Sydney Local Health District

Institute of Precision Medicine and Bioinformatics

NSW GOVERNMENT Health
Sydney Local Health District

Contents

Like the Genomics Network that precedes it, the Institute will not only encourage communication and collaboration between those providing genomic testing, but also allow other health professionals to benefit from the genomic expertise in the District.

Dr Natasha Luquin

From the Chief Executive

Sydney Local Health District has a long and successful history of collaboration and cooperation to ensure that the latest research is translated into the very best models of clinical care.

This culture ensures that talents across many disciplines can converge and develop models of care that are centred on the patient, and, in the discipline of genetics, on the family.

The District initiated a Genomics Network in 2018 to expand medical applications of genomics at the bedside, clinic, laboratory, and in the community. The Network has now evolved into the Institute of Precision Medicine and Bioinformatics to further progress genomics and develop the infrastructure for additional "omics" capability as these come on-line for patient care and research (including proteomics, metabolomics, transcriptomics and others).

Although bioinformatics is a core component of any "omics", it is specifically mentioned in the Institute's name to highlight the key role this technology plays in the analysis and storage of the large data sets generated by "omics".

The formation of institutes within Sydney Local Health District has produced many success stories, for example the Institute of Academic Surgery and Institute of Musculoskeletal Health.

The Institute of Precision Medicine and Bioinformatics will allow similar collaboration and cooperation between health professionals practising precision medicine in the District in order to optimise clinical care.

The Institute has identified the following work priorities starting 2020:

- Progress bioinformatics expertise and infrastructure
- Develop strategies for genome DNA sequencing in patient care
- Expand and strengthen connections and partnerships
- Consolidate research activities leading to greater competitiveness for research funding in genomics
- Align more closely with strategic directions identified in Commonwealth, State and Sydney Local Health District genomic plans

I wish the Institute and its broad membership group success, and I look forward to hearing how genomics and other "omics" will continue to improve patient care in our District.

Dr Teresa Anderson AM
Chief Executive
Sydney Local Health District

What is precision medicine?

Previously, our understanding of DNA and its role in human genetic disorders provided information which improved clinical diagnosis and risk assessment. Today, an individual's genetic profile can be used to select sophisticated novel therapies. This comprises precision medicine. An example would be genetic DNA testing a cancer – the DNA changes causing that patient's cancer are identified and from this the most effective treatment can be chosen. In this way, genomics or a comprehensive DNA genetic profile directly informs the decisions and treatments tailored to the individual patient.

Precision medicine strategies also include pharmacogenomics, by understanding how genes affect a patient's response to particular drugs. This allows for more effective prescribing of medications by using doses tailored to a patient's genetic makeup.

In future, an understanding of an individual's protein (proteomics) or metabolic (metabolomics) profile will provide additional "personalised" information that can be used for patient care via precision medicine.

