murdoch children's research institute

Philanthropic Funds Impact Report

Thank you

We are deeply grateful for your generosity in supporting our new initiatives at MCRI. The three funds outlined here support some of our key activities within the Institute. The Brilliant Minds Fund supports our most promising leaders, the Discovery Fund some of our best ideas and the Innovation Fund an opportunity to make a difference to our communities.

With your support, we have been able to invest in some promising researchers and their critical work. It is thanks to you that we are able to help to advance our research, bringing benefit to children, families and their communities with the ultimate goal to help children live healthier and more fulfilled lives. Thank you.

Brilliant Minds

Supporting the career of a talented researcher is undoubtedly one of the most valuable investments that can be made for the Institute, individual researchers, and the field of child health research. The Brilliant Minds Fund encourages our best and brightest researchers, who are often at critical stages in their careers to support and retain our very best people.

Dr Boris Novakovic

I am an epigeneticist, which means I study the structure of DNA (not the sequence!).

I am interested in differentiated cells – these are the ones that carry out specific functions in our body. These cells can also remodel the structure of their DNA in ways that influence their function.

To study epigenetic remodelling in differentiated cells, I use vaccine response and autoimmune diseases as a model.

Recently we found that the BCG vaccine that is commonly used against tuberculosis changes the epigenetic profile of a specific white-blood cell more than 15 months after vaccination, and this may explain the reported positive effect of the BCG vaccine on eczema development and viral infections.

I use the latest molecular techniques to obtain as much information as possible out of blood samples from children receiving care at the Children's Campus. My goal is to identify and explain regions in the genome into 'active' or 'inactive', in order to work out which molecular pathways are shared between inflammatory diseases, and which are unique to each. By understanding this basic question, we can start to predict therapeutic responses in children and even identify new treatments.

Our work relies on the generosity of children and families by providing these biospecimens. The sequencing techniques we use to study epigenetics are costly and MCRI is one of the few places in the world where we can perform this research. This is due to the generous support of our donors, without whom our research would not be possible, thank you.

What is Epigenetics?

Epigenetics is the study of how the environment can change the way your genes work. Epigenetic changes are reversible and do not change your DNA sequence, but they can change how your body reads a DNA sequence.

Dr Gareth Ball

My team and I are focused on understanding the development of brain structure and function from birth through to late adolescence.

Magnetic Resonance Imaging (MRI) provides a safe and unique way to study the developing brain. Using image processing techniques and machine learning methods, we build statistical models of typical brain development. Using these models, we can investigate when and where differences arise in common neurodevelopmental disorders, such as autism, or after early adverse events such as premature birth.

Working in collaboration with a worldwide consortium of neuroscience researchers and clinicians, we recently contributed data from brain scans of healthy babies to a worldwide study of brain development and growth over the human lifespan, published in *Nature*. This work can help us to understand the nature of complex developmental disorders, identify children most at risk of poor outcomes and to direct care to where it is most needed.

New avenues of research we are exploring include the integration of genetic data into our models. Many common neurodevelopmental disorders have a genetic basis, and in collaboration with clinicians at the Royal Children's Hospital, we aim to combine neuroanatomical measures derived from MRI with genetic analyses to better understand the consequences of disruption to early brain development on an individual level.

We strive for improvements in child health and we are grateful for the support we receive for our research at MCRI.

Discovery

The Discovery Fund supports some of the most promising projects and pilot studies. This is an exciting and proven way to accelerate groundbreaking discoveries in medical research. Many of our researchers submit promising ideas to the National Health and Medical Research Council (NHMRC). Despite recognition that these are high quality and impactful as viewed by the NHMRC, they are not funded. Thanks to your support, we are able to ensure we can support these ideas through often very competitive fields, while encouraging our talented researchers.

Dr Nicole Van Bergen

Nicole is a Team Leader in the Brain and Mitochondrial Research unit at MCRI.

Nicole's major research focus is to understand the underlying cause of neurodevelopmental disorders and to develop focused treatments for them.

I'd like to express my gratitude to all of the generous donors for their support. Your funding has helped me to undertake my research on rare genetic neurodevelopmental disorders. This will enable me to grow my research program at MCRI and will allow me to augment the focus of my research and will have a substantial positive impact on growing my track record.

