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Decoding Broken Hearts

A global partnership between two visionary institutes to accelerate precision therapies and transform the treatment of childhood heart disease.

Front cover image: Stem cell derived heart cells with their characteristic striped pattern that its formed by its beating units, the sarcomeres, as well as its nuclei in blue. Dr Antonia Zech (Heart Regeneration and Disease groups - Prof Enzo Porrello and A/Prof David Elliott).



Murdoch Children's Research Institute, Melbourne, Australia

Murdoch Children's Research Institute (MCRI) is the largest child health research institute in Australia and one of the top three in the world for research quality and impact. We are committed to transforming child and adolescent health by pioneering new treatments, trialling better vaccines and improving diagnosis and treatment methods for sick children. MCRI is located at The Royal Children's Hospital and is at the heart of the Melbourne Biomedical Precinct, Australia.

GLADSTONE INSTITUTES

Gladstone Institutes, San Francisco, California, USA

Gladstone Institutes is an independent, nonprofit biomedical research organization that uses visionary science and technology to overcome disease. Established in 1979, it is located in the epicenter of biomedical and technological innovation, in the Mission Bay neighborhood of San Francisco. Gladstone has created a research model that disrupts how science is done, funds big ideas, and attracts the brightest minds.



A new era in paediatric medicine

Murdoch Children's Research Institute (MCRI) and Gladstone Institutes are joining forces to revolutionise the treatment of childhood diseases.

This partnership will bring together the unparalleled potential of stem cell medicine with the precision and speed of artificial intelligence (AI) to usher in a new era of healthcare.

We invite you to join us in the first phase of this partnership – Decoding Broken Hearts – a research project that will advance scientific knowledge and offer tangible hope and improved outcomes for children suffering from heart disease globally.

In time, we aim to extend this program beyond the realm of heart disease to encompass a range of severe childhood conditions such as autism, cancer, disorders of kidney and muscle development and respiratory diseases.

We invite philanthropists dedicated to advancing the health and wellbeing of children to support this ambitious partnership.

Thank you for considering this proposal and we look forward to working with you to create a brighter future for all children with currently incurable diseases.

Sincerely,



Professor Kathryn North AC
Director, Murdoch Children's
Research Institute



Professor Deepak Srivastava
President, Gladstone Institutes

Image left: MCRI stem cell researchers Dr Antonia Zech (left) and Dr Julian Stolper (right) with Associate Professor David Elliott (middle) in an MCRI laboratory located within The Royal Children's Hospital in Melbourne, Australia.

Heart disease is a health issue affecting children around the world (one in 100 births)

A critical health problem

Childhood heart disease

Heart disease is the leading cause of death and disability in children, affecting up to one in 100 live births.

Childhood heart disease includes congenital heart defects that affect the structure of the heart, and disorders of the heart muscle, both of which affect the heart's ability to pump efficiently. In the most severe cases, these conditions can progress to heart failure, which is a life-threatening condition where the diseased heart is unable to pump enough blood to meet the needs of the body.

Current therapies for heart failure in children do not target the root cause of disease and only offer symptomatic relief. Therefore, the only option for patients in end stage heart failure is heart transplantation.

Unfortunately, heart transplantation has limitations including low donor tissue availability, poor medium-to-long term survival rates, lifelong immunosuppression requiring frequent hospitalisation, and poor quality of life for transplanted patients.



Meet Amelia and Elijah

Ebony is a proud Mum of two children: Amelia, who is eight years old and two-year-old Elijah.

When Amelia was two years old, her world changed as she went into heart failure and was subsequently diagnosed with cardiomyopathy, a heart muscle disease that affects the pumping power of the heart. Given the severity of her heart failure, the only option for Amelia was heart transplantation.

Several months after her diagnosis, Amelia was listed on the heart transplant waiting list. Ebony recalls thinking, "When will she get a new heart? Where will it come from? How long will it be?" Luckily, a donor heart became available for Amelia, and she underwent transplantation that year.