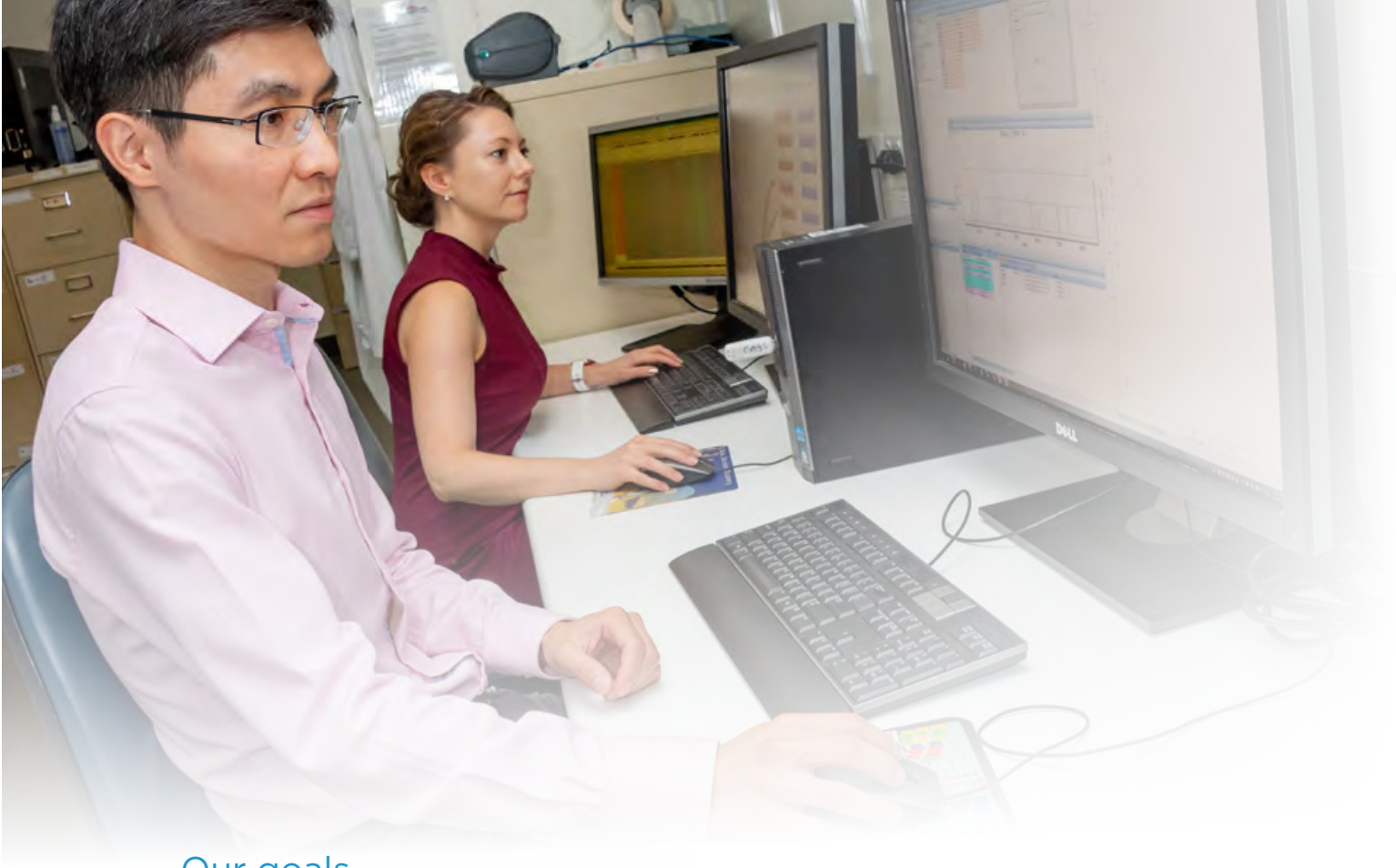
Our vision

To ensure that the benefits of precision medicine are rapidly and effectively implemented into the clinical care of patients and their families.

Initially, the Institute will utilise knowledge of an individual's DNA genetic makeup (genomics) to enhance clinical interventions required to maintain health and wellbeing. New and emerging strategies in precision medicine, including proteomics and metabolomics, will also be included in clinical models of care.

The Institute of Precision Medicine and Bioinformatics will deliver this vision through:

- Membership that is open to a wide range of health professionals within Sydney Local Health District, and partner organisations
- Strengthening the relationships between disciplines in the field of genomics
- Effective governance comprising a Director, Manager, Chief Scientist / QA Coordinator, and Management Committee
- Reporting structure to the District's Chief Executive, Director of Medical Services, Director of Research and the General Managers at RPA and Concord Hospitals



Our goals

- Enhancing medical diagnosis for a growing number of disciplines, including respiratory and cardiovascular medicine, nephrology, immunology, neurology and rare genetic disorders
- Selecting appropriate patient-specific therapies in cancer, including the ability to monitor progress by DNA testing
- Identifying risk in family members and using this knowledge to initiate early preventive or therapeutic interventions
- Prenatal screening and testing during pregnancy using non-invasive approaches
- Expanding the options for gene and cellular therapies

> The Institute will provide a platform that will assist in the development of novel strategies for identifying at-risk populations and tailoring treatment choices for individuals.
>
> **Dr Elizabeth Robertson**

History of genetics and genomics in Sydney Local Health District

1980–1990

The first molecular (DNA based) genetic tests were developed at RPA Hospital in the Department of Haematology. Initially, they were for the detection of thalassaemia but quickly expanded to include DNA genetic testing for cystic fibrosis and prenatal testing. Professor Ron Trent, who had returned after working in Oxford, led this initiative which resulted in a new Department of Molecular Genetics (later called Medical Genomics), and provided the first stand-alone DNA genetics testing service in NSW.

1991–2000

The Human Genome Project started with the goal to sequence the entire human genome. It was completed ahead of schedule in 2000. Knowledge that resulted from the sequencing of the genome of many organisms, plants, as well as the first human DNA sequence, opened up many opportunities in research. The clinical applications of these findings provided a better understanding for the genetic basis of disease, as well as new approaches to improve treatment. Although not appreciated at the time, the technological spin-offs from the Human Genome Project (high throughput DNA sequencing and bioinformatics) ensured that the genomics era (genetics = one or few genes; genomics = many or all genes) would soon follow.

2001–2010

The potential for genetic DNA based therapies became a reality and, through RPA Hospital's Gene and Stem Cell Therapy Program led by Professor John Rasko, patients with haemophilia and thalassaemia were treated with novel approaches leading to clinical improvements.
A decade later, a patient with another genetic disorder (porphyria) was treated by gene therapy in the Department of Chemical Pathology (Professor Peter Stewart). Professor Harry Iland in the Department of Haematology set up a molecular-based DNA testing initiative in patients with haematological malignancies for both diagnostic testing and post-treatment surveillance allowing earlier interventions should relapses occur.

Clinical and Cancer Genetic Services expanded at both RPA and Concord Hospitals enabling patients with genetic disorders to seek professional genetic counselling and have new diagnostic approaches through DNA genetic testing.

Genetic risks for couples planning pregnancy or risks in family members could be accurately assessed by genetic, and then genomic DNA testing.

Many specialty clinics across Sydney Local Health District now included DNA genetic or genomic testing as a component of decision making in patient care protocols. For example, neurology (Professor Garth Nicholson), cardiology (Professor Chris Semsarian), cystic fibrosis (Professor Peter Bye) and fetal medicine (Dr Tom Boogert, Professor Jon Hyett).

2011 – 2019

A collaboration between the Departments of Anatomical Pathology (Professor Sandra O'Toole) and Medical Genomics (Associate Professor Bing Yu) at RPA Hospital enabled somatic cell DNA genetic testing in cancer.

This service expanded rapidly with DNA genetic testing providing an example par excellence of how precision medicine would lead to new therapeutic approaches in cancer. This service was boosted with Professor Michael Buckland's neuropathology laboratory adding somatic cell testing for brain cancers.

Professor David Sullivan (Department of Chemical Pathology) working with the Department of Medical Genomics, started a model of preventive care allowing earlier interventions for patients with the common familial hypercholesterolaemia disorder. This approach requires the DNA genetic defects in each family to be identified. At-risk family members are then tested prior to the detrimental effects of the high cholesterol becoming established.

