Melbourne Genomics Health Alliance
&
Australian Genomics Health Alliance

Professor Andrew Sinclair
Deputy Director: Murdoch Children’s Research Institute
Executive Director: Victorian Clinical Genetics Service
University of Melbourne, Department of Paediatrics
Australian Genomics Health Alliance

Assoc. Professor Clara Gaff
Executive Director: Melbourne Genomics Health Alliance
Melbourne Genomics Health Alliance

Exec. Director: Assoc. Prof. Clara Gaff

Founding members

The Royal Melbourne Hospital

The Royal Children’s Hospital Melbourne

THE UNIVERSITY OF MELBOURNE

Walter+Eliza Hall Institute of Medical Research

Murdoch Childrens Research Institute

CSIRO

agrf

New members

Peter Mac

Austin Health

Monash Health

FUNDING: Members $3.4 million 2014-15, State Govt & Members $35 million 2016-19
Collaboration focused on health care is needed
2014 -2015 Demonstration Phase

**Build a ‘prototype’**
- Testing policies
- Counselling & consent
- Single bioinformatics platform
- Shared variant curation db
- Variants linked to clinical data
- Patient data entry
- Researcher access to data

*Multiple organisations*
*Different conditions*

**Evaluate** compared to standard care

**Process**
- what worked
- what didn’t
- potential solutions

**Impact**
- detection rate
- change in management
- Cost effectiveness

**Clinicians**
**Patients**
**Diagnostic scientists**
**Data scientists**

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Demonstration Project

Prospective: Singleton Whole Exome Sequencing with targeted analysis prospective i.e. in parallel with usual investigations

Five flagship diseases:

- Hereditary peripheral neuropathies (CMT)
- Childhood syndromes (CS)
- Focal epilepsy (Epil)
- Hereditary colorectal cancer syndromes (hCRC) - germline
- Acute myeloid leukaemia (AML) - somatic

n= 305 patients
Shared approaches

Common clinical consent form (germline)

Data standards

Curation guidelines

Lab name/logo

Diagnostic Exome Sequencing report – targeted analysis.

Patient Details:
Name:
DOB:
Sex:
URN:
Referring doctor:
[insert referring dr details]

Sample details:
Lab ID:
Source:
Date collected:
Date received:
Report date:

Clinical indication:
[insert diagnosis and family history of XXXX]

Test performed:
Whole exome sequencing (WES) with targeted analysis of [insert #] genes known to be associated with [name of condition]

Primary result:
A likely pathogenic variant consistent with a diagnosis of [condition] was detected.

Secondary result:
No secondary findings detected.

Common report format

Multidisciplinary review meetings

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Proof of concept for State-wide approach

**Analysis:** Common Bioinformatics Pipeline (Cpipe)  
**VLSCI**

**Interpretation & Variant Curation Database** (MG-LOVD)  
**NeCTAR**

**Reporting**

**Storage & compute**  
**VLSCI**

**Access to clinical data:** Data linkage  
**BioGrid**

**Access for researchers:** Research Data Storage  
**RDSI**

**Patient data entry**  
**BioGrid**
Patients: pathogenic variants – interim results

<table>
<thead>
<tr>
<th>Participants</th>
<th>Total</th>
<th>AML</th>
<th>CRC</th>
<th>CS</th>
<th>CMT</th>
<th>EPIL</th>
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<td>171</td>
<td>24</td>
<td>25</td>
<td>80</td>
<td>35</td>
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<tr>
<td>Pathogenic variant detected</td>
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<td>38%</td>
<td>20%</td>
<td>57%</td>
<td>29%</td>
<td>10%</td>
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<tr>
<td>Not detected by Std care</td>
<td>TBD</td>
<td>TBD</td>
<td>none</td>
<td>45%</td>
<td>29%</td>
<td>10%</td>
</tr>
</tbody>
</table>

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40 children with suspected syndromes

Standard investigations

A total of $190,007 was spent on diagnostic investigations, an average of $4,750 per patient.

7 diagnoses were made

Cost per diagnosis of $27,143

Singleton exome

A total of $80,000 was spent on singleton exomes at $2,000 per patient.

25 diagnoses were made

Cost per diagnosis of $3,200
Clinicians have a better understanding

- Designed to promote change in clinician behaviour
- Capability Opportunity Motivation Behaviour (COM-B) Model (Michey et al. 2011)
- All clinicians interviewed as part of the process evaluation (n=28)

“So it's given us hands-on experience with the data and being able to understand how the test works and how the curation process works. I definitely have a much better understanding about the limitations of the test and also how it's supposed to look.”
Decision support: algorithm with capacity to indicate whether exome is appropriate based on phenotype data (or recommend a different test)

Knowledge resource encompassing evidence and clinical actions

Reports integrated into hospital systems and electronic patient records that link genotype and phenotype data

Systems that prompt for review when gene lists are significantly updated

Professional upskilling, particularly opportunities for experiential learning (“learning by doing”)

