

# Clinical utility of genomics in immunological conditions

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## Background

Melbourne Genomics' 16 Clinical Flagships have been at the forefront of determining when genomic testing makes a demonstrable difference to the safety and quality of patient care.

The Melbourne Genomics Immunology Clinical Flagship investigated several immune disorders with a known genetic basis. These include primary immunodeficiencies (PIDs), systemic auto-inflammatory diseases (SAIDs) and hereditary angioedema (HAE) – conditions that severely impact daily life and are typically very difficult to diagnose accurately.

Patients with immune conditions often remain undiagnosed and without appropriate treatment for many years. This 'diagnostic odyssey' can result in patients undergoing invasive and unnecessary testing, as well as loss of good health and quality of life.

## Publications

"Delayed diagnosis and complications of predominantly antibody deficiencies in a cohort of Australian adults", Charlotte A. Slade, Julian J. Bosco, Tran Binh Giang, Elizabeth Kruse, Robert G. Stirling, Paul U. Cameron, Fiona Hore-Lacy, Michael F. Sutherland, Sara L. Barnes, Stephen Holdsworth, Samar Ojaimi, Gary A. Unglik, Joseph De Luca, Mittal Patel, Jeremy McComish, Kymble Spriggs, Yang Tran, Priscilla Auyeung, Katherine Nicholls, Robyn E. O'Hehir, Philip D. Hodgkin, Jo A. Douglass, Vanessa L. Bryant and Menno C. van Zelm, *Frontiers in Immunology* (2018), [doi.org/10.3389/fimmu.2018.00694](https://doi.org/10.3389/fimmu.2018.00694)

"Pitfalls of immunotherapy: lessons from a patient with CTLA-4 haploinsufficiency", Leisa Rebecca Watson, Charlotte A. Slade, Sama Ojaimi, Sara Barnes, Pasquale Fedele, Prudence Smith, Justine Marum, Sebastian Lunke, Zornitza Stark, Matthew F. Hunter, Vanessa L. Bryant, Michael Sze Yuan Low, *Allergy Asthma Clin Immunol.* (2018), [doi: 10.1186/s13223-018-0272-7](https://doi.org/10.1186/s13223-018-0272-7)

## Project description

The objective: to determine whether genomic sequencing can provide more accurate diagnosis for patients with immune disorders that have a suspected monogenic basis, and lead to more effective treatment and improved care for their specific condition.

Patients received genomic testing in parallel with usual testing and care for their condition.

Patients from four major hospitals participated. Most had previously been seen in an immunology, immunogenetics, genetics or other specialist clinic.

The Immunology Flagship was led by Professor Jo Douglass from The Royal Melbourne Hospital (RMH), with key coordination by Dr Charlotte Slade (RMH and WEHI) and Dr Vanessa Bryant (WEHI). The Flagship directly involved at least 26 healthcare and research professionals, plus a wider group of 36 experts (including nurses, health economists, biostatisticians, clinicians and registrars).

## Activities, outcomes and lessons learnt

Findings from this project will be made available following publication of results.

## Impact

The Flagship has driven national conversations about the identification and treatment of patients with immune system diseases, leading to development of a national immunodeficiency strategy (<https://www.nationalimmunodeficiencystrategy.org.au>).

## Clinical Flagship team

Name	Organisation	Role
Jo Douglass	RMH	Clinical immunologist
Charlotte Slade	RMH/WEHI	Clinical immunologist
Vanessa Bryant	WEHI	Researcher
Alison Trainer	RMH	Clinical geneticist
Anna Jarmolowicz	MCRI/VCGS	Genetic counsellor
Belinda Creighton	Monash Health	Genetic counsellor
Ben Van Dort	RCH	Clinical nurse consultant
Emma Creed	RMH	Genetic counsellor
Fiona Moghaddas	WEHI	Clinical immunology registrar
Gary Unglik	RMH	Clinical immunologist
Gemma Brett	MCRI/VCGS	Genetic counsellor
Giulia Valente	Austin Health	Genetic counsellor
Heather Chaliner	Austin Health	Genetic counsellor
Ingrid Winship	RMH	Clinical geneticist
Jeremy McComish	RMH	Clinical immunologist
Jo Smart	RCH	Clinical immunologist
Jonathan Akikusa	RCH	Paediatric rheumatologist
Katherine Nicholls	RMH	Clinical immunologist
Kirsty West	RMH	Genetic counsellor
Matthew Hunter	Monash Health	Clinical geneticist
Melanie Bahlo	WEHI	Bioinformatician
Michael Sutherland	Austin Health	Respiratory physician
Mimi Tang	RCH	Clinical immunologist
Peter Gowdie	Monash Health	Rheumatologist
Sara Barnes	Monash Health	Clinical immunologist
Seth Masters	WEHI	Researcher
Stephen Holdsworth	Monash Health	Clinical immunologist
Yael Praver	Monash Health	Genetic counsellor
Zornitza Stark	MCRI/VCGS	Clinical geneticist

This Clinical Flagship has also garnered involvement from a wider group of 36 professionals, including clinicians (immunologists, rheumatologists), registrars, nurses, an administrative co-ordinator, clinician-researchers, researchers, health economists and a biostatistician.