During this decade, genomics came to prominence as a direct result of the impressive technological developments allowing many to all of the human (and microbial) genes to be sequenced. The applications of genomic testing in microbiology demonstrated a novel finding when it was shown that the human microbiome, when characterised at the DNA or RNA level, showed some correlation with common clinical disorders such as diabetes. This opened a future therapeutic approach to be led by Professor Sebastiaan van Hal in the Department of Microbiology at RPA Hospital.

In addition, immunologists from Sydney Local Health District joined a consortium led by the Garvan Institute of Medical Research. CIRCA (Clinical Immunogenomics Research Consortium Australasia) enabled families with yet to be diagnosed or understood immunological disorders to be studied using whole genome sequencing approaches. The results have been impressive with new diagnoses being made and, in some circumstances, effective novel therapies implemented based on the underlying DNA genetic defects detected.

Opportunities in genomic medicine

There are many initiatives underway to include genomic (precision) medicine in new models of clinical care. These will have applications across diverse fields of medical practice such as hospital in and outpatient services, community general practice, public health, research and laboratory medicine.

The Institute of Precision Medicine and Bioinformatics will facilitate the development of new partnerships to ensure genomic capabilities are more rapidly identified and developed.

NSW Health

The NSW Health Genomics strategy was released in August 2017. The strategy articulates a shared vision for genomics in NSW, promoting collaboration to maximise opportunities for partnerships and optimal use of resources.

A Genomics Steering Committee will oversee the development of the implementation plan for Phase 1 of the strategy "Strengthen the foundations"; Phase 2 "Enhance disease management and prevention" and Phase 3 "Towards Precision Medicine".

NSW Health Pathology has published a Genomics Strategic Plan (2016-2018) based on the provision of a state-wide genomic service.

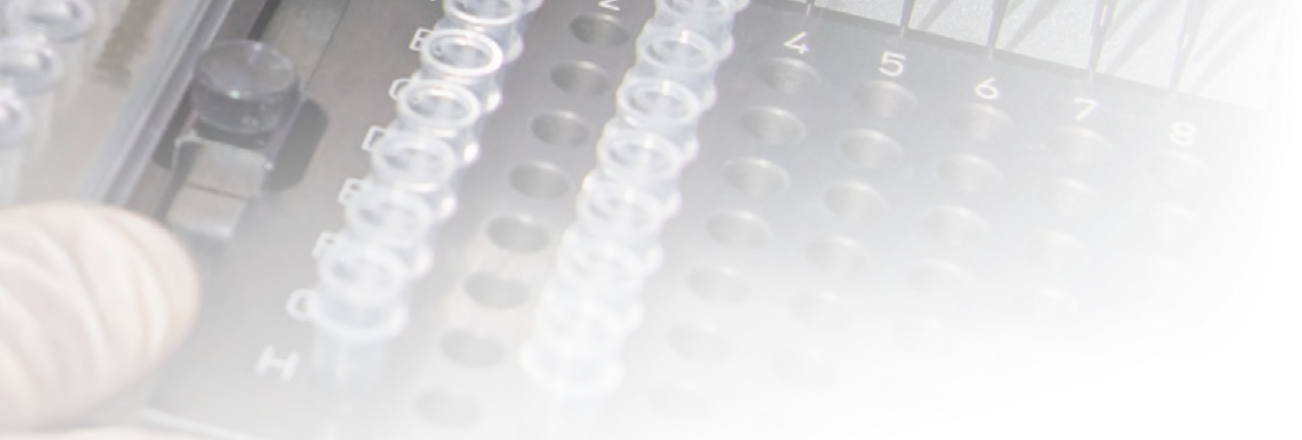
Sydney Local Health District

Sydney Local Health District has developed its own culture for clinical service delivery involving close interaction and integration of clinical, community and diagnostic services, such as imaging and laboratory medicine. Teaching and research are integral to service delivery.

The District leads many initiatives in NSW Health through its close integration of multidisciplinary services within the same location or departments and an extensive repertoire of clinical trials. This ensures staff rapidly adopt best practice for patient care. The appropriate and timely utilisation of genomic testing has benefited patients by reducing the time taken to achieve a diagnosis for complex or rare disorders, and lowering health costs by avoiding unnecessary investigations, medications and serious adverse events.

Pharmaceutical Benefits Scheme

There is a cost saving for the PBS if expensive subsidised drugs are only used for patients who are most likely to benefit from them. From this, the concept of "companion diagnostics" was developed, i.e. the prescription of a drug is dependent on a linked DNA genetic test that can confirm the drug is likely to have a beneficial effect. This precision medicine approach is increasingly being adopted by pharmaceutical companies when they develop new products or undertake clinical trials to assess efficacy and toxicity for new products. Patients in Sydney Local Health District have access to newly developed drugs through participation in clinical trials. The opportunity to stratify patients based on the relevant DNA genetic tests (pharmacogenomics) will increase access to a larger number of clinical trials.



Growing demand for genomics-based clinical services

Genetics and the health burden of chronic and rare diseases

Genetic factors are increasingly recognised as contributing to the health burden of chronic and complex diseases in our community. In this population, the utility of genomics, particularly the availability of rapid sequencing genomic technologies, is identifying new models of care. The same sequencing technologies are making inroads into the rare diseases, which are present in the population with a prevalence of approximately 1 in 2,000. Although individually rare, these disorders are collectively common. A starting point in understanding and then managing the rare genetic disorders is making the initial diagnosis, which becomes more likely if DNA genomic sequencing is added to the conventional investigations.

The move towards personalised medicine will require genetic and genomic expertise in multidisciplinary teams managing patients in a range of hospital-based and community services. Due to the mix of health professionals at Sydney Local Health District, it is essential for long-term sustainability that medical specialists, general practitioners, trainees, nurses, dieticians, pharmacists and others are engaged in genetic and genomic medicine to ensure new developments can be rapidly moved into clinical care.

