HEART CENTRE BIOBANK REGISTRY

PARTICIPANT NEWSLETTER

ISSUE 11 · FEBRUARY 2025

Your Participation

You are receiving this newsletter because you consented to be a participant of the Heart Centre Biobank Registry. We thank participants who took the time to learn about this initiative and donated samples and their medical histories to create this critical resource for researchers working at improving heart disease outcomes. Your contribution has fueled and continues to fuel important practice-changing research.

Registry Update

The Heart Centre Biobank, led by The Hospital for Sick Children (SickKids), involves 6 hospitals across Ontario. The contribution from participants continues to yield important research discoveries that benefit patients with heart disease and the research community. Newly discovered genetic findings that are medically relevant are returned to consenting participants. This newsletter provides an update on recent registry activities.

10,858
Participants

90
Research genetic findings returned

60%
Biobank participants genetically characterized

Highlighting recent genomic discoveries

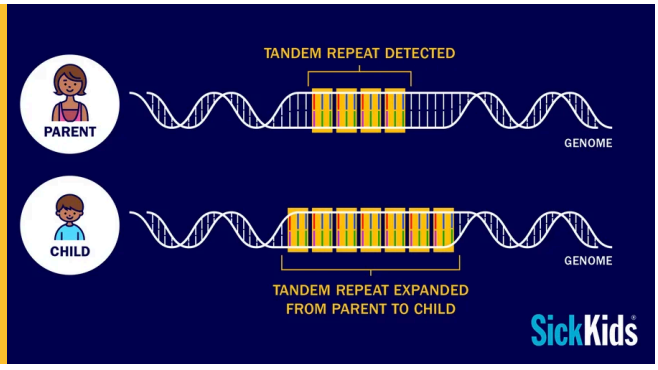
New genetic marker for cardiomyopathy - Tandem repeat expansions

Cardiomyopathy, an inherited heart condition affecting up to 1 in 500 people, can lead to heart failure. A study led by Dr. Ryan Yuen and Dr. Mital, published in eBioMedicine used DNA from biobank participants to explore tandem repeat expansions (TREs) in whole genome sequencing. It found that TREs, a form of genetic variation, are more common in those with cardiomyopathy and may cause up to 4% of cases.[1] The study also revealed that children of parents with cardiomyopathy tend to have larger TREs, a phenomenon called “genetic anticipation.” Larger TREs can disrupt gene function, leading to earlier onset and more severe symptoms. Researchers are working at ways to stop their growth which could lead to personalized therapies to improve outcomes.

The team is now studying TREs in participants with congenital heart disease with the PROCEED Study. Source SickKids News

Tandem Repeat Expansion 101

Tandem repeats are sequences of two or more DNA base pairs repeated immediately adjacent to one another. Tandem repeats can expand when they are passed from one generation to the next. As a repeat sequence expands, the likelihood that it may disrupt a gene's function increases.



Using Artificial Intelligence to uncover genetic causes of congenital heart disease

Congenital heart disease (CHD) is the most common birth defect, yet nearly 90% of cases remain genetically undiagnosed. A study led by Drs. Lesurf and Mital, published in Genome Medicine used genome and RNA sequencing of heart muscle from CHD patients to identify heart-specific genetic variants affecting 95 genes. By applying artificial intelligence (AI), the team developed a model that detected these variants in 12% of CHD patients, significantly improving diagnostic accuracy.[2] The study, part of the PROCEED project, involved over 1,100 patients from Canada, the Netherlands, Germany, and Australia. This breakthrough study demonstrates how AI can enhance diagnosis where standard tests fail and lays the foundation for precision therapies targeting these genetic defects in CHD patients.

Source Ted Rogers Centre for Heart Research

Heart Centre Biobank

Thank you for participating and for your continued support!

For the most up-to-date news, check us out at www.theheartcentrebiobank.com

Phone: at 416-813-8428 Email: heartcentre.biobank@sickkids.ca

TED ROGERS CENTRE FOR HEART RESEARCH

If you are a parent that isn’t already participating or you have parents that would like to, please call or email the Biobank team for information.

Celebrating 10 Years of the Ted Rogers Centre for Heart Research!

This year, we celebrated the 10th anniversary of the Rogers Foundation's inaugural gift to the Ted Rogers Centre for Heart Research (TRCHR). The Cardiac Genomic & Precision Medicine Program, based at SickKids and one of three programs at the Centre, collaborates with the University Health Network and the University of Toronto. The Heart Centre Biobank Registry plays a key role in supporting the program, ensuring that your research contributions make a meaningful impact towards precision child health!

Publications

1. *Mitina A, et al. Genome-wide enhancer-associated tandem repeats are expanded in cardiomyopathy. EBioMedicine. Mar 2024*
2. *Lesurf R, et al. A validated heart-specific model for splice-disrupting variants in childhood heart disease. Genome Med. Oct 2024*
3. *Kinnear C, et al. Myosin inhibitor reverses hypertrophic cardiomyopathy in genotypically diverse pediatric iPSC-cardiomyocytes to mirror variant correction. Cell Rep Med. May 2024*
4. *Kobayashi J, et al. Flow-targeted pediatric ex vivo heart perfusion in donation after circulatory death: A porcine model. J Heart Lung Transplant. Mar 2020*
5. *Kadowaki S, et al. A modified intraventricular balloon method for functional assessment of hearts from donation after circulatory death. JTCVS Open. Jan 2024*
6. *Kadowaki S, et al. Cardioprotective Actions of a Glucagon-like Peptide-1 Receptor Agonist on Hearts Donated After Circulatory Death. J Am Heart Assoc. Feb 2023*

Precision Cardiac Therapies for Children in the Works

New medication found to be an effective targeted treatment for pediatric hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a genetic condition that causes abnormal thickening of the heart muscle, leading to heart failure and sudden cardiac death, particularly in children. A study led by Dr. Ellis and a team of clinical, genomics, stem cells and bioengineering researchers published in Cell Reports Medicine explored myosin-targeted drugs, such as myosin ATPase inhibitors, as potential treatments for pediatric HCM. These drugs, previously trialed in adults, were tested on beating heart cells generated from patient skin or blood cells. The myosin inhibitors fully rescued abnormalities and restored normal heart cell function, matching the effects of gene correction.[3] These novel therapies are now in clinical trials in children with HCM and provide hope for the future.

Source Ted Rogers Centre for Heart Research

Expanding the donor pool to keep hearts alive

A third of infants on the heart transplant waitlist die while waiting due to a shortage of donors and lack of suitable mechanical support devices. To address this, a pioneering pediatric ex-vivo (outside the body cardiac perfusion system) was developed to resuscitate and repair hearts from marginal or circulatory death donors before transplantation.[4,5] The team is also exploring how exenatide, a medication that protects the heart, can improve function in hearts deprived of oxygen. The study, led by Dr. Honjo, published in the Journal of the American Heart Association, showed that exenatide-treated hearts had better oxygen use and less damage, suggesting it could enhance transplant outcomes.[6] These advances could significantly increase the number of donor hearts available in Canada.

This work is supported by the Ted Rogers Centre for Heart Research Cardiac Genomic & Precision Medicine Program. Listen to the podcast here.

A Message from the Heart Centre Biobank

The discoveries made through the research highlighted in this newsletter would not have been possible without your participation in the Heart Centre Biobank Registry. Your contribution is a gift that keeps on giving as your samples and data are used to support research in all types of childhood onset heart disease. The Heart Centre Biobank is thankful to you for your contribution to these discoveries.

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