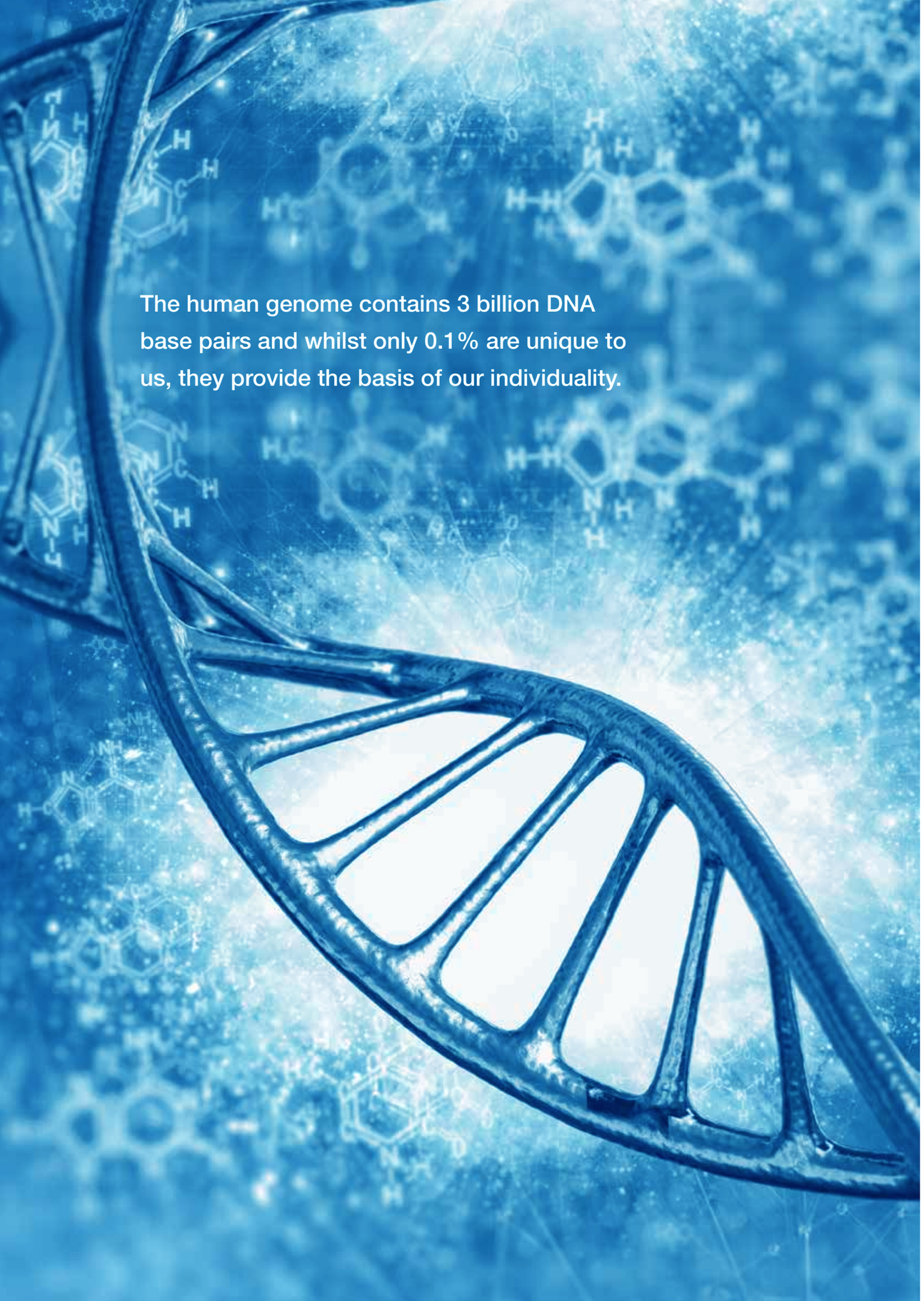
MHTP Medical Genomics Facility

Biennial Review 2018/2019

MHTP Monash Health Translation Precinct | MONASH University | HUDSON INSTITUTE OF MEDICAL RESEARCH | MonashHealth



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MHTP Medical Genomics Facility

Our facility provides access to sophisticated technologies and expertise to determine the structure and function of DNA and its role in health and disease.