Precision medicine and comprehensive cancer care

The use of genetic/genomic testing in cancer is now a well-accepted component in the model of care for inherited (germline) and the more commonly acquired or somatic cancers.

Genetic/genomic testing has proven valuable for cancer management with:

- Re-classification of cancers based on their DNA genetic mutations. The selection of treatment options is then guided by the cancer's underlying genetic defect rather than the tissue or organ involved.
- Screening at-risk family members with familial type cancers to enable more effective follow-up and prevention.
- Follow-up of patients with a broad range of cancers (solid and haematological), so any relapses are detected quickly and treatment recommenced.
- Enrolling patients in clinical trials which require prior stratification based on DNA genetic or genomic testing.

Novel models of care

Genetic or genomic DNA diagnosis should be considered as only the beginning of a journey. The ultimate in precision medicine is the use of cellular and gene therapies to correct or modify abnormal gene function. Sydney Local Health District is well positioned in this relatively novel form of treatment through its Department of Cell and Molecular Therapies and its collaboration with the Department of Haematology at RPA Hospital.

A feature of the clinical care provided through RPA and Concord Hospitals is the development of specialised clinics including hyperlipidaemia, porphyria, cystic fibrosis, cardiac genetics, fetal medicine, neurogenetics, alcohol dependence and cancer genetics. Each clinic has demonstrated the benefits of genetic and now genomics knowledge in driving innovative prevention and treatment programs using a multidisciplinary approach. Increasingly, access to new investigational drugs requires the stratification of patients based on genetic/genomic testing before entering clinical trials.

Clinical care and research in genomics at Sydney Local Health District

Genomics applications	Medical discipline or disorder	Patient benefits
DNA genetic testing	Clinical and Laboratory Genetics Cardiology Neurology Haematology Respiratory Immunology Renal	The DNA genetic test can be used to confirm clinical diagnoses without further investigations, e.g. haemochromatosis, prenatal testing. The same test can be used to screen at-risk individuals in the community or during pregnancy. Another important application is in predicting the risk for illness in those with a family history of genetic disease.
Implementing proven preventive strategies	Chemical Pathology	Families with Familial Hypercholesterolaemia have a genetic basis for their disorder and so family members are at risk. DNA genetic testing is now used to screen at-risk family members before the damaging effects of the high levels of cholesterol are established. Prevention is improved by early drug and dietary treatments. Recently a new generation of anti-lipid drugs were funded through the PBS. These will only be accessible if the relevant genetic abnormality is confirmed by DNA genetic/genomic testing.

Genomics applications	Medical discipline or disorder	Patient benefits
Personalised medicine in treatment	Oncology Haematology Tissue Pathology Neuropathology Pharmacogenetics	Treatment of cancer (melanoma, lung and bowel) has now a well-established DNA genetic test to ensure that the right drugs are selected based on the DNA abnormality in the patient's tumour. The personalised part is demonstrated here because it is not tumour X that is being treated (based on tissue or organ affected) but the patient's tumour as defined by its genetic/genomic defects against which specific drugs can be selected. Rare cancers for which there are no known treatment are now investigated for DNA genetic defects. Once detected, these form the basis for treatments that are off-label. In the haematological malignancies the potential for more accurate diagnosis is now supplemented with the ability to monitor early relapse through genetic DNA surveillance. The metabolism of potent drugs (anticancer or immunosuppressives) can be influenced by the underlying genetic structure for each individual. Based on the gene profile, the appropriate drug doses can be modified to prevent side effects or alternative medications are selected.
Gene-based therapies	Immunodeficiency Thalassaemia Haemophilia Porphyria	Treatment options for some genetic defects can now include the correction of the genetic defect to cure the disorder or make it significantly less severe. This approach is impacting across multiple disciplines including immunology, haematology and chemical pathology.

Our objectives

Two objectives for the Institute of Precision Medicine and Bioinformatics are:

Strategic

To deliver innovative health care and research

- Aligning more effectively the expertise found at RPA and Concord Hospitals
- Maintaining the multidisciplinary mix that encourages novel research discoveries and their rapid translation into clinical care
- Utilising precision medicine strategies to improve clinical outcomes
- Developing more innovative models of care
- Expanding options for genomics-based therapies
- Educating health professionals, students and trainees in genomics
- Facilitating more competitive research grant applications

Operational

To create a Sydney Local Health District administrative and governance structure for health professionals working in genomics, funded by the District but not aligned with a Clinical Stream

