Australian Genomics
Kathryn North
The Australian Health Care System

Health service funding and responsibilities

Australia’s Health 2014, AIHW
NHMRC Genomics
TARGETED CALL FOR RESEARCH

• Demonstrate how patient benefit could be maximized through application of genomic data in one or more human diseases.

• Provide evidence to inform analysis on the cost effectiveness of implementing genomic data into the Australian health system.

• A significant increase in the understanding of practical strategies that could be used by Australian health system planners and policymakers.

• Building Australia’s research and research translation capacity in the area of genomics and healthcare.
Australian Genomics
PROGRAMS, FLAGSHIPS AND PROJECTS

Program 1
National diagnostic & research network
Developing the best diagnostic approach for each disease area

Program 2
National approach to data federation & analysis
Linking genomic and clinical data

Program 3
Economics & health policy
Health economics, policy development, implementation, science & communication

Program 4
Genomics workforce, education & ethics
Mapping education & training needs, addressing ethical implications of genomic medicine

Rare Disease Flagship
Existing Activities

Cancer Flagship
Clinically driven
Patient focused
Enabling research

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

Analysis
To provide a strong ethically informed evidence base for applying genomics to clinical practice

Policy
Practical strategies to inform Australian health system planners and policy makers

genomicsandhealth.org
Program One
A NATIONAL DIAGNOSTIC & RESEARCH NETWORK

Purpose – the delivery of a coordinated and sustainable system for the provision of genomic testing in the clinical environment – technology agnostic.

Primary activities – Unified approach to test ordering, minimal clinical data set required, ethics, consent.
Supporting the delivery of the Flagship projects through a national referral network,
Building evidence to inform policy change

• National Clinical Consent
• MSAC Application Pipeline
• Functional Genomics Network
Program Two
A NATIONAL APPROACH TO DATA FEDERATION AND ANALYSIS

Purpose – Development of standards and practices to exchange, share and unify genomic data from Flagship projects: at both a national level and harmonised with international efforts.

The group is developing a flexible, scalable national clinical genomics data infrastructure to unify data across our health systems to allow higher-order use of this information for research and improved healthcare outcomes.
Program Three
POLICY, HEALTH ECONOMICS AND IMPLEMENTATION SCIENCE

Purpose – To successfully integrate genomic medicine into the Australian health system we must understand the economic implications. We are analysing and modelling the health and social impact of genomic medicine to inform policy development, and – in alignment with the Australia’s National Health Genomics Policy Framework, building evidence to support the efficient, effective, ethical and equitable implementation of genomics into the Australian health system.

Primary activities over three domains:
• Health Economics
• Policy Development
• Implementation Science
  • Health Implementation Research
  • Network Analysis: Understanding Complexity
# National Health Genomics Policy Framework

## Vision

**Helping people live longer and better**

Through appropriate access to genomic knowledge and technology to prevent, diagnose, treat and monitor disease.

## Mission

To harness the health benefits of genomic knowledge and technology into the Australian health system in an efficient, effective, ethical and equitable way to improve individual and population health.

## Strategic Priority Areas

<table>
<thead>
<tr>
<th>Area</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-centred approach</td>
<td>Delivering high-quality care for people through a person-centred approach to integrating genomics into health care</td>
</tr>
<tr>
<td>Workforce</td>
<td>Building a skilled workforce that is literate in genomics</td>
</tr>
<tr>
<td>Financing</td>
<td>Ensuring sustainable and strategic investment in cost-effective genomics</td>
</tr>
<tr>
<td>Services</td>
<td>Maximising quality, safety and clinical utility of genomics in health care</td>
</tr>
<tr>
<td>Data</td>
<td>Responsible collection, storage, use and management of genomic data</td>
</tr>
</tbody>
</table>

## Enablers of Success

- Collaborative governance and leadership
- Stakeholder engagement
- National and international partnerships

## Principles

1. The application of genomic knowledge is ethically, legally and socially responsible and community trust is promoted.
2. Access and equity are promoted for vulnerable populations.
3. The application of genomic knowledge to health care is supported and informed by evidence and research.
Program Four
ETHICS

Purpose – While the Australian Genomics ethics domain has two key projects, listed below, ethics intersects with all our programs of work. Ainsley Newson, Ethics Lead, contributes to the Dynamic Consent project, the National Clinical Consent project of Program 1, collaborates with Program 2 on the Genomic data sharing project below, influences Policy Development with Program 3, and her work intersects with Flagship methodology design.