Vision

To provide collaborative and agile genomic services of the highest quality to enable basic and translational research.

Mission

To support innovative medical research through the delivery of specialised genomic technology services, knowledge and expertise.

We encourage you to learn more at mhtpmedicalgenomics.org.au

Our Medical Genomics facility, incorporating the Gandel Genomics Centre, is a recognised platform technology leader in Australia. With 20 years of experience, we have continually evolved and innovated to reflect the dynamic changes in the field of genomics that deepen our understanding of human health and disease.

Located within the MHTP Translational Research Facility (TRF), we support scientific discovery and insight into how disease and disability can be diagnosed, prevented and treated.

MHTP Medical Genomics Team – L-R, Ms Jodee Gould, Dr Selva Kumari Ramasubramanian, Dr Trevor Wilson, Ms Vivien Vasic, Ms Amesha Silva, Dr Sen Wang, Ms Angela Phan, Dr Niro Pathirage, Dr Catherine Itman

Message from the Platform Manager

I present this annual report with pride as our facility celebrates 20 years as a recognised platform technologies leader in Australia. Our journey began in 1999 using Sanger sequencing technology, and has since expanded in scope to incorporate real time PCR, microarray, high throughput microfluidics, single cell DropSeq, and Next Generation Sequencing capabilities.

With an emphasis on supporting research and clinical projects through internationally accredited laboratories, our success has been achieved through collaboration between Monash Health Translation Precinct (MHTP) partners in concert with philanthropic donors and government. Their support, for which we are sincerely grateful, has enabled us to continuously advance our technology over the span of the last two decades, and remain at the forefront of a changing healthcare landscape.

Gandel Philanthropy, in particular, has been a dedicated supporter of genomics at the MHTP for 15 years. Their most recent grant, dedicated to supporting the advancement of genomics research, enabled the establishment of the Gandel Genomics Centre, which we proudly launched in June 2017. Since this time, the Centre has supported the work of numerous researchers across a wide range of projects, including the Hudson Institute and Monash University research programs, Melbourne Genomics, and AIM BRAIN projects.

Our excellence in clinical genomics was highlighted and strengthened recently when the facility was awarded NATA (National Association of Testing Authorities) accreditation for whole clinical exomes, building on the original accreditation achieved in 2003. We closed our Sanger sequencing and Microarray technology, after many years of service, to enable us to focus on advancing our Next Generation Sequencing technologies. In the coming year, we are excited to be introducing NextSeq technologies, to support timely, high impact research and clinical outcomes for the precinct.

The facility has contributed to many innovative projects that have made important progress in critical research areas such as cancer, inflammation, reproduction and child health, microbiome, regenerative and neurodevelopmental disorders. We look forward to sharing some of the outcomes of this research within this review.

My heartfelt thanks go to our governance and leadership committees for their continued support, and to Dr Trevor Wilson, the lead of our expert scientific team.

The success of our platform is reinforced by the continued dedication and diligence of all members, for which I am extremely grateful.

Thank you, once again, to all our supporters; your commitment and continued engagement allows us to thrive and extend our outreach from basic research through to translational and precision medicine.

Vivien Vasic
MHTP Medical Genomics Facility Manager
MHTP Platform Strategic Initiatives Manager

MHTP Platform Strategic Initiatives Manager: Ms Vivien Vasic

1999

Wellcome Trust Sequencing Centre established - a joint initiative of the Monash Institute of Medical Research (MIMR) and Prince Henry's Institute (PHI)

2000

Applied Biosystems 377 sequencer capability is increased three fold

2004

dHPLC technology for mutation detection introduced

2005

Real-Time PCR technology for gene expression established

2006

Launch of the **Gandel Charitable Trust Sequencing Centre**

2007

Qualification of RNA / DNA analysis commenced

2008

Second Genetic Analyzer purchased with Monash Health

2010

MIcroSeq genetic microbial ID system established and Next Gen Sequencing introduced

2011

Integration of Next Gen Sequencing, High Content Screening and Microarray within the **MHTP Medical Genomics Facility**

