

Jeffrey Modell Diagnostic and Research Centers - Activity Report

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



Center Information:

Date:	16 May 2022
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.
 - Three sessions held in 2021 with rotating hosts from JMF founding members (Royal Melbourne Hospital, Royal Children’s Hospital, Alfred Health, Monash Health):
24 June, 23 September, 25 November 2021
- Invited presentations by Dr Samar Ojaimi and A/Prof Menno van Zelm at the AusPIPs annual forum entitled PID: More than just a single disease. Chaired by Dr Emily Edwards. 18 September 2021
- Dr Emily Edwards wrote an article for The Conversation (September 2021; Appendix 1) raising awareness of the need for a third dose of the COVID-19 vaccine for protection of immune-compromised individuals. This resulted in multiple media interviews covering this topic including national news coverage on the ABC News Channel, and online articles for ABC Science.

Patient Support:

- All activities and reports are communicated through the Centre’s website <http://www.jmf-melbourne.org.au/> 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 the centre’s activities
 - Serve as portal to guide patients and professionals to the right resources and information
- Continued activities of Centre member Dr. Emily Edwards as Vice President of AusPIPs Inc., an Australian charitable organisation that advocates for and supports people and their families, who have Primary Immune Deficiency (PID). JMF Melbourne Centre director Menno van Zelm, and members Jo Douglass, Charlotte Slade, Jeremy McComish and Theresa Cole were active as volunteer members in the Medical Advisory Panel of AusPIPs. These

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individuals provided crucial input in to the AusPIPS patient centred brochure: About Immunoglobulin (Ig) drafts (see attachment 2).

Research:

➤ Collaborative Studies

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

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 policy implications to the health system, and to build a genomics workforce, education and ethics.
- Recruitment of 150 patients with suspected PID for whole-exome sequencing completed in 2020 – final analysis ongoing.

Genomics collaboration with 3billion Inc.

- JMF exec members involved: Dr Bosco and A/Prof Van Zelm, in collaboration with Dr Ojaimi and Dr Edwards
- 132 patients whole-exome sequenced in 2021 – genetic hits identified in 34 patients
- Aim to genetically characterize predominantly antibody deficient patients, and establish assays to interrogate functional consequences of genetic variants, building a framework for a functional genomics approach to patient diagnostics, provide supportive information for the incorporation of genomics and functional assays in healthcare-supportive diagnostics.
- Analysis of raw datafiles ongoing

Other Collaborative research studies between JMF Exec members:

- Examination of immunological memory in immunodeficient patients following COVID-19 vaccination (ongoing)
- Collaboration Sergio Rosenzweig (NIH) on monoallelic TCF3 mutations.
- Collaboration Hiro Kanegane (Tokyo, Japan) on an UNC13D duplication (manuscript submitted)

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➤ 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 including genomics (genetic variants from Whole Exome sequencing) of adults with predominantly antibody deficiency
- Identification of immunological changes associated with non-infectious complications in adult PAD patients
- Establishment of technologies for detection of antigen-specific B-cell and T-cell memory following COVID-19 vaccination in patients with immunodeficiency

➤ Published Manuscripts

1. E.S.J. Edwards, J.J. Bosco, S. Ojaimi, R.E. O’Hehir, M.C. van Zelm. (2021) Beyond monogenetic rare variants: tackling the low genetic diagnoses in predominantly antibody deficiency. *Cell Mol Immunol* 18(3):588-603 DOI: 10.1038/s41423-020-00520-8
2. E. Tosune, T. Nakano, K. Moriya, D. Sato, D. Suzuki, A. Miura, S. Katayama, H. Niizuma, J. Kanno, M.C. van Zelm, K. Imai, H. Kanegane, H. Sashara, S. Kure (2021) Case Report: Infantile-Onset Fulminant Type 1 Diabetes Mellitus Caused by Novel Compound Heterozygous *LRBA* Variants. *Front Immunol* 12(8):688572 DOI: 10.3389/fimmu.2021.677572
3. A. Nishimura, T. Naruto, S. Miyamoto, A. Grigg, J.J. Bosco, A. Hoshino, K. Amano, S. Iwamoto, M. Hirayama, M. Migita, O. Ohara, M. Takagi, T. Morio, M.C. van Zelm, H. Kanegane (2021) Genomics analysis of leukaemia predisposition in X-linked agammaglobulinemia. *Brit J Haem* 193(6):1277-1281 DOI: 10.1111/bjh.17459
4. R. Ameratunga, H. Longhurst, K. Lehnert, R. Steele, E.S.J. Edwards, S.T. Woon (2021) Are All Primary Immunodeficiency Disorders Inborn Errors of Immunity? *Front Immunol* 12(6):706796 DOI: 10.3389/fimmu.2021.706796

World Primary Immunodeficiency Week:

- Radio interview Emily Edwards on 25 April 2021 with Dr Shane on Triple R 102.7FM “Einstein A Go Go” about Primary Immunodeficiency.

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➤ Government Outreach

- A/Prof Van Zelm invited to consult the Australian Department of Health and Nour Group regarding complete overhaul of the Newborn Bloodspot Screening Programs (scheduled 22 January 2022)

Future Goals:

➤ Activities planned for next budget period

Education / outreach

- Four PID Discussion group meetings in 2022: 7 April, 16 June, 8 September, 24 November
- ASCIA breakfast meeting, 31st ASCIA Annual Conference. 1-3 September 2021. Melbourne Convention Center
- 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 provision of COVID-19 prophylactic Evusheld to protect patients from severe SARS-CoV-2 infection
- 3rd annual JMF Melbourne Immunodeficiency symposium to be held in November 2022

Diagnostics / research

- Complement whole-exome sequencing with functional immunological tests to evaluate the role of common gene variants in modifying disease presentation, especially with regards to autoimmunity and gastrointestinal disease in predominantly antibody deficiency.
- Pilot studies supplementing existing diagnostics, including:
 - Functional tests to supplement accredited tests (genetic diagnoses of uncertain significance) for diagnosis of PID and provide rationale for treatment with biologicals.
 - Extensive flow panels to supplement diagnostics of selected cases
- SARS-CoV-2-specific antibody content in Australian immunoglobulin product and relationship with levels in international product, with the aim of showing that Australian product can augment SARS-CoV-2-specific antibody levels in PID patients.

Other:

Attachments:

1. Dr Emily Edwards - Conversation article
2. About Immunoglobulin (Ig) Brochure – AusPIPS