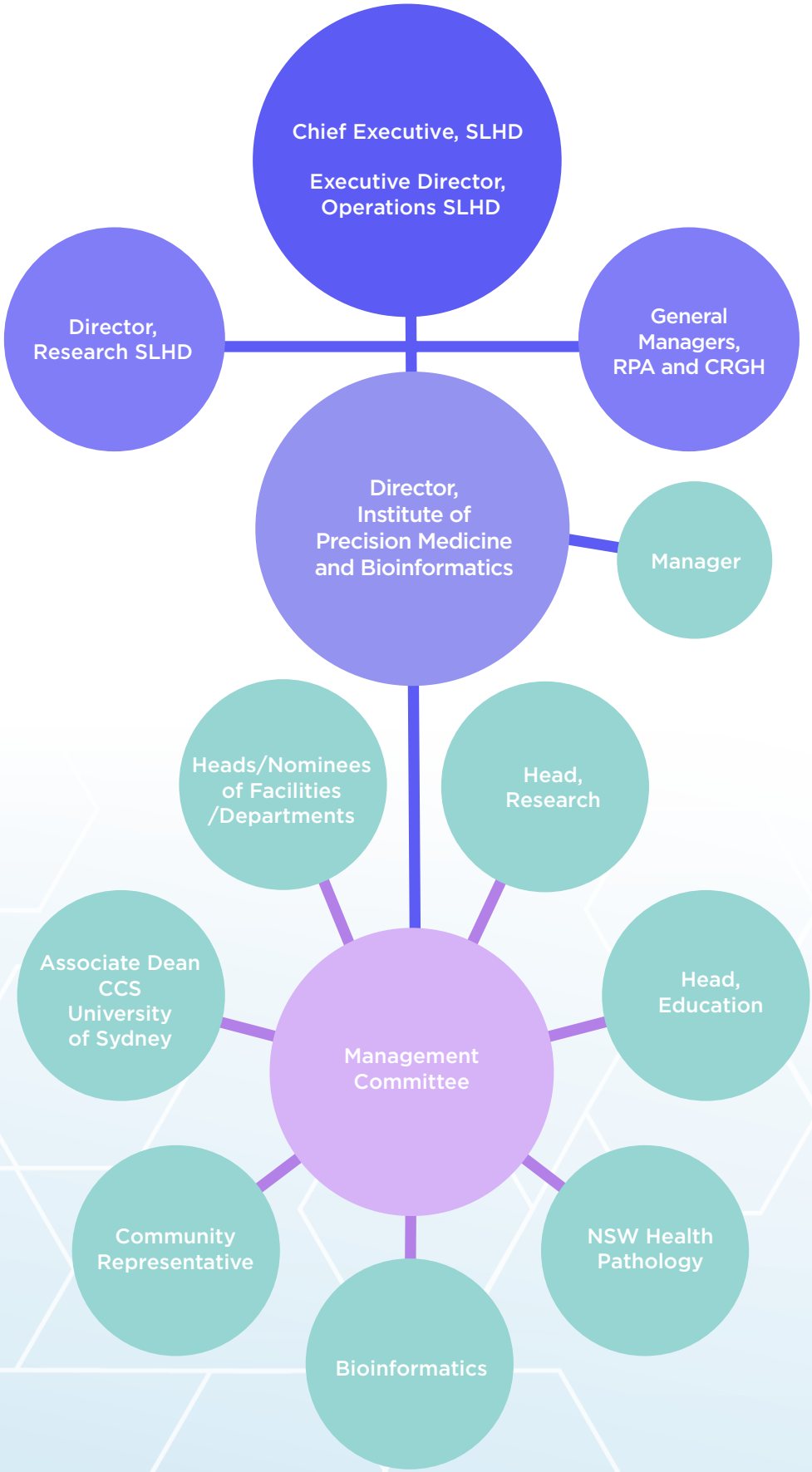
- Health professionals working in genomics (and other omics) can join the Institute to obtain a more relevant administrative and career pathway.

The Institute will strengthen our genomic research activities by improving communication and collaboration with molecular biological laboratories and bioinformaticians within the District.

Professor Harry Iland

Our membership

Our organisational structure



Future models of care with precision medicine

The Institute of Precision Medicine and Bioinformatics will function as an incubator for NSW Health Pathology through its work in developing innovative models of clinical care. This would enable NSW Health Pathology to respond with state-of-the-art technology and laboratory support.

The Institute will work more closely with The University of Sydney which has a strong track record for investing in new technologies and ideas that are mutually advantageous to the University and its partners including Sydney Local Health District.

While many developments have occurred in genomic medicine, there is more to come especially as the “omics” approach is broadened into other areas as described below.

Applications	Opportunities	Patient benefits
Developing new models of care	Charles Perkins Centre Vascular Health Clinic	An innovative vascular prevention clinic will develop along a shared-care model facilitated by a "virtual clinic" in which laboratory reports are supported by real-time clinician query and reply capabilities. This will provide a supportive framework for the developing field of cardio-metabolic medicine.
Metabolomics for clinical diagnosis and management	Obesity Diabetes Liver disease	Collaboration with the Charles Perkins Centre has led to the creation of a clinic to address the increasingly prevalent problem of non-alcoholic fatty liver disease. This will allow the evaluation of candidate biomarkers identified by sophisticated metabolomic analysis of samples from the Framingham Offspring study.
Epigenetics and molecular programming	Obstetrics Nutrition	Projects such as "Baby 1000" illustrate the combined expertise of researchers who are investigating the possibility that in utero factors may program life-long metabolic status. This type of endeavour requires the analytical and statistical expertise of a consortium-type model.
Cutting edge imaging capability	Neuropathology	Collaboration with mass-spectroscopists and researchers from the University of Sydney Nano Institute will create opportunities for sample analysis. Mass-spec imaging may be of particular relevance to Neuropathology. These collaborations can also address the field of drug discovery. Like most of the other initiatives listed here, this capability has much broader relevance within the context of Sydney Research as shown by collaborations within the BioHEART project.
Enhancement of Biobanking services	High throughput analysis to support Mendelian Randomisation etc	The principles of Mendelian Randomisation provide a strategy for the selection of informative biomarkers and promising therapeutic targets. Bioinformatics in an era of open data will allow many appropriate analyses to be conducted in silico. This capability can assist strategic decisions for clinical trials.

Our leadership team

Prof Ron Trent

PhD, MB BS, BSc(Med) (Sydney), DPhil (Oxon),
FRACP, FRCPA, FFSc, FTSE
Director

Ron is Head of the Department of Medical Genomics at RPA Hospital. He brings to the Institute considerable experience from his 12 years on NHMRC principal committees including Council, Research Committee and Chair of the Human Genetics Advisory Committee. He was a Director for the Garvan Institute of Medical Research from 1998-2009 and was recently re-appointed for another triennium. In 1991, he became the Foundation Professor of Medical Molecular Genetics at the University of Sydney. He has a strong interest in medical education and published his book Molecular Medicine in 1993, with a 4th edition in 2012. In 1996 he developed a training course leading to Fellowship in Genetic Pathology in the Royal College of Pathologists of Australasia. This program provided, for the first time, an opportunity for medical graduates to pursue a career in laboratory genetics.