2012

Launch of the **ACRF Centre for Cancer Genomic Medicine**

2014

MIMR and PHI merge to form the Hudson Institute of Medical Research

2015

Launch of the **Fluidigm Single Cell Centre of Excellence**

2015

Relocation to new laboratories within the MHTP Translational Research Facility

2016

Expansion of Next Gen -Illumina HiSeq, MiSeq and Ion Proton systems

2016

DropSeq technology introduced

2017

Functional Genomics capabilities established

2017

Launch of the **Gandel Genomics Centre**

2019

CELEBRATING 20 YEARS SUPPORTING MEDICAL RESEARCH

Gandel Genomics Centre

We recently celebrated the founding of the Gandel Genomics Centre, launched to recognise the long-standing relationship with Gandel Philanthropy that now spans almost 15 years. Gandel Philanthropy is one of Australia's largest independent, family philanthropic funds and has been a committed and fervent supporter of genomics at the Hudson Institute.

In 2005, Mr John and Mrs Pauline Gandel could see the potential of genomics to transform healthcare. They provided a grant to fund a 16 capillary Genetic Analyser using the latest DNA Sanger sequencing technology and the Gandel Charitable Trust Sequencing Centre was launched in appreciation of their generosity.

This technology led the way for a Victorian-first initiative using the MicroSeq Genetic Microbial Identification System for the rapid diagnosis of bacterial or fungal infections. With the support of additional funding provided by Gandel Philanthropy in 2010, this initiative enabled test results to be achieved in hours rather than days.

The Hudson Institute's genomic research capabilities were given a significant boost in 2017, with a further grant by Gandel Philanthropy to support the Gandel genomics health research program to develop genomic technologies from basic research through to diagnostics and precision medicine.

We were extremely honoured that three generations of the Gandel family were able to participate in the launch of the Gandel Genomics Centre. This demonstrates the deep commitment to philanthropic funding for medical research that is shared among all members of the family, and the importance of Gandel Philanthropy's legacy in the field of advanced medical research and transformative diagnosis and treatment technologies, as affirmed by Mr John Gandel:

"Helping set up this Centre to enable future significant research in genomics and precision medicine was a natural next step in our productive and long-standing relationship."

2006 - Mr John Gandel AC, Mrs Pauline Gandel AC, Ms Vivien Vasic and Professor Byran Williams at the Gandel Charitable Trust Sequencing Centre launch.

2017 - The Gandel Family at the launch of the Gandel Genomics Centre.

Top: L-R: *Ms Vivien Vasic, Mr Bob Edgar, Mrs Pauline Gandel AC, Mr Frank McGuire, Mrs Lisa Thurin, Mrs Helen Gandel, Mr Vedran Drakulic OAM, Professor Bryan Williams*
Lower left: L-R: *Professor Paul Zimmet AO, Professor Henry Burger AO (Augural Director, Prince Henry's Hospital Medical Research Centre), Professor David de Krester AO (Augural Director Monash Institute of Reproduction and Development renamed the Monash Institute of Medical Research (MIMR)) – Prince Henrys Institute and MIMR merged in 2014 to form the Hudson Institute of Medical Research*
Lower middle: *Dr Joanne Lundy*
Lower right: L-R: *Mr Thurin Mrs Pauline Gandel AC, Mrs Helen Gandel, Ms Vivien Vasic*

Research Highlights
2018 - 2019

Dr Joanne Lundy
Medical Oncologist and PhD candidate, Cancer and Immune Signaling Group, Hudson Institute

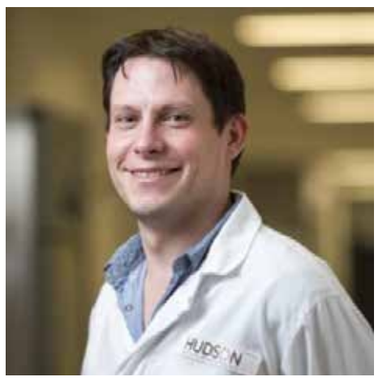
Advancing Precision Medicine in Pancreatic Cancer

Dr Joanne Lundy is a medical oncologist undertaking a PhD at Hudson Institute focused on “Advancing Precision Medicine in Pancreatic Cancer”.

