

# Jeffrey Modell Diagnostic and Research Centers - Activity Report

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



## Center Information:

|                          |                           |
|--------------------------|---------------------------|
| Date:                    | 11 December 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.
  - Three sessions held in 2020 with rotating hosts from JMF founding members (Royal Melbourne Hospital, Royal Children’s Hospital, Alfred Health, Monash Health):  
18 June, 10 September, 19 November
- Primary Immunodeficiency Diagnostics workshop 1-2 Feb 2020. This intensive weekend program provided a practical and comprehensive overview of current cellular/functional and molecular diagnostic assays for PID, facilitated by 13 Australian and international experts in the field. The 28 participants from Australia, New Zealand and South-East Asia were provided educational sessions that included short lectures, interactive case-based discussions and small group discussions (programme details in attachment 1).

### **Patient Support:**

- Invited presentations by Prof Jo Douglas, Dr Charlotte Slade and A/prof Menno van Zelm at the AusPIPs COVID19 information sessions on 15 May 2020 and 26 November 2020
- 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 activities
  - Serve as portal to guide patients and professionals to the right resources and information
- Centre member Dr. Emily Edwards was recruited 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 was recruited as volunteer to the Medical Advisory Panel of AusPIPs.

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## 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 for whole-exome sequencing completed in 2020 – final analysis ongoing.

#### Other Collaborative research studies between JMF Exec members:

- Examination of immunological memory in PAD patients following influenza vaccination (see publications below)
- Invited Review on the challenges of genetics in patients with Predominantly Antibody Deficiency and directions for future research into this (see manuscript 4).
- International collaboration with the groups of Prof Jose Franco (Colombia) and Prof. Martin van Hagen on the immunological nature of selective IgA deficiency (see manuscript 1)

### ➤ Protocols Overview

N/A

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## ➤ 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
- Detection of antigen-specific B-cell memory following influenza vaccination or SARS-CoV2 infection (see manuscripts 2 and 3)

## ➤ Published Manuscripts

1. C. Grosserichter-Wagener, A. Franco-Gallego, F. Ahmadi, M. Moncada-Vélez, V.A. Dalm, J.L. Rojas, J.C. Orrego, N. Correa Vargas, L. Hammarström, M.W. Schreurs, W.A. Dik, P.M. van Hagen, L. Boon, J.J.M. van Dongen, M. van der Burg, Q. Pan-Hammarström, J.L. Franco, M.C. van Zelm. (2020) Defective formation of IgA memory B cells, Th1 and Th17 cells in symptomatic patients with selective IgA deficiency. *Clin Transl Immunology*. 9(5):e1130.
2. G.E. Hartley, E.S.J. Edwards, J.J. Bosco, S. Ojaimi, R.G. Stirling, P.U. Cameron, K.L. Flanagan, M. Plebanski, P.M. Hogarth, R.E. O’Hehir, M.C. van Zelm (2020) Influenza-specific IgG1+ memory B cell numbers increase upon booster vaccination in healthy adults but not in patients with Predominantly Antibody Deficiency *Clin Transl Immunology*.
3. G.E. Hartley, E.S.J. Edwards, P.M. Aui, N. Varese, S. Stojanovic, J. McMahon, A.Y. Peleg, I. Boo, H.E. Drummer, P.M. Hogarth, R.E. O’Hehir, M.C. van Zelm (2020) Rapid and lasting generation of B-cell memory to SARS-CoV-2 spike and nucleocapsid proteins in COVID-19 disease and convalescence. *medRxiv* 2020.11.17.20233544.
4. E.S.J. Edwards, J.J. Bosco, S. Ojaimi, R.E. O’Hehir, M.C. van Zelm (2020) Beyond monogenetic rare variants: Tackling the low rate of genetic diagnoses in Predominantly Antibody Deficiency. *Cellular & Molecular Immunology*
5. Hosking LM, Quach A, Slade CA, Galea MA, Richards S, Choo S, Ferrante A. (2020) Proceed with Caution: STAT1 GOF Diagnosis Missed Due to Intronic SNP. *J Clin Immunol*. 40(3):547-550.
6. J.C.M.M. Villanueva, K-W. Chan, R.C. Ong, A.G. Andaya, Y-L. Lau, M.C. van Zelm, H. Kanegane (2020) Hyper IgE Syndrome Associated with Warts: A First Case of Deficator of Cytokines 8 Deficiency in the Philippines. *Front. Pediatr*. DOI: 10.3389/fped.2020.604725

## World Primary Immunodeficiency Week:

- Radio interview Menno van Zelm on 26 April 2020 with Dr Shane on Triple R 102.7FM Einstein A Go Go about Primary Immunodeficiency.

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## ➤ Government Outreach

- JMF Melbourne is one of the stakeholders in the ASCIA Immunodeficiency Strategy for Australia and New Zealand, which was published on 5 November 2020 ([www.nationalimmunodeficiencystrategy.org.au/](http://www.nationalimmunodeficiencystrategy.org.au/)) and has been submitted to the Parliamentary Inquiry into approval processes for new drugs and novel medical technologies in Australia (see attachment 2).

## Future Goals:

### ➤ Activities planned for next budget period

#### Education / outreach

- Four PID Discussion group meetings in 2020: 18 March, 17 June, 9 September, 18 November
- ASCIA breakfast meeting, 31st ASCIA Annual Conference. 1-3 September 2021. Melbourne Convention Center (see attached prelim programme in attachment 3)
- 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.
- 3<sup>rd</sup> annual JMF Melbourne Immunodeficiency symposium to be held either in June or October 2021

#### 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.
  - Improve measurements for detection of impaired vaccination responses using recombinant antigen tetramers. Focus on booster vaccinations with influenza and neoantigen vaccinations for SARS-CoV2
  - Extensive flow panels to supplement diagnostics of selected cases

## Other:

### Attachments:

1. Programme and participants PID diagnostics course 2020
2. ASCIA Immunodeficiency Strategy for Australia and New Zealand
3. Programme ASCIA 2021 conference