Dr Natasha Luquin

BSc(Hons) PhD
Chief Scientist, WHS and QA Coordinator

Natasha is a senior hospital scientist in the Department of Medical Genomics (NSW Health Pathology) at RPA Hospital. She obtained her PhD in Neurogenetics at RPA, followed by post-doctoral research in the neuroanatomy of Parkinson's disease, returning to RPA in 2013 to continue her work in molecular genetics. She is involved in germline genetic testing, primarily pharmacogenetics and next generation sequencing and is the QA officer for the Department. Natasha collaborates in a research study with the Discipline of Addiction Medicine at RPA, investigating the pharmacogenetics of alcohol dependence treatment. She hopes to expand pharmacogenetic testing from reactive single-gene testing to pre-emptive testing of a panel of genes. This model of precision testing reduces adverse drug reactions and improves drug efficacy for better patient outcomes.

Ms Melissa Cole

BAppSci (Information)
Operations Manager

Melissa joins the Institute after a 20 year career in legal and business publishing. Melissa has worked extensively in the areas of business communication, administration, marketing, public relations and project management. She is looking forward to immersing herself in the administration and management of the Institute to ensure successful member collaboration and effective promotion of the Institute.

Our clinicians and researchers

Prof David Sullivan

MB BS, FRACP, FRCPA
Clinical Associate Professor, Dept of Chemical Pathology, RPA Hospital

David is a physician and chemical pathologist with a long-term interest in lipid metabolism with particular emphasis on the dietary component of gene–environment interactions contributing to cardiovascular disease and other chronic degenerative disorders. He has been involved in the early use of many forms of lipid-lowering intervention. He supports the improvement of detection and management of severe inherited dyslipidaemia, such as that seen in familial hypercholesterolaemia.

David has international experience including World Health Organization (WHO) Fellowship at the MRC Lipoprotein Unit, Royal Postgraduate School of Medicine, Hammersmith Hospital in London. He co-ordinated international clinical studies from the WHO reference lipid laboratory in Wageningen, Netherlands where he worked with the originator of the technique known as Mendelian Randomisation. This technique has become fundamental to precision medicine because it harnesses bioinformatic techniques to identify causative biomarkers and promising therapeutic targets. In addition to his clinical and teaching activities, David has served on numerous clinical committees including the management committees of the LIPID and FIELD trials. Current research interests include biomarkers and post-prandial metabolism. He also dabbles in potential therapeutic uses for chocolate.

Prof Clement Loy

BA, MB BS, MMed(Clin Epi), FRACP, PhD
Professor, Brain and Mind Centre, University of Sydney
and Huntington Disease Clinical Program, Westmead Hospital

Clement is a cognitive neurologist with subspecialty training at the Dementia Research Centre, National Hospital for Neurology and Neurosurgery, Queen Square, London; and laboratory training in molecular genetics at the Garvan and Prince of Wales Medical Research Institutes. He has a longstanding interest in the genetic forms of dementia, having provided care for families with familial Frontotemporal Dementia, familial Alzheimer Disease and Huntington Disease, in London and Sydney, since 2003. He has summarised his approach to the familial dementias in a first-authored review in the Lancet (2014). Clement's current research interests include gene-silencing trials for people with Huntington Disease, and design of clinical trials for pre-manifest expansion carriers using a genotype-based enrichment/ precision medicine approach. He serves the wider community as a member of the Pharmaceutical Benefits Advisory Committee.

Integration of laboratory, bioinformatic and clinical activities will drive rapid translation of genetic technology to personalised diagnosis, prognosis and treatment.

Professor Clement Loy

Prof John E.J. Rasko AO

BSc (Med), MB BS (Hons), PhD, MAICD, FFSc(RCPA), FRCPA, FRACP, FAAHMS
Head, Dept of Cell and Molecular Therapies, RPA Hospital and Stem Cell Therapy Program at the Centenary Institute, University of Sydney

John is an Australian pioneer in the application of adult stem cells and genetic therapy. He is a clinical haematologist, pathologist and scientist with an international reputation in gene and stem cell therapy, experimental haematology and molecular biology. In over 170 publications he has contributed to the understanding of stem cells and blood cell development, gene therapy technologies, cancer causation and treatment, human genetic diseases and molecular biology.

John serves on hospital, state and national bodies including Chair of GTTAC, Office of the Gene Technology Regulator – responsible for regulating all genetically-modified organisms in Australia – and immediate past Chair of the Advisory Committee on Biologicals, Therapeutic Goods Administration. He is the President (2018-20) of the prominent International Society for Cell & Gene Therapy.

Contributions to scientific organisations include co-founding (2000) and past-President (2003-5) of the Australasian Gene & Cell Therapy Society; Vice President (2008-12) and President-Elect (2016-18) International Society for Cell & Gene Therapy; Scientific Advisory Committees and Board member for philanthropic foundations; and several Human Research Ethics Committees. He is the recipient of national (RCPA, RACP, ASBMB) and international awards in recognition of his commitment to excellence in medical research, including appointment as an Officer of the Order of Australia.