Advanced pancreatic cancer is an aggressive disease with few effective therapeutic options. Unfortunately, obtaining high quality biopsy material from pancreatic tumours is challenging, and can lead to delayed cancer diagnosis that subsequently limits treatment options. The Cancer and Immune Signaling Group has developed a research pipeline in which fine needle biopsies are used to isolate high quality genetic material. The group processes samples using Next Generation Sequencing technologies in Medical Genomics to characterise the range of tumour mutations and abnormally expressed genes that are present in each individual cancer.

The group uses this information to create a genetic signature of pancreatic cancer, which they hope will decrease the time to diagnosis, avoid the need for repeat biopsies, and potentially open new targeted treatment pathways for patients facing this devastating disease. A targeted therapy trial for patients with tumours featuring a specific genetic profile is currently open and recruiting patients. The team are planning to open a new precision medicine study in the coming months, applying their genetic signature and targeted gene panel testing to all consenting patients presenting with a new diagnosis of pancreatic cancer. By rapidly detailing clinically relevant molecular tumour features, the group hopes to match patients to the most suitable targeted treatments for their disease.

Berry, W.; Lundy, J.; Croagh, D.; Jenkins, B.J. Reviewing the Utility of EUS FNA to Advance Precision Medicine in Pancreatic Cancer. Cancers 2018, 10, 35.



Dr Sam Forster
Head, Microbiota and Systems Biology Group, Hudson Institute

Bacterial communities in metropolitan, rural and indigenous Australians

Gastrointestinal microbiota play an essential, though poorly understood role in many aspects of human biology. Emerging evidence suggests the bacterial community structure can impact diseases as diverse as autoimmune diseases, cancers and infections. Despite their importance, many species of bacteria that inhabit this environment have not yet been successfully grown in the laboratory, nor had their genome sequenced or interactions with the human immune system characterised.

Research within the Microbiota and Systems Biology Group led by Dr Sam Forster, applies genomics, computational and systems biology, microbiology and immunology to develop an understanding of these bacteria, their genomes and the reciprocal interactions with the human immune system that either leads to disease or maintains health.

The Medical Genomics Facility supports whole genome sequencing of diverse bacterial isolates cultured from the microbiomes of metropolitan, rural and indigenous Australians. The project aims to isolate, genome sequence, classify, characterise and permanently archive 1500 bacterial species in the Australian Microbiome Culture Collection. This will provide insights of previously undiscovered bacterial species, improve methods to measure the bacterial species that inhabit the human gut and a detailed understanding of the gut microbiota of Australians. This resource will enhance knowledge of human associated bacteria, identify species with potential medical applications and preserve these species for future generations.

Forster, S.C., Kumar, N., Anonye, B.O. et al. A human gut bacterial genome and culture collection for improved metagenomic analyses. Nature Biotechnology 37, 186–192 (2019).

Dr Rachel Hill
Head, Behavioural Neuroscience Laboratory, Monash University

Psychiatric disorders

Psychiatric disorders are thought to be caused by a combination of genetic and environmental disturbances or ‘risk-factors’.

Dr Rachel Hill, heads the behavioural neuroscience laboratory which investigates these risk factors in cell and animal models to help understand how these disturbances contribute to mental illness at the molecular, physiological and behavioural level. One specific important risk factor associated with the development of autism and schizophrenia is the exposure of the fetus to infection during pregnancy.

Using Microfluidic Technology within Medical Genomics, Rachel and her team investigate the immediate and long-term effects on the brain of exposure to infection.

Published findings by the team show a cluster of genes involved in controlling the movement of inhibitory neurons in the brain were altered following exposure to an infection. The expression of the ARX gene was specifically reduced, suggesting this gene is particularly susceptible to the effects of infection during early development.

The team also analysed whole genome data in collaboration with the Australian Schizophrenia Research Bank and identified a person with schizophrenia carrying a missense mutation in the ARX gene. Using the same Microfluidic Technology, a target gene in the animal model was identified showing promise for this novel human mutation to be associated with schizophrenia.

Jay P. Nakamuraa, Anna Schroedera, Matthew Hudson, Nigel Jones, Brendan Gillespie, Xin Dua, Michael Notaras, Vaidy Swaminathan, William R. Reay, Joshua R. Atkins, Melissa J. Green, Vaughan J. Carr, Murray J. Cairns, Suresh Sundram, Rachel A. Hill, The maternal immune activation model uncovers a role for the Arx gene in GABAergic dysfunction in schizophrenia. Brain, Behavior, and Immunity 81, 161-171 (2019).