My major interest is to address fundamental molecular questions relating to orphan neurodevelopmental diseases and to harness this knowledge to aid in the development of new therapeutics. I have always had a strong desire to contribute my knowledge and experience as a molecular biologist to improving the health outcomes of children by uncovering the molecular basis of rare diseases.

CDKL5 Deficiency Disorder is a debilitating progressive seizure disorder affecting young children, causing infantile-onset, difficult to control seizures, severe cognitive impairment and profound lifelong disability. There are no effective treatments and current knowledge of this rare disorder is limited. My research project will use several pioneering techniques to unravel CDKL5 function to a level never before attempted. We hope to study molecular pathways using human brain cells grown in a 3D environment to better mimic the human brain. In addition, a high-throughput drug screening program will be used to identify potential targeted therapies for children with CDD.

Professor David Amor

Professor Amor is a clinical geneticist working in the field of neurodevelopmental medicine.

Neurodevelopmental disorders (NDD) are one of the largest unmet challenges in healthcare due to their lifelong nature, high management costs, prevalence and recurrence within families.

My vision is to advance the field of neurodevelopmental research, to improve understanding of cause, enable prevention, and ensure that children and their families have access to effective treatments.

Although neurodevelopmental disorders have many causes, many are genetic. Over the last decade, genetic testing technologies have greatly increased diagnosis of these disorders, providing answers and specific care needs through to personalised treatment and management. Although therapies for NDDs have seemed a distant possibility, the current generation of children with NDDs are the first for which targeted therapies, based on accurate genetic diagnoses, will be available.

I have contributed to the discovery of three new genes for neurodevelopmental disability, along with major international publications outlining the contribution of genetics to the cause of cerebral palsy, disorders of speech and language and acutely unwell infants. As the focus of my team shifts towards treatment, I have established a program of work that aims to better understand a group of intellectual disability syndromes caused by faults in a family of 'chromatin' genes. In my clinics, the lack of treatment for children with these conditions is a major unmet need – yet these conditions may be amenable to treatment. In the last year my team has established stem cell models for 12 neurodevelopmental disorders caused by faults in chromatin genes and are currently using these cell models to better understand the biology of these conditions. Soon we will start to test specific treatments in these models. My ultimate vision is to return findings to my clinic via clinical trials.

