

Jeffrey Modell Diagnostic and Research Centers - Activity Report

Recommended “best practices” for Public Awareness, Physician Education and Research



Center Information:

Date:	30 March 2020
Name of Center Director:	A/Prof. Menno C. van Zelm
Name of Institution:	JMF Centre Melbourne
City/Country:	Melbourne / Australia

Progress and Updates:

Educational Activities:

- PID Discussion group meetings
 - City-wide initiative of 4 evening sessions per year to discuss PID and difficult cases, aimed to educate clinical specialists, academics and registrars, exchange of expertise.
 - Four sessions held in 2019 with rotating hosts from JMF founding members (Royal Melbourne Hospital, Royal Children’s Hospital, Alfred Health, Monash Health): 21 March, 20 June, 12 September, 21 November
- JMF Centre Melbourne 2nd Annual Symposium “Bridging Research and Care for Patients”
 - Half-day event on 11 October 2019 with short talks from early-mid-career scientists and clinical registrars, and a keynote lecture from Dr Mirjam van der Burg (LUMC, Leiden). Mirjam is current Secretary of ESID and her visit was supported by a visiting speaker grant of the Australia and New Zealand society for Immunology (ASI).
 - Attended by 50 delegates, including clinicians, scientists, patients and patient organisations from across Melbourne, Victoria
- Sponsoring of PID breakfast session at annual meeting of the Australasian Society for Clinical Immunology and Allergy (ASCI) on 7 September 2018 (please see attached full programme, picture and news article on website <https://www.jmf-melbourne.org.au/news-events>)

Patient Support:

- Invited lectures by Dr Vanessa Bryant (WEHI) and Dr Emily Edwards (Monash University) at the annual conference of the Immune Deficiency Foundation of Australia (IDFA) in April 2019 in Brisbane, QLD.
- Invited presentations by Prof Jo Douglas, Dr Vanessa Bryant and A/prof Menno van Zelm at the annual board meeting of AusPIPs
- All activities and reports are communicated through the Centre’s website <http://www.jmf-melbourne.org.au/>

Jeffrey Modell Diagnostic and Research Centers - Activity Report

Recommended “best practices” for Public Awareness, Physician Education and Research



as well as the Facebook page

(<https://www.facebook.com/jmf.melbourne/>) for optimal interactions with stakeholders (esp. JMF, and patient organisations).

Together the website and Facebook page are aimed to:

- Promote activities
- Serve as portal to guide patients and professionals to the right resources and information

Research:

➤ Collaborative Studies

JMF Melbourne Exec member initiatives include local and Australia-wide genomic screening programs highlighted below.

Immunology Flagship Program of Melbourne Genomics Health Alliance

- JMF Exec members: Dr Vanessa Bryant, Dr Charlotte Slade, Dr Joanne Smart
- An Alliance of 10 leading healthcare and research organisations (including JMF Melbourne network Walter & Eliza Hall Institute, Royal Melbourne Hospital, Royal Children’s Hospital, Monash Health).
- Dedicated to bringing global knowledge of genomics to benefit individual care of Victorians by demonstrating clinical utility and value of accredited clinical genomic sequencing for Victorians with suspected PID
- Preliminary findings of whole-exome sequencing for 200 Victorians include new diagnosis for 12% participants, changes to patient for 13% patients.
- <https://www.melbournegenomics.org.au/news/providing-better-care-more-victorians-genomic-sequencing>

Genetic Immunology Flagship Program of Australian Genomic Health Alliance

- Flagship lead: Prof Matthew Cook, Centre for Personalised Immunology, ACT
- Members from JMF Melbourne exec committee: Dr Bosco, Dr, Bryant, Dr Slade, Prof Smart and A/Prof Van Zelm
- Aim to provide a national diagnostic and research network, a national approach to data federation and analysis, economic analysis and poly implications to the health system and build a genomic workforce, education and ethics.
- Recruitment of 150 patients with suspected PID June -December 2019 for whole-exome sequencing.