However, following Amelia's heart transplant, Ebony was to discover that her son, Elijah, has the same cardiomyopathy. Elijah is being closely monitored by the cardiology team, but Ebony and the family face the uncertainty of not knowing whether he might go into heart failure one day.

Children like Amelia and Elijah face a lifelong health journey, as heart transplantation unfortunately does not offer a cure for these patients. For this reason, Ebony finds comfort in knowing that new therapies are in the pipeline to give patients more options in the future.

"It's good to know that there are people working on things that will help the lives of my kids and other kids."

Ebony Mallinson



Our solution

A global partnership between two of the world's leading research institutes in children's health, computational biology and stem cell medicine to accelerate precision therapies for childhood heart disease.

This new collaboration aims to transform childhood heart disease treatment by targeting molecular pathways predictive of patient outcomes, allowing tailored treatment for each patient to prevent progression to heart failure.

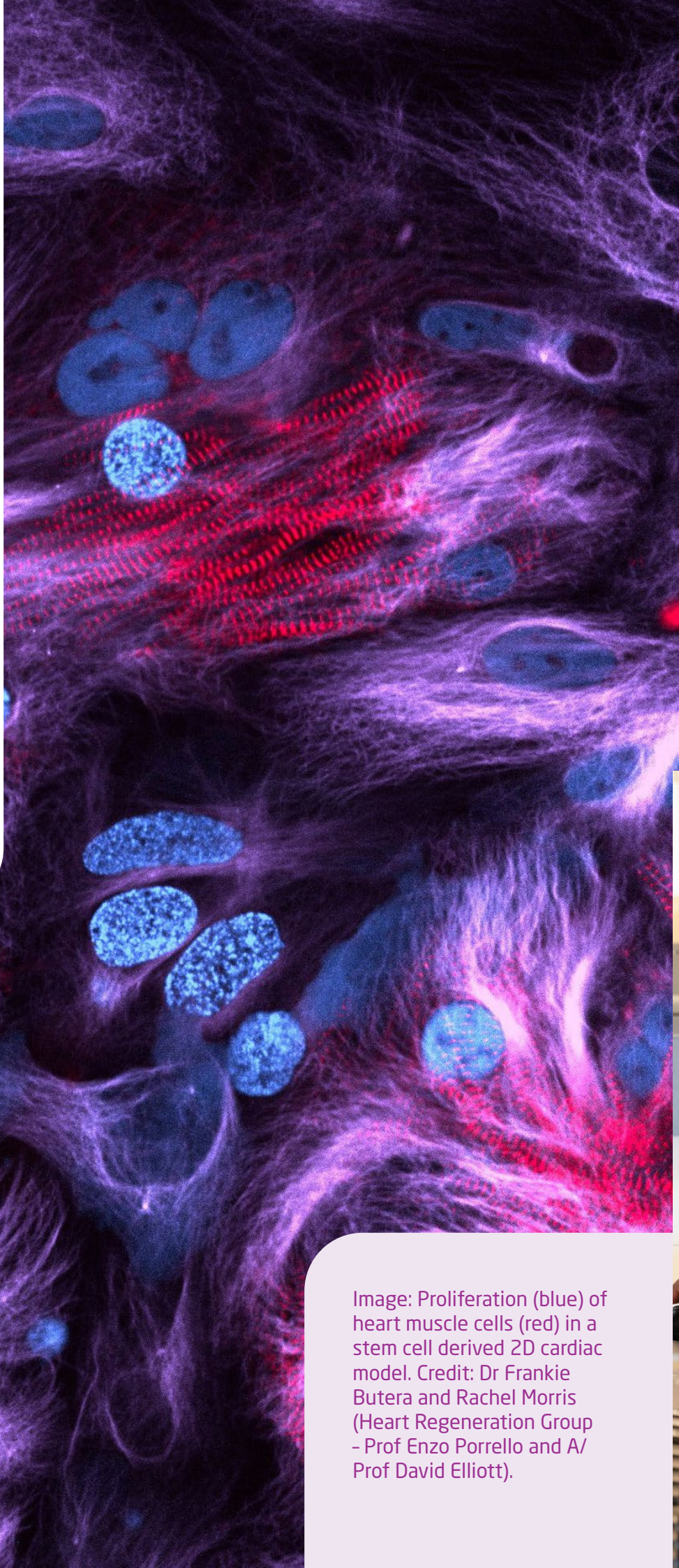


Image: Proliferation (blue) of heart muscle cells (red) in a stem cell derived 2D cardiac model. Credit: Dr Frankie Butera and Rachel Morris (Heart Regeneration Group - Prof Enzo Porrello and A/ Prof David Elliott).

