SA Genomics Health Alliance

Submission to South Australian Productivity Commission

2020 Health and Medical Research Inquiry

From the SA Genomics Health Alliance

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Purpose
To reinforce to the South Australian Productivity Commission:

- The exciting opportunities for the engagement by the SA Government in genomic medicine
- How this is important in the relatively newly announced $500M in leveraged funds available via the federally funded Genomic Health Futures Mission,
- current status of genomic medicine in SA and;
- activities of the SA Genomics Health Alliance (https://www.sagenomics.org/).

Recommendations

- That the SA Government considers specialised fiscal support for peer reviewed local genomic medicine activities and the alliance so that SA has an equal voice on the national stage.

1. **Genomic medicine:** an emerging medical discipline that involves using genomic information about an individual as part of their clinical care (e.g., for diagnostic or therapeutic decision-making) and the health outcomes and policy implications of that clinical use. Genomics includes the use of techniques to sequence DNA (e.g. whole exome sequencing or whole genome sequencing) as well as techniques to sequence RNA (e.g. RNA-seq) as well as many additional high-throughput 'omics technologies.

   Genomics is a disruptive and enabling technology, with demonstrated applicability across multiple sectors including agritech, energy, mining, forestry and fisheries. Within the biomedical and health industries, genomics has the potential for immediate impact, with at least 50% (but most likely much more) of the Australian population predicted to benefit from genomic medicine and related technologies within their lifespan.

   Genomic medicine facts:
   - Genomic medicine has the greatest impact at the beginning (inherited disorders) and end of life (cancer, neurodegenerative disorders), when healthcare costs are high.
   - Although genetic diseases are individually rare, they comprise 7-8% of all childhood disorders and 30% of children in hospital have a genetic disorder.
   - The diagnostic rate for rare diseases has risen from ~10% 15 years ago to ~50% in 2018 because of genomic advances.

- A genetic diagnosis provides reproductive confidence: in a study of 80 couples who had a child with a complex disorder, 1/32 no diagnosis vs 9/48 with diagnosis went on to have another pregnancy within 18 mths. (Stark et al. 2017, 2018)
- Early diagnosis using genomics in Australia saves ~$21,000 per diagnosis (Stark et al, 2017, 2018).
- 50% of cancers are rare, poorly treated and account for the majority of cancer-associated death. Genomic testing indicates that at least 50% of cancers can be better treated.

Applications of genomics in health:

- **Rare disease:** Rare disease patients often experience a 'diagnostic odyssey', where it takes an average of 4-6 years to identify a patient's disorder. There are now thousands of stories from rare disease patients, such as Ollie, Louis and Ariana who have immediately benefitted from genomic testing with life changing results.

- **Cancer:** Genomic testing allows for 'personalised medicines' in cancer—offering individualised and targeted treatment that is based on the specific genetic makeup of an individual's cancer or rare disease. For instance, successfully stopping or reducing therapy at the right time has long-term benefits for patients, since drug side-effects are relieved and millions of dollars are saved on drug treatment. The case of South Australian boy, Angus, demonstrates the power of this process. Led by UniSA Professor Hamish Scott, the ACRF Cancer Genome Facility was able to pinpoint the DNA mutation causing Diamond-Blackfan Anaemia (a rare genetic bone marrow disorder) in Angus, and work with clinical specialists to understand the progression of the disease in Angus, including providing a biological basis for the previously baffling remission experienced by Angus. It was an understanding of the cellular basis for this spontaneous remission that is now supporting ongoing work to translate this into a personalised treatment regime for Angus, and more widely, offers better chances to develop effective cell-therapy approaches in other Diamond-Blackfan Anaemia sufferers.

- **Infectious Disease:** Genomic sequencing of microbes offers the opportunity to rapidly and accurately identify the cause of infection, without a need for cell culture. For example, genomics can be used to monitor the spread of disease, trace the origin of an epidemic or to identify multi-drug resistant species. Rapid testing devices are in development that will allow microbial detection at the point of care. For example, genomics can be used to identify infectious causes of stillbirth or illness in acute care.

