. Characteristics and Initial Outcomes of a Multidisciplinary Renal Genetics Clinic (RGC)

   a. 2015 American Society of Nephrology Kidney Week, San Diego (USA), November 2015. Published as JASN; 26(S1 ):995A.


   a. 2015 American Society of Nephrology Kidney Week, San Diego (USA), November 2015. Published as JASN; 26(S1 ):480A.


   a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra, September 2015. Published as Nephrology; 20(S3):74.

   b. 2015 Royal Brisbane and Women's Hospital Healthcare Symposium, October 2015.


   a. 2015 Royal Brisbane and Women's Hospital Healthcare Symposium, October 2015.


   a. 2015 Royal Brisbane and Women's Hospital Healthcare Symposium, October 2015.


   a. 2015 Royal Brisbane and Women's Hospital Healthcare Symposium, October 2015.
   a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra. Published as Nephrology; 20(S3):79.
   a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra. Published as Nephrology; 20(S3):65.
   a. 2015 Australian and New Zealand Society of Nephrology Annual Scientific Meeting, Canberra. Published as Nephrology; 20(S3):65.
   a. 2015 Human Genetics Society of Australasia Annual Scientific Meeting, Perth, August 2015.
   a. 2014 Royal Brisbane and Women's Hospital Healthcare Symposium, October 2014.
   a. 2014 Australian and New Zealand Annual Scientific Meeting, Melbourne. Published as Nephrology; 19(S4):68.
   a. 2014 Australian and New Zealand Annual Scientific Meeting, Melbourne. Published as Nephrology; 19(S4):71.

a. 2014 Australian and New Zealand Annual Scientific Meeting, Melbourne, August 2014. Published as Nephrology; 19(S4 ):67.


a. 2014 Australian and New Zealand Annual Scientific Meeting, Melbourne, August 2014. Published as Nephrology; 19(S4 ):68.


a. 2014 Australian and New Zealand Annual Scientific Meeting, Melbourne, August 2014. Published as Nephrology; 19(S4 ):94.


a. 2014 American Society of Nephrology Kidney Week, Philadelphia (USA), November 2014. Published as JASN; 25(S1 ):422A.


a. 2013 Royal Australasian College of Physicians Annual Scientific Meeting, Perth, May 2013. Published as Internal Medicine Journal; 43(S3):42.


a. 2013 American Society of Nephrology Kidney Week, Atlanta (USA), November 2013. Published as JASN; 24(1 ):893A.

b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.


a. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.


a. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.
   a. 2013 American Society of Nephrology Kidney Week, Atlanta (USA), November 2013. Published as JASN; 24(1):304A.
   b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.
   a. 2013 American Society of Nephrology Kidney Week, Atlanta (USA), November 2013. Published as JASN; 24(1):685A.
   b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.
   a. 2013 American Society of Nephrology Kidney Week, Atlanta (USA), November 2013. Published as JASN; 24(1):824A
   b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.
   b. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.
   a. 2013 Royal Brisbane and Women's Hospital Symposium, October 2013.