Uniting global research excellence

Pioneering stem cell technologies and patient access

MCRI stands at the forefront of paediatric health research, globally renowned for its pioneering stem cell technologies in cardiac organoid platforms and unique patient engagement embedded within research. MCRI's achievements in deciphering the complexities of heart disease have positioned the institute as a beacon of hope for developing innovative, life-saving treatments for children.

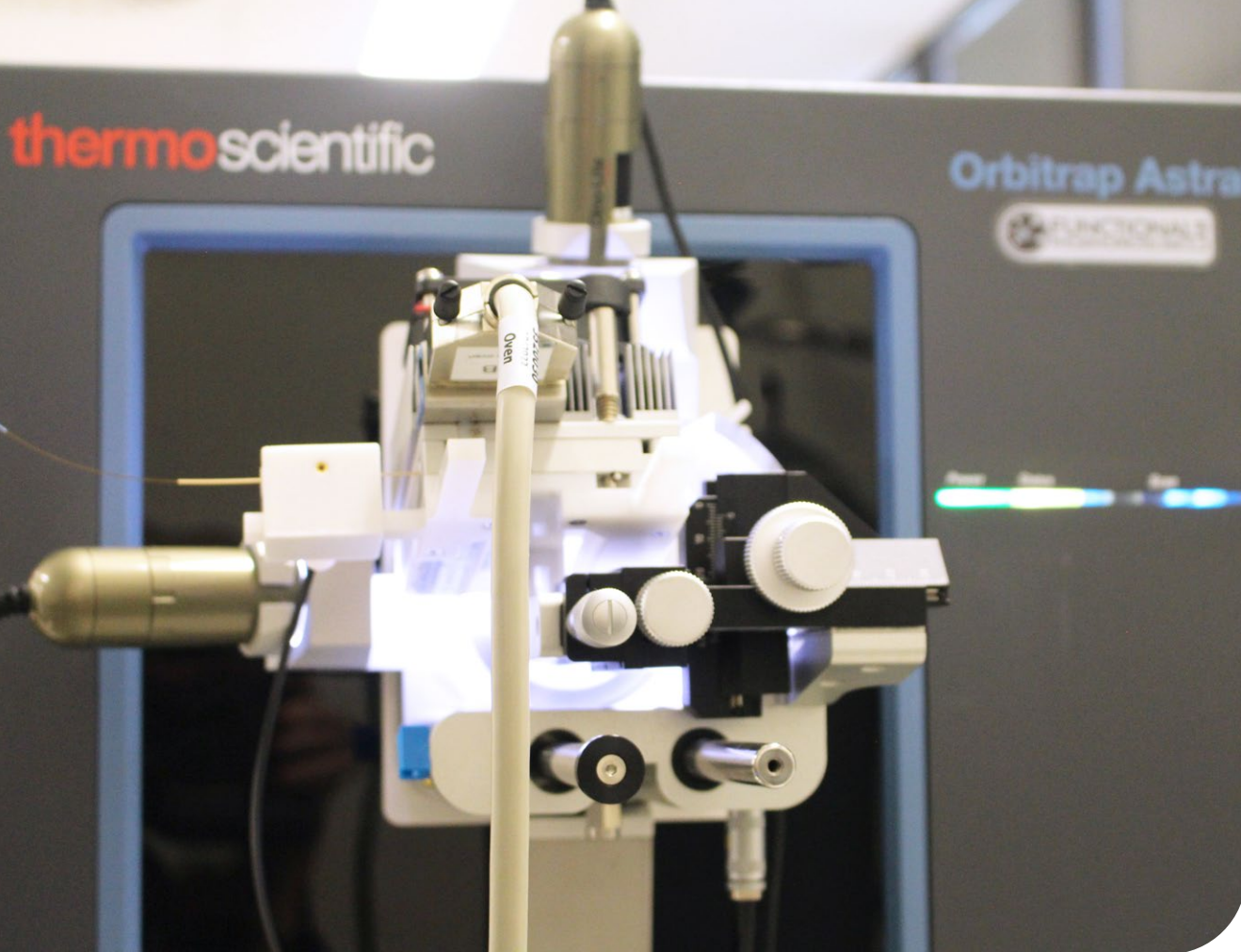


AI and computational biology expertise

Renowned for cutting-edge use of artificial intelligence (AI) in medical research, Gladstone Institutes represents the pinnacle of innovation in identifying the biological underpinnings of diseases and the discovery of potential drug targets. Research at Gladstone has the potential to redefine the boundaries of science and medicine.

Image top right: MCRI stem cell medicine researcher Thomas Martinez (right) with Professor Enzo Porrello (left) in MCRI's stem cell laboratory located within The Royal Children's Hospital in Melbourne, Australia.

Image left: Assistant Professor Christina Theodoris with Gladstone researcher in laboratory



Bridging gaps in cardiac research

This novel collaborative approach allows for an unprecedented exploration of heart disease at its most fundamental level. It opens new pathways for discovering potential drug targets and treatment strategies, overcoming longstanding obstacles such as the intricate mechanisms of disease progression and the slow pace of research translation into clinical practice.

Image above: The first Thermo Scientific™ Orbitrap™ Astral™ Mass Spectrometer (MS) installed in Australia, and one of the first in the world, will enable researchers to study proteins faster and with more precision, accelerating discoveries into stem cells and childhood diseases.

The power of technology in solving age-old problems

Technological advancements, particularly in AI, have transformed our ability to process and analyse vast amounts of data.

These tools enable researchers to decode complex biological information, predict disease outcomes and identify new therapeutic targets at speeds and accuracies previously unimaginable. In the realm of heart disease, this means faster, more precise diagnoses and the development of personalised treatments that could significantly improve patient outcomes.