Dr Simon Chu, Neve and Ms Tasha Amour
Head, Hormone Cancer Therapeutics Research Group, Hudson Institute

Rare Ovarian Cancer

Dr Simon Chu heads the Hormone Cancer Therapeutics Research Group that investigates a rare form of ovarian cancer known as granulosa cell tumours (GCT). Due to its low incidence, less is currently known of this deadly disease, which is particularly distressing for patients as it has a recurrent nature and requires a lifetime of monitoring. Sadly, the recurrences are generally resistant to chemotherapy and tend to be highly aggressive with a poor prognosis.

To help kick start research into a subset of the tumours called juvenile GCT, Australia’s youngest juvenile GCT patient, five-year-old Neve (pictured) handed over a $10,000 cheque to Dr Simon Chu, on 17 January 2019. Neve was first diagnosed with the tumour when she was 11 months old. The research will involve the world’s largest group of juvenile GCT patients with participants ranging in age from infants to adult women.

The group will genetically sequence the tumour genome of juvenile GCT patients in order to identify which mutations cause the tumours to arise and which could provide specific diagnostic markers for the tumours that arise. This information could lead to a more personalised treatment strategy utilising drugs that target specific gene mutations and has the potential to change the future for children and women with juvenile GCT around the world.

Rare Ovarian Cancer (ROC) Incorporated, led by CEO Ms Tasha Amour, was created to raise awareness of these cancers and much needed funds for research. The Medical Genomics facility was proud to host Ms Amour, Neve and her family when they visited the laboratories last year.

Research Highlights
2018 - 2019

Professor Mark Bellgrove
Director of Research, Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, President, Australian ADHD Professionals Association (AADPA) Ltd

AIM BRAIN PROject
Associate Professor Elizabeth Algar, Dr Christine White and Molly Buntine, ANZCHOG, Hudson Institute and Monash Health

Dr Gareth Gregory
Clinical Lead, Haematology Clinical Trials Unit, Monash Health

Dr Stacey Ellery
Post-doctoral Scientist, Embryology and Placental Biology / Maternal and Perinatal Medicine groups, Hudson Institute

The Genetics of ADHD and ASDs

Professor Mark Bellgrove leads a multidisciplinary team within the Turner Institute for Brain and Mental Health studying the genetic basis of neurodevelopmental disorders including attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASDs). His group uses a range of genomic methodologies from candidate genes, to genome wide association and more recently next generation sequencing.

Professor Bellgrove spearheaded the expansion of next generation sequencing capability at Monash University and the Monash Health Translation Precinct in 2015 through the purchase of a MiSeq and HiSeq 3000 technologies.

He has longstanding relationships with Illumina Genomics and secured funding via an Australian Research Council Linkage Project to study the genetics of cognitive function. Professor Bellgrove is currently amassing 1000 strong family-based cohort of children with ADHD and ASD with funding received from the Medical Research Futures Fund. The long-term goal of this project is to use whole genome sequencing (WGS) in partnership with national and international collaborators, to uncover common and unique genomic signatures across these disorders.

AIM BRAIN PROject

The AIM BRAIN PROject (Access to Innovative Molecular diagnostic PROfiling for paediatric brain tumours) seeks to develop genomic testing for children diagnosed with brain tumours. The project was initiated in 2017 at the Hudson Institute and Monash Health under the auspices of the Australia and New Zealand Children's Haematology and Oncology (ANZCHO) Group.

The project explores the feasibility of establishing genomic testing for children with Central Nervous System (CNS) tumours in Australia and New Zealand. It draws on emerging evidence from the German Cancer Research Centre (DKFZ) that shows many CNS tumour subtypes are not distinguishable by traditional histopathology and immunohistochemistry alone, and that molecular profiling is required for complete diagnosis.

Analysis using whole genome methylation profiling of more than 2500 CNS tumours by DKFZ revealed there are more than 80 distinctive subtypes. This information is now being used to refine CNS tumour diagnoses in Europe and America.

In collaboration with DKFZ, the AIM BRAIN PROject is now using whole genome methylation profiling and targeted next generation sequencing to help establish testing in Australasia. Medical Genomics is hosting the team in the NATA accredited laboratories to assist with this endeavour.