Prof Sebastiaan van Hal

MB ChB, FRACP, FRCPA, PhD
Senior Staff Specialist, Infectious Diseases and Microbiology, RPA Hospital

Sebastiaan is a Senior Staff Specialist in the Department of Infectious Diseases and Microbiology and a member of the Institute of Precision Medicine and Bioinformatics at RPA Hospital. He has an extensive research record in molecular epidemiology focusing on multi-resistant Gram positive organisms (MRSA and VRE) and fungal pathogens.

Sebastiaan successfully established a NATA accredited whole genome sequencing service for bacterial pathogens. This service has aided patient care by assisting in the diagnosis of causative pathogens and identification of antimicrobial resistance genes assisting medical practitioners' choice of antibiotics for treatment options. It is also a valuable tool for infection control in outbreak investigations.

He continues to explore new diagnostic ways of utilising whole genome sequencing technology examining viral diagnostics; microbiome and metagenomic testing. In addition, he continues to explore long-read sequencing (Oxford Nanopore technologies) to assist in genome closure and in our understanding of transmission dynamics of mobile genetic elements carrying antibiotic resistance genes between pathogens.

Prof Harry Iland AM

MB BS(Hons), FRACP, FRCPA, MHGSA
Haematologist, Sydney Local Health District

Harry's current appointments include Senior Staff Specialist in the Institute of Haematology and the Institute of Precision Medicine and Bioinformatics at RPA Hospital where he heads the Molecular Haematology Laboratory, and Clinical Professor in the Sydney Medical School, University of Sydney.

Harry established one of the earliest diagnostic molecular haematopathology laboratories focusing on haematological malignancies in Australia, and his laboratory has identified and published novel molecular variants in acute promyelocytic leukaemia (APL), core binding factor acute myeloid leukaemia, and the McLeod syndrome. His major clinical and laboratory passion has been the investigation and management of APL, and he has been responsible for the Australasian Leukaemia and Lymphoma Group (ALLG) clinical trial program in APL since 1997. The APML4 regimen, which has been a major achievement of that program, has received international recognition, and has proven to be practice-changing in the US, Canada and Australia.

Harry has served on numerous national and international committees including the European LeukemiaNet's panel of experts in APL, the Australian Drug Evaluation Committee, and the Molecular Haematology and Molecular Genetics Advisory Committees of the RCPA Quality Assurance Program. His awards include the Haematology Society of Australia and New Zealand (HSANZ) Robert Pitney Travelling Fellowship, the HSANZ Carl de Gruchy Oration, Life Membership of the ALLG, and Member of the Order of Australia (AM).

Prof Garth Nicholson

MB BS, FRACP
Director, Northcott Neuroscience Laboratory,
ANZAC Research Institute, Concord Repatriation General Hospital

Garth is an academic and clinical neurologist who directs both research and diagnostic neurogenetic laboratories. His research group has mapped and located a number of neurogenetic disorders, particularly hereditary neuropathies (HSAN1, CMT X1, X3 and distal hereditary myopathy, dSMAX), spastic paraplegias, and inherited ataxias (including Machado-Joseph disease) and motor neurone disorders including the fatal form known as amyotrophic lateral sclerosis.

He established the Molecular Medicine Laboratory, a reference neurogenetics diagnostic facility, at Concord Hospital. His group has shown that only about 50% of families with inherited neurodegenerations have gene coding mutations. His research group at the ANZAC Northcott Neurobiology laboratory are examining noncoding DNA abnormalities causing disease in the missing 50% of families.

Present research work focuses on exploring avenues to treat specific hereditary neuropathies with well-defined cell biology and amenable metabolic pathways, including HSAN1 X1 and CMTX6A and C, CMTX1.

Assoc Prof Michael Buckland

MB BS, PhD, FRCPA
Clinical Associate Professor and
Head, Dept of Neuropathology, RPA Hospital

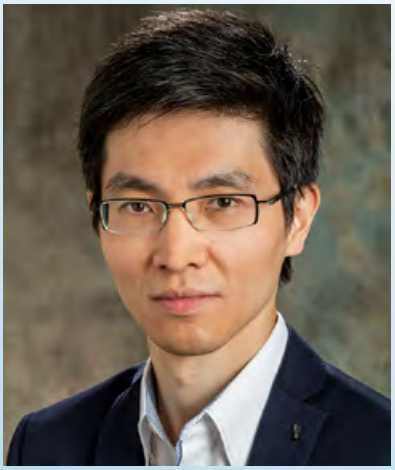
Michael is a Senior Staff Specialist and Head of the Department of Neuropathology at RPA Hospital. During his medical training he undertook a PhD in neurobiology and postdoctoral work in molecular biology.

He commenced his role as a dedicated neuropathologist at RPA Hospital in 2009. He has a longstanding interest in the biology and molecular pathology of brain tumours and neurodegenerative disease, and has published widely in this area. Under his leadership, RPA Neuropathology established Australia's first clinical diagnostic service for brain tumour molecular testing in 2013. Today the service attracts referrals from throughout Australia and New Zealand. Michael is excited to be part of the Institute of Precision Medicine and Bioinformatics: he believes that precision medicine is fundamental to accurate brain tumour diagnosis, which is the essential first step to any meaningful clinical trial in brain tumour treatment.

Assoc Prof Bing Yu

MD, PhD, FFSc (RCPA)
Associate Professor, Central Clinical School, University of Sydney
and Honorary Principal Hospital Scientist, Dept of Medical Genomics,
RPA Hospital

Bing is a Fellow of both the Faculty of Science, Royal College of Pathologists of Australasia, and Human Genetics Society of Australasia. Bing leads one of the two state-wide centres for cancer somatic DNA testing based in the Department of Medical Genomics at RPA Hospital, NSW Health Pathology. This type of testing provides critical information about genetic DNA changes in tumour cells and facilitates precision treatment for patients with advanced stages of lung, melanoma and colorectal cancer. Bing has published over 100 papers and book chapters and has a strong interest in bioinformatics. He is the editor for the book "In silico tools for gene discovery" and author for book chapters in two editions of "Clinical Bioinformatics".