- **Pharmacogenomics:** Variations in the human genome can cause individuals to respond differently to drugs. Genomic testing can be used to identify those individuals at risk for a serious adverse reaction. For example, ~6% of individuals have a life-threatening hypersensitivity response to the anti-HIV drug abacavir because they carry a specific DNA variation in the HLA region of the genome. Patients can now be screened for this variant prior to treatment with abacavir reducing the risk of death associated with treatment.

2. **Genomics can reduce health care costs:** A series of recent national and international studies have demonstrated that genomics, when implemented appropriately, can be used to substantially reduce healthcare costs.
   - Genomic testing can decrease the cost of diagnosing a rare inherited childhood disease from $27,050 to $6,003 if used as a first in line test. (Stark et al. 2017)
   - Changes in clinical management due to diagnostic WES results led to a cost saving of AU$1,578 per QALY (or AU$8,118 per QALY when additional indirect costs are included) (Stark et al. 2018)
   - Rapid genome sequencing of infants in acute case alters management in 31% of cases and substantially decreases inpatient costs (Farnaes et al. 2017)
   - Early exome sequencing in infantile epilepsy led to a cost saving of USD$7047 per diagnosis. (Howell et al. 2018)
   - Genomic sequencing reduced the cost per diagnosis for paediatric neuromuscular disease from USD$16,495 to USD$3706. (Schofield et al., 2017)

   A single chemotherapy dose in cancer is ~$10,000 and a $1,000 genomic test is increasing used to predict response.

It is notable that the clinical utility of genomic testing is increasing, whilst costs are decreasing. It is therefore likely that the economic benefit of genomic testing will continue to improve over the short to medium term.

3. The national genomics landscape:

Total investment in genomics across Australia totals $714M ($570 federal, $144 state).
There currently exist the following major genomics initiatives across Australia:

- **Genomic Health Futures Mission** ($500M over 10 years). The $500 million Australian Genomics Health Futures Mission is the centrepiece of the Government's $1.3 billion National Health and Medical Industry Growth Plan announced in the 2018-19 Budget. The first genomics project is Mackenzie's Mission, with $20 million being provided for a preconception screening trial for rare and debilitating birth disorders including Spinal Muscular Atrophy, Fragile X and Cystic Fibrosis.
- Australian Genomic Cancer Medicine Program ($50M, Federal Government)
- Zero Childhood Cancer ($50M, partner funding + $20M, Australian Government))
- Melbourne Genomics Health Alliance ($25M, Vic government + $8M from partner institutes)
- The Australian Genomics Health Alliance ($25M, NHMRC)
- Queensland Genomics Health Alliance ($25M, QLD government)
- Sydney Genomics Collaborative ($24M, NSW government)
- Canberra Clinical Genomics ($7.3M, ACT Government)

Further information on the Australian genomics landscape is available through the recently released reports:

- *Australia 2030, Prosperity through Innovation (Innovation & Science Australia)*
- *The Future of Precision Medicine in Australia (ACOLA)*.

A National Health Genomics Policy Framework (NHGPF) was ratified by COAG in October 2017 and an associated Implementation Plan is currently under development.