Research is supported by the Robert Connor Dawes Foundation (RCD) Carrie's Beanies 4 Brain Cancer (CB4BC) and the "Sorry Boys", as well as support from Cancer Australia.

Melbourne Genomics - Lymphoma Flagship

Established in 2013, Melbourne Genomics is an alliance of ten leading healthcare, academic and medical research organisations working together to create the widespread change needed to deliver genomic medicine within Victoria's healthcare system. A Demonstration Project undertaken in 2014- 2015 illustrated that the vision to integrate genomic medicine into healthcare was clearly possible, promoting additional support from the Victorian Government in 2016.

Medical Genomics was proud to be involved with the Lymphoma Flagship managed by Dr Gareth Gregory from Monash Health. The study involved the sequencing of approximately 100 patients with aggressive non-Hodgkin lymphomas (aNHL), a diverse group of blood cancers with varied clinical outcomes.

The aim of the flagship was to assess the diagnostic utility of next generation sequencing (NGS) to improve diagnostic accuracy for aNHL patients, explore its potential to guide future management and establish interpretive capacity. Tests compared gene sequencing of the cancer cells to that of non-tumour cells from the same patient. The flagship showed that NGS testing altered diagnosis for a fifth of the patients tested with the potential to impact care for half of all patients with further research

Changes made to processes during the flagship reduced turn-around times from months to two weeks.

Baby Health

Dr Stacey Ellery undertakes research at the Hudson Institute to unravel how maternal and placental factors influence fetal growth and development and contribute to new-born wellbeing. Her focus is on maternal nutrition, placentology, factors leading to fetal growth deficiencies as well as energy homeostasis during pregnancy.

Dr Ellery's team use the Medical Genomic facility's Microfluidic Technology to characterise the function of mitochondria following stress on the human placenta and to investigate how two nutritional supplements (creatine and sulforaphane) maintain placental energy (ATP) homeostasis. These studies have shown that sulforaphane could possibly be used to assist with common pregnancy complications, including fetal growth restriction and pre-eclampsia. Data generated from the Biomark helped lead to a phase II clinical trial to investigate whether sulforaphane can be used to improve fetal wellbeing in women with pre-eclampsia.

Dr Ellery also uses the Microfluidic Technology to investigate higher rates of new-born morbidity and mortality South Asian babies face compared to their Caucasian peers by comparing gene expression between Caucasian and South Asian women. Data suggests ethnicity of the mother and conditions during labour may alter genes that affect the maturation of the fetus.

Other data generated from the Microfluidic Technology looks at genes associated with hypoxic-ischemic brain injury in new-born babies and whether the use of creatine is able to stabilise ATP homeostasis when the fetus is deprived of oxygen which can lead to brain injury. Preventing this injury could reduce the rates of long-term neurodevelopmental complications, such as cerebral palsy.

Education and Outreach

Monash Tech School students visited Hudson Institute as part of a six-week trial program to learn about the technologies that enable medical research and the many different career options available in science.

As part of the Superhealth program at Monash Tech School, groups of up to twenty Year 9 students toured the Microscopy, Cell Therapies and Medical Genomics facilities. Ten local secondary schools in the City of Monash were also involved in the program, which is designed to give students exposure to real-world experiences in STEM areas, in order to complement and build upon their existing studies.

The Superhealth program encourages students to understand science through practical, real-life applications, thereby adding context and value to the theory they learn in class. Students are also exposed to potential career pathways they could pursue in the future.