Geneformer, an AI model developed by Dr. Theodoris, learns from data from over 30 million individual cells to make predictions about gene activity in cells or tissues where there is limited data and identify candidate therapeutic targets.

World class leaders

Meet Enzo

Professor Enzo Porrello is Theme Director of Stem Cell Medicine and Head of the Heart Regeneration Group at Murdoch Children's Research Institute.

He also directs the Melbourne Node of the Novo Nordisk Foundation Centre for Stem Cell Medicine (reNEW) and he is the founding Co-Director of the Melbourne Centre for Cardiovascular Genomics and Regenerative Medicine (CardioRegen).

Professor Porrello's research focuses on the development of regenerative therapies for children and adults with heart failure. Over the course of his career, he has made important contributions to our understanding of mammalian heart regeneration and has pioneered the development of human organoids for drug discovery.

Professor Porrello is a co-founder of Dynamics, a biotechnology company focused on the development of new heart failure treatments using organoid technologies.



Meet Christina

Assistant Professor Christina Theodoris is an Investigator at the Gladstone Institutes and a pediatric geneticist at the University of California, San Francisco.

Her lab investigates how dysregulation of whole networks of genes causes cardiovascular disease. With a strong foundation in pediatric cardiac genetics, her group moves from bedside to bench by using experimental models to understand the mechanisms underlying disease.

Leveraging cutting-edge experimental genomics and computational modeling, they map the gene networks that drive disease progression to identify central regulatory nodes that, when targeted, have a broad restorative effect on the disease network.

They then use AI to identify novel therapeutics that target these nodes to treat the core disease mechanism. This approach led to the identification of a candidate therapeutic for cardiac valve disease, the most common birth defect in humans.





Pathway to impact

We are building upon significant technological advancements to make this program possible.



Identify

Identification of potential drug targets

Use AI to discover what causes a specific heart disorder in children with specific genetic mutations.