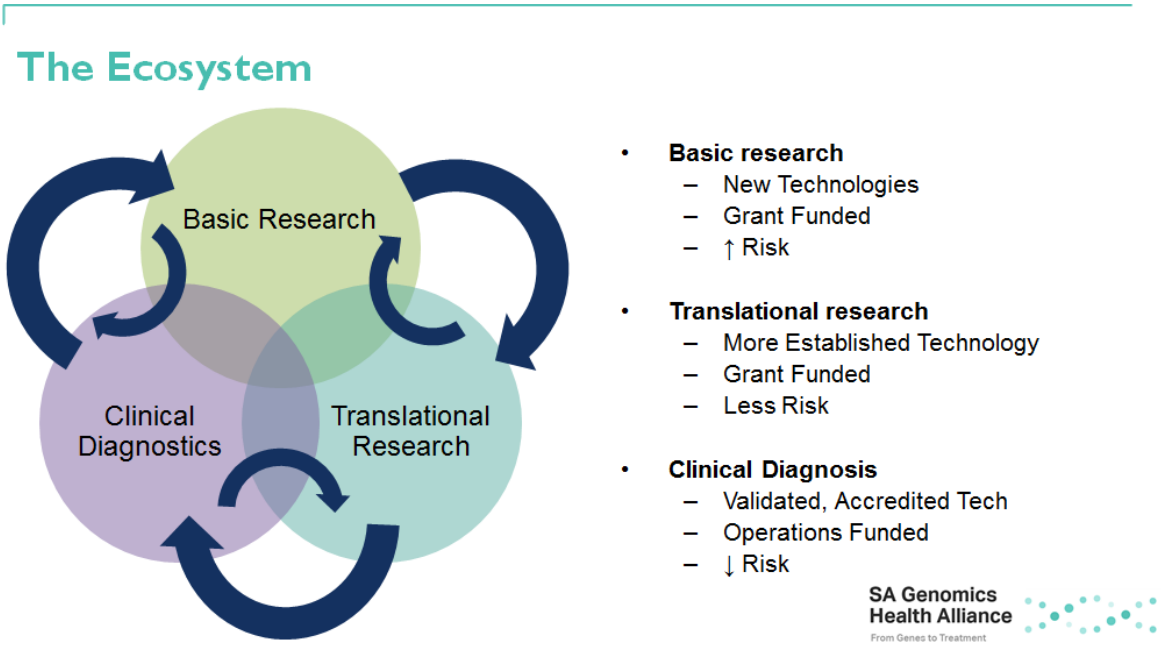
4. South Australian Excellence in Genomics including Diagnostics: SA has been an international leader in the field since the mid-20th century and punches well above its weight. The Human Genetics Society of Australia was conceived at an SA meeting, SA was the only state to have a representative, Prof. Grant Sutherland AC, on the highly prestigious 40 member founding council of the Human Genome Organisation and SA was also the only state to contribute to the Human Genome Sequencing project. This legacy has continued to today. SA was the first state to offer accredited clinical genomic sequencing in 2015, and we continue to lead the field, with SA Pathology having recently received the first accreditation in Australia for a series of advanced genomics tests (RNA-seq, copy number variation analysis, matched tumour-normal somatic sequencing and sequencing from fixed tissue, 2018). This means that SA **COULD** have been and also now offer the most advanced **ACCREDITED** genomic testing for genetic disease and cancer in the nation **if suitably empowered** by SA Pathology/SA Health/treasuary. State government budgetary and administrative processes (cumbersome, slow), attitudes (risk adverse) and state government infrastructure (including in IT) and processes hamper competitiveness and commercialization/monitization. Expectations for commercialization in the HMR and diagnostic area without flexible co-funding are all limiting. However, many National and international firsts are not monetised due to lack of support between public benefit and commercial profit. SA is and has been home to some the world's preeminent specialists in neurogenetics (Prof. Jozef Gecz, University of Adelaide) and the genetics of eye disease (Prof. Jamie Craig, Flinders University). Additionally, Prof Hamish Scott and A/Prof Barnet are Chief Investigators on an NHMRC funded study, in collaboration with the Broad Institute/Harvard Medical School (No 1 ranked academic institute in the world), investigating genetic causes of stillbirth/perinatal death. Thus far a genetic cause has been identified in over 50% of cases. Just this week, this was awarded a $3.4M MRFF Genomics Health Futures Mission grant as a nation project with SA leadership. The quality of research draws scientists from interstate and overseas and attracts significant funding. In the period 2013-2017 alone, SA genomics researchers received over $ 80M in grant funding (see fig).

5. Current clinical genomics practice in SA: SA has an exemplary clinical genomics service. Genomic testing has been funded via the LHN in SA for a number of years,, as part of the SA Clinical Genetics Service. This service has recently been separated from SA Pathology and split into the Adult Genetics Unit (AGU) at the RAH, and the Paediatric Genetics & Reproductive Unit (PRGU) at the WCH. The close relationship between SA Pathology, research laboratories, and

the LHNs (particularly the WCH, RAH and FMC) has allowed genomic testing to be embedded in the genetics service with expansion to a limited number of non-genetics specialists. There is opportunity to formally recognise this contribution to testing and the benefit which it has provided for SA patients. With the participation of SA Pathology but lead by Australian Genomics, on the 1st of May this year a new MBS funded item number was funded.