Primary activities: two sub-projects

• Ethical, Legal & Policy Issues in Genomic Data Sharing – following the Health Legal report commissioned into the legal barriers to genomic data sharing, Program 4 extends this analysis to consider the non-legal barriers impeding data sharing in Australia.

• Ethical Analysis of Clinical Genomics – this body of work considers the ethical aspects of implementing genomic testing in healthcare, including the ethical appropriateness of the technology’s use and it’s breadth of application.
Australian Genomics: Progress

- Australian Genomics launched
- NHMRC TCR
- Jan 14
- Jan 15
- Jan 16
- May 16
- Sep 16
- Jan 17
- May 17
- Sep 17
- Jan 18

**Staff**
- 1 in 2014
- 55 in 18 months

**Investigators**
- 50 in 2014
- 230 in 18 months

**Partner Institutions**
- 30 in 2014
- 80 in 18 months

**Projected recruitment of 2000 in two years**

**Projects**
- 80% growth in 18 months
### Clinical Flagship Projects
**AUSTRALIAN GENOMICS**

11 Flagship projects currently active across Rare Disease and Cancer, with additional Rare Disease projects to be launched in 2018.

<table>
<thead>
<tr>
<th>Flagship</th>
<th>Duration</th>
<th>Sites</th>
<th>Number</th>
<th>Methodology</th>
<th>Lead(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromuscular Disorders</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, VIC, WA</td>
<td>250</td>
<td>Custom Capture Panel / WES</td>
<td>Nigel Laing</td>
</tr>
<tr>
<td>Mitochondrial Disorders * with AMDF</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, VIC, WA</td>
<td>210</td>
<td>Half: WES + mtDNA Half: WGS</td>
<td>John Christodoulou David Thorburn</td>
</tr>
<tr>
<td>Neurodevelopmental Disorders</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, VIC, WA</td>
<td></td>
<td></td>
<td>Jozef Gecz</td>
</tr>
<tr>
<td>Epileptic Encephalopathy</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, TAS, VIC, WA</td>
<td>100</td>
<td>WES</td>
<td>Ingrid Scheffer</td>
</tr>
<tr>
<td>Brain Malformations &amp; Leukodystrophies</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, VIC, WA, NT</td>
<td>170</td>
<td>WES</td>
<td>Rick Leventer Paul Lockhart</td>
</tr>
<tr>
<td>Intellectual Disabilities</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, VIC, WA</td>
<td>~50 (trios)</td>
<td>WES / WGS</td>
<td>Tony Roscioli Mike Field</td>
</tr>
<tr>
<td>Renal Genetics * with Kidgen</td>
<td>2016 - 2018</td>
<td>NSW, QLD, SA, VIC, WA</td>
<td>550</td>
<td>WES / Panel</td>
<td>Andrew Mallett</td>
</tr>
<tr>
<td>Genetic Immunology</td>
<td>2016 - 2018</td>
<td>ACT, NSW, SA, VIC, WA</td>
<td>~150</td>
<td>WES / WGS</td>
<td>Matthew Cook</td>
</tr>
<tr>
<td>Acute Lymphoblastic Leukaemia</td>
<td>2016 - 2020</td>
<td>NSW, NT, QLD, SA, VIC, WA, WLD</td>
<td>~300</td>
<td>RNA Seq</td>
<td>Deborah White</td>
</tr>
<tr>
<td>Somatic Cancer * with MGHA</td>
<td>2016 - 2018</td>
<td>NSW, QLD, VIC, WA</td>
<td>400</td>
<td>Large Capture Panel</td>
<td>Stephen Fox</td>
</tr>
<tr>
<td>Germline Cancer - Paed / AYA * with NSW Cancer Genomics</td>
<td>2016 - 2020</td>
<td>NSW, QLD, VIC, WA</td>
<td>1400</td>
<td>WGS</td>
<td>David Thomas</td>
</tr>
<tr>
<td>Hereditary Cancer Syndromes * with ICCon</td>
<td>2016 - 2020</td>
<td>NSW, QLD, SA, VIC, WA</td>
<td>200</td>
<td>WGS</td>
<td>Robyn Ward</td>
</tr>
</tbody>
</table>

**Total Recruitment:** ~3880 (5 years)
Program Two
PROJECT 1 - CLINICAL VARIANT CLASSIFICATION & SHARING

Purpose – *Sharing of variants of known pathogenicity*
- Working to establish a **national consensus approach to variant classification**
- Provide a means and guidelines by which testing laboratories may **share reportable variant classifications consistently**, and in keeping with best practices internationally.