13 September 2018
Monash Tech School students

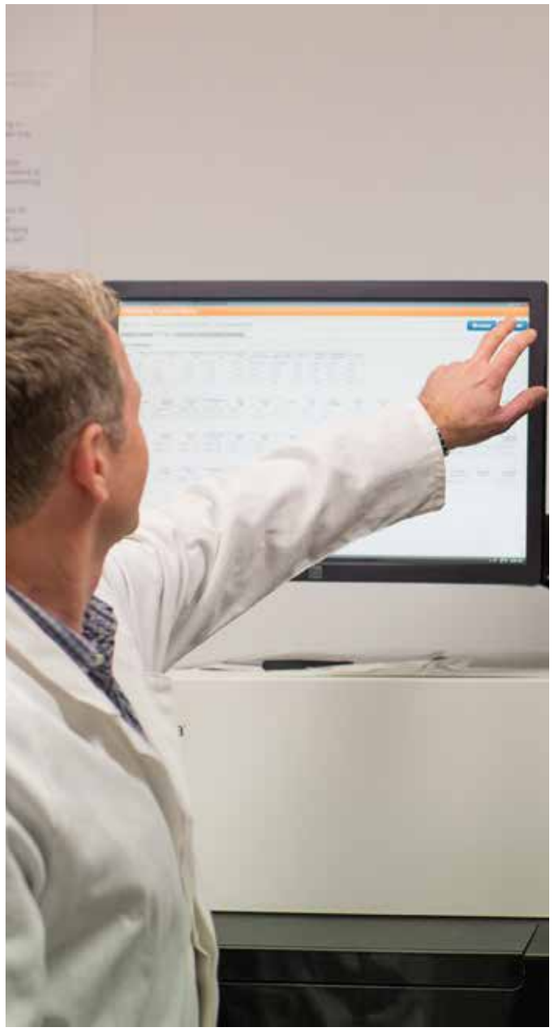
19 September 2019
Probus Club Tour

On 19 September, fifteen members of the Monash Central Combined Probus Club toured the Cell Therapies and Medical Genomics facilities at the MHTP. They learnt about the state-of-the-art facilities available to support medical research, as well as participating in a presentation on the ground-breaking research being conducted into bowel cancer. The tour was part of the Institute's community outreach program.

27 April 2018
Day of Immunology

The Day of Immunology is a world-wide event, celebrated annually on April 29th. It aims to strengthen public awareness of the importance of the immune system to our health and wellbeing, as well as the benefits of medical research.

As part of the Day of Immunology activities in Victoria, public visits to the Monash Health Translation Precinct were held. During organised tours, Medical Genomics showcased technologies used to support research and deepening our understanding of immunity and infection.



26 November 2019
Psychiatric Genetics Workshop

In conjunction with Monash University's Department of Psychiatry, Medical Genomics hosted a 'Genomics in Psychiatry workshop'. Featuring expert speakers in the field, the workshop showcased the value of using genetic tools to understand the biology of many psychiatric disorders.

Our Operations

Sanger Sequencing and Fragment Analysis samples

17,489

2018

Microarray samples

2,008

2018

Next Generation Sequencing

2,007

2018

2,333

2019

Real Time qPCR runs

1,032

2018

1,033

2019

Agilent Bioanalyser – Quality Control

2,525

2018

3,241

2019

Single Cell projects

9

2018

15

2019

Ms Valerie Zahra, Researcher

Governance

The MHTP Platform Advisory Committee's role is to provide strategic advice, leadership and financial management.

Ordinary members

Professor Melissa Southey, BSc (Hons), PhD, Grap Dip Law, FHGSA, FFSc (RCPA), Chair, Precision Medicine, School of Clinical Sciences at Monash Health, Monash University - Chair

Associate Professor Ron Firestein, MD, PhD, Head, Centre for Cancer Research, Hudson Institute of Medical Research and Consulting Pathologist, Monash Health

Dr Sam Forster, BSc (Hons), PhD, Research Group Leader, Microbiota and Systems Biology Laboratory, Hudson Institute

Dr Angus Henderson BSc (Hons), PhD, Director, Enterprise Strategy and Development, Monash Health

Dr Rachel Hill, BSc (Hons), PhD, NHMRC Career development fellow, Head, Behavioural Neuroscience Laboratory, Department of Psychiatry, Monash University

Professor Richard Kitching, MB ChB, PhD, FRACP, FASN, FAAHMS, Nephrologist and Paediatric Nephrologist, Monash Health and Department of Medicine, Monash University

Associate Professor Rebecca Lim, BSc (Hons), PhD, Deputy Centre Head, The Ritchie Centre, Research Group Leader, Amnion Cell Biology, Hudson Institute

Professor Ian Smith BSc (Hons), PhD, Vice Provost (Research and Research Infrastructure), Monash University

Ex Officio

Dr Eugene Fredericks, BSc (Hons), PhD, Manager, School Manager, School of Clinical Sciences at Monash Health, Monash University