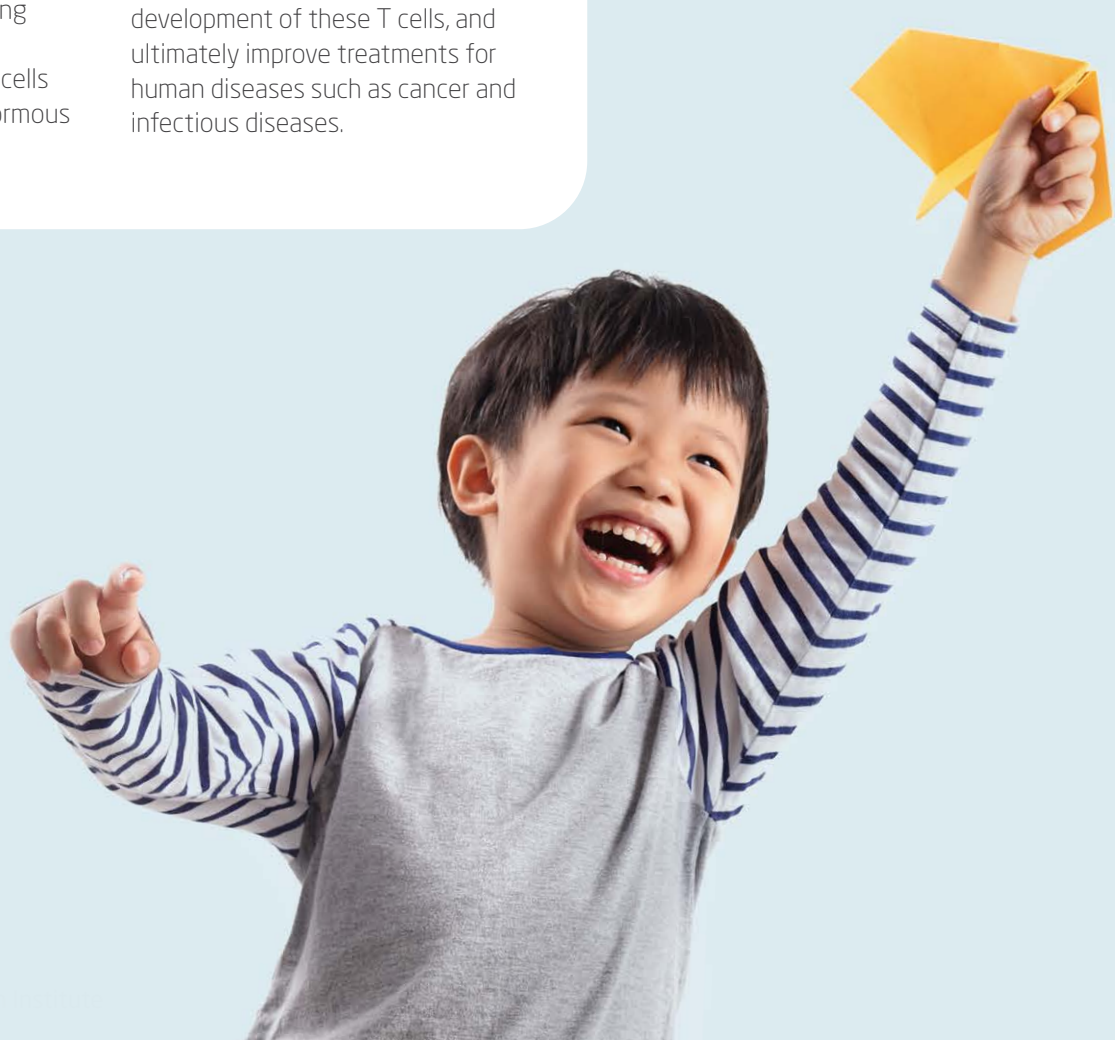
I am immensely grateful for the opportunity to pursue research into the causes of neurodevelopmental disability, and to work towards finding new and effective therapies. My position at MCRI has proved to be very effective for incorporating new genetic knowledge into the neurodevelopmental clinics at RCH and the accompanying research programs at MCRI, as well as being rewarding for me personally.

Dr Dan Pellici

Dan Pellicci works within the Infection and Immunity team and his work explores specifically understanding the biology of unconventional T cells.

These cells are responsible for rapidly mounting potent immune responses.

My project is based around the blood and tissue that contain diverse populations of T cells, which are critical for providing effective immunity against invading pathogens. These cells are recognised for their enormous clinical potential. Presently, understanding the factors that lead to the development of functionally mature specific T cells could provide critical new information on how best to develop the T cells for clinical benefit. The development of T cells is poorly understood, in part due to a long standing theory that T cells develop in foetal tissues such as the liver and not within the postnatal thymus. However, this understanding is largely based on studies undertaken decades ago, and we believe that this can be greatly improved with modern technologies. Our preliminary data has shown that these T Cells do develop within the postnatal thymus. Given the advances in technology, our work will provide unprecedented insights into how these specific T cells develop within the human body. We expect this research project will identify factors that can influence the frequency, function and development of these T cells, and ultimately improve treatments for human diseases such as cancer and infectious diseases.



Dr Deirdre Gartland

Dr Deirdre Gartland co-leads the Resilience and Mental Health stream within Intergenerational Health.

Her role in the Childhood Resilience Study team has resulted in the Child Resilience Questionnaire, co-designed with partner organisations and communities to ensure the resilience measure is culturally sensitive, effective and relevant for children from diverse backgrounds, including refugee background and Aboriginal children.

My dynamic program of work straddles resilience, mental health and family violence. Today 1 in 3 children will arrive at primary school from a home in which violence is occurring, and 1 in 5 children live with a mental disorder. The clustering of violence and social adversity has devastating impacts on children's mental health and development across the life course. Yet most child mental health needs remain unmet, even in high income countries such as Australia. A common and significant error is confusing resilience with mental health. Resilience is an incredibly powerful moderator between risks and child mental health and wellbeing.