Other Collaborative research studies between JMF Exec members:

- CD19 complex deficiencies: how do specific mutations lead to mild and severe clinical phenotypes?
- Immunological analysis of a newly established cohort of adult patients with predominantly antibody deficiency in the State of Victoria (see publications below)

Jeffrey Modell Diagnostic and Research Centers - Activity Report

Recommended "best practices" for Public Awareness, Physician Education and Research



- Immunodeficiency and autoimmunity in patients with predominantly antibody deficiency
 - Examination of immunological memory in PAD patients following vaccination
- Protocols Overview
N/A
- Specific Aims
- Providing a genetic diagnosis for patients with PID
 - Define the functional effects of pathogenic mutations
 - Understanding the contradictory presence of autoimmunity in patients with predominantly antibody deficiency
- Objectives Achieved
- Multi-centre research database of adults with primary antibody deficiency
 - Identification of immunological changes associated with non-infectious complications in adult PAD patients
- Published Manuscripts
1. M.C. van Zelm, M. Pumar, P. Shuttleworth, P.M. Aui, J.M. Smart, A. Grigg, J.J. Bosco (2019) Functional Antibody Responses Following Allogeneic Stem Cell Transplantation for TP53 Mutant pre-B-ALL in a Patient With X-Linked Agammaglobulinemia. *Front Immunol.*;10:895.
 2. M.C. van Zelm, J.J. Bosco, P.M. Aui, S. De Jong, F. Hore-Lacy, R.E. O'Hehir, R.G. Stirling, P.U. Cameron (2019) Impaired STAT3-Dependent Upregulation of IL2R α in B Cells of a Patient With a STAT1 Gain-of-Function Mutation. *Front Immunol.*;10:768.
 3. W. van de Veen, C.E. Krätz, C.I. McKenzie, P.M. Aui, J. Neumann, C.J.M. van Noesel, O.F. Wirz, B. Hagl, C. Kröner, B.D. Spielberger, C.A. Akdis, M.C. van Zelm, M. Akdis M, E.D. Renner (2019) Impaired memory B cell development and antibody maturation with a skewing towards IgE in patients with STAT3 hyper-IgE syndrome. *Allergy*; 74(12):2394-2405.
 4. R.H.J. Verstegen, P.M. Aui, E. Watson, S. De Jong, S.J.W. Bartol, J.J. Bosco, P.U. Cameron, R.G. Stirling, E. de Vries, J.J.M. van Dongen, M.C. van Zelm (2019) Quantification of T-Cell and B-Cell Replication History in Aging, Immunodeficiency, and Newborn Screening. *Front Immunol.* 10:2084.
 5. E.S.J. Edwards ESJ, J.J. Bosco, P.M. Aui, R.G. Stirling, P.U. Cameron, J. Chatelier, F. Hore-Lacy, R.E. O'Hehir, M.C. van Zelm (2019) Predominantly Antibody-Deficient Patients With Non-infectious Complications Have Reduced Naive B, Treg, Th17, and Tfh17 Cells. *Front Immunol.*;10:2593.

World Primary Immunodeficiency Week:

- Global Balloons & Bubbles Launch – Coordination with Local Patient Groups

Jeffrey Modell Diagnostic and Research Centers - Activity Report

Recommended "best practices" for Public Awareness, Physician Education and Research



➤ Government Outreach

- PID strategy document (attached letter to Hon Greg Hunt MP))

Future Goals:

➤ Activities planned for next budget period

Education / outreach

- Four PID Discussion group meetings in 2020: 19 March, 18 June, 10 September, 19 November
- Diagnostics course 1-2 Feb 2020
- ASCIA breakfast meeting
- Annual PID Update Day in April 2019 for Clinical specialists, registrars, laboratory scientists
- Continued engagement with patient organisations and families affected by the absence of SCID newborn screening in Australia to advocate for implementation of newborn screening for PIDs; for funding of SCIG in Victoria.
- JMF Melbourne is one of the stakeholders for a National Immunodeficiency Strategy for Australia. Initiative started on March 8, 2019
- 3rd annual JMF Melbourne Immunodeficiency symposium to be held either in June or October 2020

Diagnostics / research

- Pilot studies supplementing existing diagnostics, including:
 - Functional tests to supplement accredited tests (genetic diagnoses of uncertain significance) for diagnosis of PID.
 - Improve measurements for detection of impaired vaccination responses using neoantigens (e.g. Salmonella) or cell-based assays (collaboration with Prof. Sergio Rosenzweig, NIH, USA)- pilot
 - Extensive flow panels to supplement diagnostics of selected cases

Other:

Attachments:

1. Programme National Immunodeficiency Strategy meeting, March 8, 2019
2. Programme ASCIA 2019 conference
3. Letter to Hon Greg Hunt MP
4. Flyer 2nd annual JMF Melbourne symposium