Dr Anthony Cheong

MB ChB, BMedSc(Hons), MPhil, DPhil
Registrar, Dept of Medical Genomics, RPA Hospital

Anthony developed an interest in exploring genetic abnormalities underlying human diseases when he characterised the function of the first human cytochrome c mutation causing familial thrombocytopenia. He discovered ABCB6 as one of the genetic modifiers on patients suffering from life-threatening attacks from porphyria in collaboration with St Jude Children's Research Hospital.

He was a Nuffield Medical Fellow between 2014-2018 at the University of Oxford, where he developed a single cell CRISPR-Cas9 genome editing protocol to study acquired alpha thalassaemia in patients with myelodysplastic syndrome.

He sees the Institute of Precision Medicine and Bioinformatics as the venue where cutting edge research will be performed and translated to refine clinical care for patients at Sydney Local Health District and beyond.

Dr Amali Mallawaarachchi

MB BS, FRACP, PhD
Staff Specialist, Clinical Geneticist & Nephrologist,
Sydney Local Health District

Amali is a Staff Specialist Clinical Geneticist at RPA Hospital. She is Australia's first dual-trained Clinical Geneticist and Nephrologist and has a clinical and research interest in the genetics of inherited kidney disease.

Amali completed her PhD focused on genomics in polycystic kidney disease and is continuing this work as a post-doctoral scientist in the Division of Genomics and Epigenetics at the Garvan Institute of Medical Research.

Her current research focuses on understanding the molecular basis of polycystic kidney disease and is supported by a Viertel Foundation Clinical Investigator Award and The PKD Foundation. She has particular expertise in genomic analysis and variant interpretation and developed the first validated whole-genome sequencing based genetic testing for polycystic kidney disease, which allowed families in Australia access to diagnostic testing for this condition for the first time. Amali works with Genetic Counsellors to provide personalised care for patients and families with inherited disease. She has established specialised Renal Genetics clinics across Sydney Local Health District and is the NSW state lead of the KidGen collaborative, a collaborative that coordinates multidisciplinary renal genetics clinics across Australia.

Dr Elizabeth Robertson

BBiomedSc (Hons), MB BS (Hons), PhD, FRACP
Cardiologist, Central Sydney Cardiology and
Clinical Senior Lecturer, University of Sydney

Elizabeth is a Cardiologist with an interest in genetically triggered disease that affects the vasculature, including Marfan syndrome and familial hypercholesterolaemia.

Her particular precision medicine interests include the contribution of epigenetics to these genetic conditions, in particular microRNA expression profiles, with a view to identifying novel therapeutic targets. In addition to her clinical and research commitments, Elizabeth is also involved in teaching medical students.

Ms Cassandra Kavanagh

BSc
Hospital Scientist, Cancer Somatic DNA Mutation Testing,
Dept of Medical Genomics, RPA Hospital

Cassandra's work is focused on profiling the DNA mutations that contribute to solid tumour growth in advanced cancer patients. Once this is known, the individual mutation profile of a patient's tumour can be used to help clinicians decide the best treatment options for the patient, including targeted therapies.

Cassandra and her fellow scientists under the supervision of Prof Bing Yu (Dept of Medical Genomics and University of Sydney) have been working on implementing new technologies such as next generation sequencing and circulating cell-free tumour DNA analysis which allow individualised tumours to be analysed in a more dynamic way. This means that the potential for their work now extends beyond just finding therapeutic targets, to providing useful information about patient prognosis, therapeutic response, surveillance and drug resistance.

Dr Kishore Kumar

MB BS, PhD, FRACP
Staff Specialist in Molecular Medicine,
Concord Repatriation General Hospital

Kishore is a Staff Specialist in neurology with a strong focus on neurogenetics. His PhD on "Advances in Genetic Studies of Movement Disorders" was undertaken at the Institute of Neurogenetics, University of Leubeck and Kolling Institute of Medical Research. With an NHMRC Early Career Fellowship at the Kinghorn Centre for Clinical Genomics, his research focused on the use of whole genome sequencing for the diagnosis of neurogenetic disorders. He has interpreted the genomes of more than 400 individuals, ranging from hereditary cerebellar ataxia, myotonic dystrophy to amyotrophic lateral sclerosis. He continues his connection with the Kinghorn Centre for Clinical Genomics as an honorary visiting scientist.

Repeat expansion disorders are particularly relevant for the field of neurogenetics but they represent a challenge to diagnose. In collaboration with Prof Garth Nicholson, Kishore is involved in providing clinical expertise for the diagnosis of such disorders at Concord Molecular Medicine, and he will build on this experience to establish Concord as an international research centre for repeat expansion disorders.

Ms Lauren Olafson

BSc, MBiomedSci
Genomics Bioinformatician, Institute of Precision Medicine and Bioinformatics, Sydney Local Health District

Lauren is a Genomics Bioinformatician at RPA Hospital. Her interest in harnessing computational potential to investigate the genetic components of disease led her to pursue the field of bioinformatics.

Her early career began in medical research at the University of New South Wales where she specialised in adult glioblastoma and high-risk paediatric cancers. There she conducted genomic analysis using a precision medicine approach to characterise cancer and identify molecular drivers.

She recognises the increased feasibility and relevance of applying bioinformatics and precision medicine in a clinical setting and is excited to be a part of Institute of Precision Medicine and Bioinformatics.

The translation of somatic cell DNA genetic testing into clinical care requires leadership and advocacy for the many disciplines involved.

Ms Cassandra Cavanagh

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