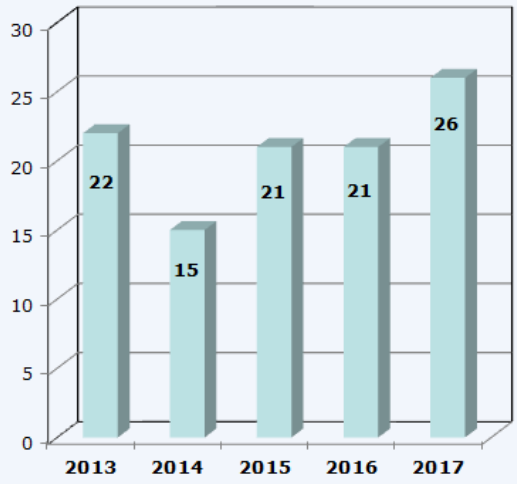
6. **SA Genomics Health Alliance:** As detailed in the attached brief, an SA Genomics Health Alliance was established in August 2017. This Alliance was formed by genomics specialists in the state in order to recognise the state contribution to the field and to address gaps that are emerging as the field evolves. A formal Alliance agreement is currently under development with member parties and SA Genomics is in the process of applying for Affiliate status with the SA Academic Health Science and Translation Centre. Collaboration through SA Genomics is designed to aid in the establishment of a research-diagnostic network centred around a genomics infrastructure hub. The Alliance is currently seeking funding to establish a genomics taskforce to further support genomics research and clinical implementation.

SA has a single state pathology service and has historically maintained close relationships between hospitals, laboratories, researchers and patient groups. This places SA in a unique position to capitalise on the developments in genomics. A wonderful opportunity exists for the SA government to back genomics in SA through leveraged support of national initiatives such as the Genomics Health Futures Mission, with the aim to continue SAs a leader in this field, but also to participate in as many projects as possible..

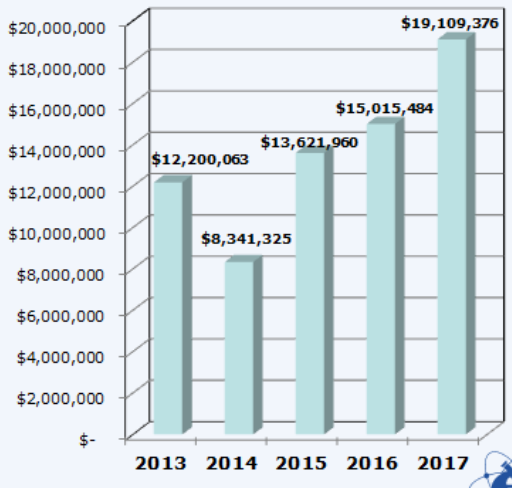


SA Grant Funding

Number of Grants With ACRFGF Budget



Amount of Grants With ACRFGF Component



105 Grants at > $68,000,000

SA PATHOLOGY

For our patients and our population

SA Genomics Health Alliance

From Genes to Treatment

Development Team: Prof. David Adelson, Sharon Bain, A/Prof. Christopher Barnett, A/Prof. Susan Branford, Prof. Alex Brown, Prof. Michael Brown, Prof. Jamie Craig, Dr. Janice Fletcher, Prof. Jozef Gecz, Joel Geoghegan, Prof. Greg Goodall, Prof. Eric Haan, Prof. Tim Hughes, Dr. Karin Kassahn, Sarah King-Smith, Prof. Angel Lopez, Prof. Ross McKinnon, Dr. Michael Michael, Sarah Moore, A/Prof. Andrew Ruszkiewicz, Dr. Andreas Schreiber, Prof. Hamish Scott, Prof. Steve Wesselingh, Prof. Deborah White (in alphabetical order).