Resilience is the process by which children and adults draw on their inner strengths (e.g. problem solving, optimism) and external strengths (e.g. a close bond with a parent/partner, friendships, school/work) to regain, sustain or improve their functioning or mental health despite the challenges they are experiencing.

For my project, I will use data collected with my world-first evidence-based child resilience questionnaire to examine the poorly understood relationship between resilience and child mental health. It is my goal to have a widely understood concept of resilience. In my framework, resilience is not 'bouncing back', as trauma and ongoing adversity will always impact individuals. By understanding what factors support resilience in children, particularly children experiencing adversity, we can identify areas where building skills or connections will help them to better navigate good mental health or functioning over their life course.

The new measure of child resilience we have developed will help show whether school or community programs are helping to build child resilience or where they might need to be improved. My team and I have published three papers and have already been approached by researchers and clinicians both internationally and locally wanting to use these measures to better understand child resilience.

We have collected data from over 1000 families to describe resilience in some of our most vulnerable communities including Aboriginal children, children from refugee backgrounds and children exposed to family violence. We are now analysing this data to help us understand child resilience, and what factors are particularly important in different contexts.

Innovation

The goal of the Innovation Fund is to kick-start research projects at the cusp of translation, allowing our experts to complete essential pre-clinical trial testing of novel therapeutics or interventions, and facilitate community implementation and policy reform.

So far, we have awarded a grant for a project based in Laos and will continue to provide crucial support for these exciting projects.

Based within Global Health, the project is looking to put best practice guidelines for the care of children in the hands of those who need it most, at the lowest level of care. Dr Amy Gray, who is leading this project, is a General Paediatrician who lived and worked in Lao PDR between 2009 and 2011 while undertaking her PhD through the Centre for International Child Health. During her time in Laos she coordinated the Lao Paediatric Residency Training program and provided support to other medical education and child health activities. This led to the project she is now working on to improve capacity for health care workers in Laos.

There are more than 5 million preventable deaths in children each year globally, and Laos has among the highest child mortality rates in the Asia-Pacific region. Improving health outcomes for children benefits families - who are often financially burdened by accessing care, the broader community, and the health systems themselves. Models for how to do this at scale in health systems under strain are required if we are to have the greatest impact and keep pace in the future with rapidly evolving health care needs.

The support from the Innovation Fund will enable the optimisation of an existing smartphone application containing best practice guidelines for health workers on the ground in Lao PDR. It will allow us to scale up access and use of the application nationwide and demonstrate the use case for other countries.

This will cover new features to the existing application to optimise the end user's function and scale the application nationwide with Lao PDR, with user feedback to prove the concept.

Features include:

- Full-text search throughout guidelines
- Ability to bookmark specific content that enables quick access to frequented guidelines
- Ability to share specific content carer-friendly care instructions (dosage/timing) content via messaging app to carer/carer's family

We are grateful to the donors of the fund. Your contribution means a health worker in a remote area, often working in isolation, will be able to deliver care that saves the lives of children.

Pictured: Our Lao colleagues and team members training face to face in a remote hospital.

Curve Tomorrow have played a critical role in delivering a healthcare tool appropriate for workers in Laos.

Curve Tomorrow spearheaded the app development for the Laos project. We caught up with George Charalambous, Executive Director Curve Tomorrow.

Curve is a purpose-driven company with the goal of improving 1 billion lives. Curve builds digital health solutions, using our 13 years of experience to deliver engaging, compliant and secure solutions.

Dr Amy Gray contacted the Curve team about getting new paediatric healthcare knowledge to the lowest-level healthcare workers in Laos. This project was a unique experience for our team. Working with the UNICEF Laos team through COVID-19 restrictions and intermittent internet connectivity was a worthwhile challenge. Additional obstacles continued in designing the app content into digital form and translating it into Lao, but we are pleased to have delivered a for purpose product that will assist healthcare workers to deliver the best outcomes for children and their families in Laos.

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