Support and reallocation of resources within the workforce
Single shared Statewide platform

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Benefits of a single platform

- Economies of scale
- Scalable according to need
- Rapid adoption of new knowledge and discoveries
- Meets the needs of and provides consistency for all users
- Facilitates sharing and use of data internally and externally
- Adaptable for other -omics
- Collaborative approach optimises funding opportunities
Others are adopting our model

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Queensland genomics alliance

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Vision: to provide evidence based genomic medicine that will improve healthcare outcomes in the most cost-effective way

Partners

Harry Perkins Institute of Medical Research
Path West
Genetic Services of Western Australia
Telethon Kids Institute
University of Western Australia

South Australian Health & Medical Research Institute
SA Pathology / Centre for Cancer Biology
University of Adelaide

The University of Queensland
Institute for Molecular Bioscience
QIMR Berghofer Medical Research Institute
Genetic Health Queensland
Diamantina Institute
Pathology Queensland

Sydney Children's Hospitals Network
Garvan Institute of Medical Research
NSW Health Pathology
Children's Cancer Institute Australia
The University of Sydney
Children's Medical Research Institute
University of New South Wales Centre for Genetics Education

Australian National University
Murdoch Childrens Research Institute
Victorian Clinical Genetics Services
Melbourne Health
The University of Melbourne
Walter and Eliza Hall Institute
Peter MacCallum Cancer Centre
Royal Children's Hospital
Victorian Life Sciences Computation Initiative

Peak Professional Bodies
Royal College of Pathologists of Australasia
Human Genetics Society of Australasia

National Partners
Bioplatforms Australia
Australian Genome Research Facility
BioGrid Australia
National Computational Infrastructure
Commonwealth Science and Industrial Research Organisation
Rare Voices Australia

International Partners
Broad Institute of MIT and Harvard
Baylor College of Medicine
Institute of Child Health, UCL
Global Alliance for Genomics and Health
Global Genomic Medicine Collaborative
Program 1
A national diagnostic and research network
Developing the most appropriate diagnostic approach for each specific disease area.

Program 2
A national data repository
Registries and linkage to genomic data.

Program 3
Evidence and policy for genomics in healthcare
Health economics, policy development, communication and engagement.

Program 4
Genomic education and workforce
Training for healthcare professionals, development of online information tools for clinicians and public.

Disease Area I
Existing Activities

Disease Area II

Rare Disease
Clinically driven
Patient focused
Enabling research

Cancer

Clinical Outcomes
Early Diagnosis
Prevention
Early Intervention
Surveillance
Targeted intervention or therapy

Analysis
To provide a strong evidence base for applying genomics to clinical medicine

Policy
Practical strategies to inform Australian Health system planners and policy makers
# Melbourne Genomics Acknowledgements

## CEOs/Leadership
- Gareth Goodier (RMH)
- Christine Kilpatrick (RCH)
- Stephen Smith (University of Melbourne)
- Doug Hilton (WEHI)
- Kathryn North (MCRI)
- Lynne Cobic (CSIRO)
- Sue Forrest (AGRF)

## Steering Group
- James Angus (Chair)
- Julian Clark
- Sue Forrest
- Trevor Lockett / David Hansen
- Andrew Sinclair
- Mike South
- Paul Waring / Jon Emery
- Ingrid Winship

## Community Advisory Group
- Ingrid Winship (Chair)
- Louisa Di Pietro
- Heather Renton
- Margaret Sahhar
- Janney Wale
- Christine Walker
- Liat Watson

## Project Team
- Clara Gaff (Exec Director)
  - Ivan Macciocca (Clinical)
  - Brenda Greyling (Clinical)
  - Natalie Thorne (Bioinf)
  - Tim Bakker (Info Mgmt)
  - Karen Meehan (Comms)
  - Michele Cook (Admin)

## Advisory Groups
- Genomics and Bioinformatics
  - Chair: Graham Taylor / Alicia Oshlack
- Clinical Interpretation and Reporting
  - Chair: Paul James
- Information Management
  - Chair: David Hansen

## Evaluation Team
- Melissa Martyn
- Bill Wilson
- Emily Forbes
- Nessie Mupfeki

## Genetic Counsellors
- Gemma Brett
- Emma Creed
- Ella Wilkins

## Advisory Groups
- AML
  - Andrew Roberts
  - Ian Majewski
  - Seong Lin Khaw
  - Francoise Merchin
  - Eddie Chew
- CMT
  - Monique Ryan
  - Paul James
  - Tim Day
  - Lynette Kiers
  - Adrienne Sexton
- CRC
  - Alex Boussioutas
  - Finlay Macrae
  - Alison Trainer
  - Ingrid Winship
  - Michael Bogwitz
- CS
  - Sue White
  - Zornitza Stark
  - Paul Ekert
  - Christiane Theda
  - David Amor
  - Tiong Tan
  - Maie Walsh
  - Patrick Yap
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