Dr Joe Pereira, BSc (Hons), PhD, Senior Operations Manager, Hudson Institute

Ms Vivien Vasic, BSc, MHTP Medical Genomics Facility Manager, MHTP Platform Strategic Initiatives Manager, Monash Health Translation Precinct

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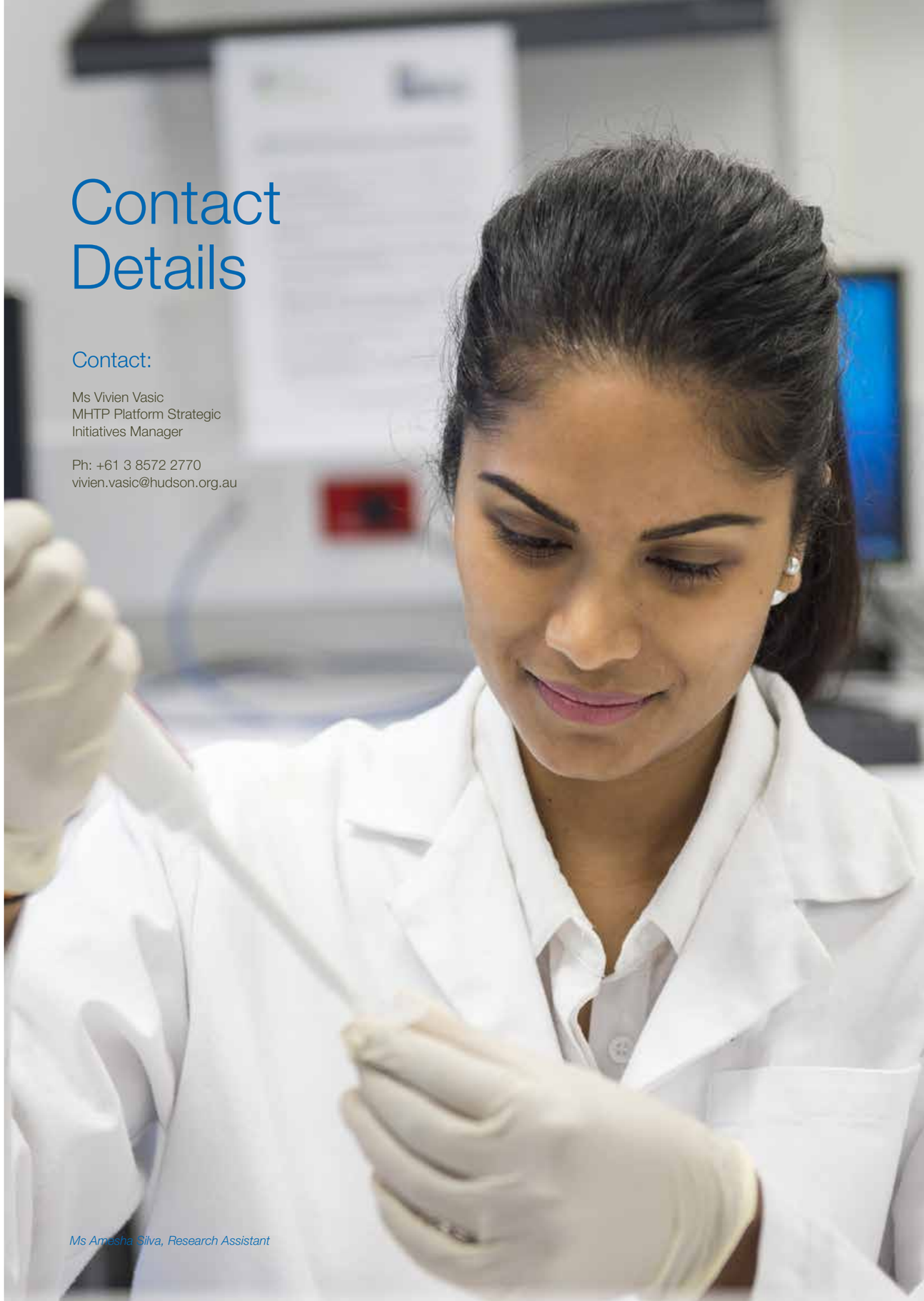

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