Primary activities –
- **National survey re: standard variant practices** from accredited laboratories nationally
- Working towards an Australian ‘clearing house’ tool to support sharing of curated variants, and **link with ClinVar internationally**
Program Two
PROJECT 2 - GENOTYPE-PHENOTYPE DATA CAPTURE AND ANALYSIS

Purpose – *Variant and phenotype information for cohorts of patients*
- ‘variant atlas’ framework for capturing phenotype-variant associations
- Developed at the Garvan Institute for Medical Research
- Allows genomic cohorts to be queried, filtered and analysed against large control datasets,
- Enables complex queries: new genotype-phenotype associations.

Primary activities – [https://variantatlas.org.au](https://variantatlas.org.au)
**Program Two**

**PROJECT 3 - PHENOTYPE ONTOLOGIES & eHEALTH**

**Purpose — Describe the clinical phenotype**

- Developing, testing and evaluating tools to aid **standardised capture of patient phenotype**
  - presentation,
  - symptoms
  - test results
- Contributing to Australian Genomics’ national database of **genotype-phenotype associations**.

*Phenotype ontologies and eHealth*

- **Tudor Groza** (co-chair)
- **Alejandro Metke** (co-chair)
- Denis Bauer
- Donna Truran
- Hugo Leroux
- Jilong Zhang
- Joshua Agudo

*Technical Work Streams*

- Clinical & Phenotypic Data Capture & Discovery
- **Driver Projects**: MME and Monarch
Program Two
PROJECT 3 - PHENOTYPE ONTOLOGIES & eHEALTH

Primary activities –
• Iteratively mapping clinical observations ‘phenotype’ with standardised digital descriptors ‘ontologies’ (SNOMED-CT, HPO)
• Developed “FHIRcap” to automatically extract and convert phenotypic information from the study database into the Gen-Phen datasets (complete)
• Designing a microservice to capture and manage quantitative phenotypes

• Patient Archive / MME platform
  https://mme.australiangenomics.org.au
• Our Beacon http://beacon.australiangenomics.org.au
Program Two
PROJECT 4 - VARIANT PIPELINE EVALUATION & QUALITY ASSURANCE

Purpose – **Quality and provenance of sequence data**: To address the diverse bioinformatic pipelines, we developed a framework for the quality control, performance assessment and description of pipelines.

Primary activities –
• Shared analysis framework for Dx pipelines
• The pipeline registry has been developed
• A prototype for an **interactive visualisation of pipelines** has been developed
• A prototype, web-accessible, **pipeline quality and performance (PQP) system** has been developed, and is ‘live’, evaluating Flagship-derived data quality
Program Two
PROJECT 5 - DATA GOVERNANCE, AGGREGATION, ARCHIVING & SHARING

Purpose – *Storing sequence and health data for future use*
Evaluate the legislative and data governance landscape, and build nationalised infrastructure to allow the ethical sharing, querying and archiving of standardised clinical genomic data.

Primary activities –
• Review into the legal and ethical barriers to genomic data sharing in collaboration with P4
• We’ve established a secure, accessible, federated tool that stores Flagship genomic data, using ‘Arvados Keep’ (live).
Program Two
PROGRAM LOGIC

Illustrating the activities and interrelationships between the Program 2 projects (P1 – P5)
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Illustrating the activities and interrelationships between the Program 2 projects (P1 – P5)
Thank you
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australiangenomics.org.au
Information Security Strategy
NATIONAL IMPLEMENTATION COMMITTEE

Purpose – The Australian Genomics Information Security Strategy attempts to address the conflicting challenges of preservation of individual privacy and the advancement of public health through data sharing.

Specifically relates to data collected on participants recruited into Australian Genomics clinical Flagships


• Data Types: Participants recruited into Flagships have consented to access to clinical records (EMR), administrative, hospital and MBS/PBS data, results of participant surveys, and access to genomic data
• Sharing of re-identifiable genomic and clinical data (genotype-phenotype information) nationally and internationally
• Future ethically approved research studies (de-identified)
• These data have been approved for collection and storage (HREC/16/MH/251)
Program Three
POLICY DEVELOPMENT

Purpose – Development of **policy relating to genomic medicine** so that it is scalable, equitable, accessible and cost effective.

Primary activities —:
• Policy development informed by **landscape analysis of frameworks** used to evaluate decisions around genomic testing internationally.
• Working in conjunction with international experts through a **G2MC Policy working group**. The group is considering:
  • A **road map** for implementation of genomics into healthcare.
  • A review of evaluation methods and criteria for genomics tests in order to consider if a **core set of values can be adopted globally**.
  • The establishment of a **knowledge transfer partnership** that would facilitate sharing and testing/evaluating existing knowledge and processes between jurisdictions.