Affiliations: Centre for Cancer Biology (CCB), South Australian Health and Medical Research Institute (SAHMRI), The University of Adelaide, The University of South Australia, Flinders University, SA Pathology, Women's and Children's Hospital.

The Challenge: Genomic testing is a key diagnostic and prognostic tool in medicine, yet SA lacks a unified voice or brand for genomic medicine. Extensive federal and interstate investment (>$714M) means that SA is at risk of losing genomics experts, clinical testing, and research funding. Further, in the absence of a coherent plan, SA will be unable to economically and sustainably implement genomic testing in mainstream medicine.

The Solution: An SA Genomics Health Alliance bringing together SA Research Institutes, Universities, SA Health, consumers and philanthropists to deliver better value healthcare through genomics.

Genomics - Key Facts

- Genomic testing is unique because it can analyse all genes in the human genome at once.
- SA was the first state in Australia to gain NATA accreditation for whole exome sequencing in 2015. In 2018, SA is again a leader in clinical genomics, being the first to validate a series of advanced genomic tests including RNA-seq and matched tumour-normal testing for cancer.
- Genomic testing can decrease the cost of diagnosing a rare inherited childhood disease from **$27,050 to $6,003** if used as a first in line test. (Stark et al. 2017).
- Although these diseases are individually rare they are common as a group, affecting up to 1 in 17 people. It takes on average 4-6 years to diagnose a Rare Disease. (Rare Disease UK)
- Pharmaceutical companies and healthcare providers are using genomic testing to identify the best treatment for cancer patients. This is referred to as 'personalised medicine' and it is one of the most promising developments in cancer therapy.
- SA is a key player in national genomics initiatives including the Australian Genomics Health Alliance & the Australian Genomic Cancer Medicine Program (AGCMP)

SA already provides limited genomic testing, why do we need an Alliance? The genomic medicine landscape has vastly changed in recent times and an Alliance is required to ensure SA patients have equitable access to cutting edge diagnostic technology. In the absence of an Alliance SA risks:

- Missing significant business development opportunities to innovate and attract capital to SA.
- Quickly becoming unable to compete.
- Disruption to existing services.
- Being unable to address the challenges posed by unregulated overseas online testing.

Can you give examples of activities an Alliance would undertake?

- Develop materials and host seminar series to educate healthcare professionals and the public about genomic medicine.
- Support a genomic medicine hotline and regional genomic telehealth services.
- Provide a conduit for funding collaborative research in the genomic medicine space.
- Act as a gatekeeper for the appropriate use of genomic tests.
- Help to develop infrastructure and linkages so pathologists, researchers and clinicians can work together for maximum benefit.
- Run demonstration projects to pilot the implementation of genomics in specific clinical scenarios.
- Support evidence based medicine for a sustainable healthcare system.

Interstate Comparison: SA has one of the most mature clinical genomic programs in Australia, yet lacks the dedicated investment seen in other states ($25M VIC, $25M NSW, $25M QLD, $9M ACT, $25M NHMRC funding) and is the only state without a genomics representative in government.

Why now? The cost of sequencing the human genome has decreased from $3bn to $1000 USD since 2003 meaning that widespread clinical implementation of genomic testing is now feasible.

Why is genomic medicine a special case? Genomic testing is in some ways the modern blood test: it is broadly applicable across almost all medical disciplines and can be used to diagnose and monitor many diseases. The technology poses special challenges not previously seen in the research or clinical space:

- The development and use of these tests requires **direct integration** of pathology, research , ICT and clinical activities.
- The tests generate **large amounts of data**. This means that they can be challenging to interpret, and requires that comparisons be made between patients. As a result optimal testing relies on the integration of specialist databases with eHealth records.
- An individual's test result can impact other family members and therefore has **unique ethical implications**.
- The genomic medicine field is **developing at an unprecedented rate** and requires dedicated investment in experts and equipment to keep pace.

SA Genomics Health Alliance aim: To deliver better value health care through genomics – by 2022 we aim to integrate genomics across all medical disciplines.

Contact: enquiries@sagenomics.org
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SA Genomics
Health Alliance

SA Genomics – Membership