\$5m

3 years



Develop

Early stage development of precision therapies

Development of AI-predicted drug targets as potential precision therapies to treat heart disorders affecting children.

\$10m

5 years



Expand

Predict genetic drivers of other inherited disorders in children

Use AI to predict which range of genes will cause a variety of disorders affecting the brain, muscles, blood immune system and kidneys of children.

\$25m+

US\$

5-10 years



Image top left: MCRI stem cell medicine researcher (left) and MCRI's Professor Enzo Porrello (right) working with a cardiac stem cell model.

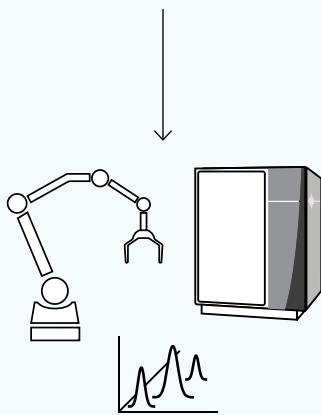
Image above: Research Associate II Tsion Abay works with a Fusion Cell Sorter in the Flow Cytometry Core room at Gladstone Institutes.

Decoding Broken Hearts: research program

Analysing patient samples and data



Biobanked samples and data from patients with childhood heart disease



State-of-the-art transcriptomic and phosphoproteomic analysis to decipher biological pathways involved in childhood heart disease

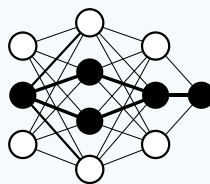


Artificial Intelligence (AI) to identify drug targets



Combining this data with genomic data sets

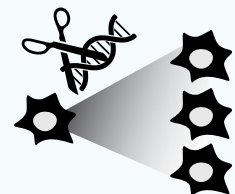
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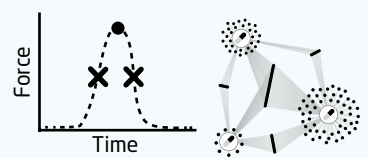
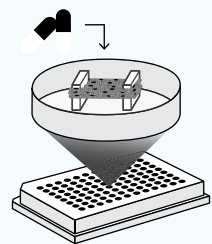
AI to identify possible drug targets in these biological pathways

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Testing drug targets in stem cell models



Patient-derived iPSC lines



Cardiac organoid functional read-outs

Collaborative drug screening in stem cell-derived heart tissues to develop new therapies for childhood heart disease





Image: Professor Shinya Yamanaka in Gladstone Institute's laboratory



Philanthropic investment opportunity

This unique collaboration offers a groundbreaking opportunity for philanthropists to contribute to a pivotal shift in pediatric heart disease research, paving the way for new treatments.

Your support can help bridge the gap between traditional research methodologies and the innovative approaches needed to tackle complex diseases like childhood heart disease.

We invite you to be part of this transformative journey, where your investment will impact the lives of children suffering from heart diseases and potentially set a new standard in pediatric healthcare.

We call upon all who are committed to advancing pediatric healthcare to support this ambitious partnership. Your contribution is not just a donation; it's an investment in the future of heart disease treatment, offering hope to children worldwide.

For more information on how you can make a difference, please reach out to us.

Join us now, as together we have the power to transform the landscape of paediatric cardiac care.

Image above: (Left to right) Ken Wallace and Anne Marie Gasbarro, Trustees of the Stafford Fox Medical Research Foundation, with MCRI's Dr Henry Beetham in the stem cell laboratory based in Melbourne, Australia. SFMRF has helped the stem cell medicine branch of MCRI see tremendous growth over the past ten years – from a faculty of just four research groups to the 160+ researchers today.



Contact us

We would love to discuss with you how we might work together to deliver groundbreaking research that has a long-lasting, positive impact.

**To discuss further,
please contact:**

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Image: MCRI stem cell medicine researcher Thomas Martinez, collecting samples from the -80-degree freezer.

Image back cover:
Gladstone Institutes researcher Ritu Kumar in the Stem Cell Core Tissue Culture Room.

