We’ve been busy: Genomic Discoveries from the Heart Centre Biobank

**CAPN2 involvement in hypoplastic left heart syndrome (HLHS)**
A large international study showed that defects in the CAPN2 gene can cause HLHS. Defects in this gene often occurred in combination with defects in other genes suggesting that in order to find what causes HLHS, one must look at the entire genome to find these multiple small defects.³

**MIB1 gene is associated with bicuspid aortic valve (BAV)**
MIB1 gene encodes a protein that plays a unique role in heart development. An international research team identified an association of defects in MIB1 as a cause of BAV, the most common type of congenital heart disease.⁴

**Improved understanding of the genetic causes of Tetralogy of Fallot**
As the lead of an international project led by our biobank team on personalized genomics for congenital heart disease, also known as, PROCEED, we performed whole genome sequencing in over 1,600 families with tetralogy of Fallot (TOF) and transposition of the great arteries (TGA). This work revealed that defects in two genes, NOTCH1 and FLT4, together account for the cause of TOF in close to 10% of patients.¹ These findings have been returned to families and new gene defects are being identified that will continue to help families in the future.

Read more about the [PROCEED Study](https://tedrogersresearch.ca/2022/05/global-project-led-by-sickkids-seeks-personalized-genomics-for-congenital-heart-disease/) which is funded by ERA PerMed, McLaughlin Centre, Data Sciences Institute and the Ted Rogers Centre for Heart Research here:

**How Immune cells help heart repair**
Single cell analysis of heart tissues from children with heart disease uncovered how scavenger cells called macrophages help repair an injured heart. This has exciting implications for future regenerative therapies for heart disease.²

Through whole genome sequencing, we have identified the genetic cause of heart disease in over 200 participants. 86 participants have already had clinically relevant genetic findings returned to them so that they can inform clinical care and family screening. We are now using even more advanced sequencing technology to search the dark or hidden matter of the genome. This is likely to be a game-changer in our ability to find even more missing genetic causes of heart disease.

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**Thank you for participating and for your continued support!**
For the most up-to-date news, check us out at [www.theheartcentrebiobank.com](http://www.theheartcentrebiobank.com)
Phone: at 416-813-8428   Email: [heartcentre.biobank@sickkids.ca](mailto:heartcentre.biobank@sickkids.ca)

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.
The Future: Genomics, Big Data, and Artificial Intelligence

In an era of data driven medicine, biobanks are an invaluable resource. They allow physicians and researchers to jointly analyze large and complex biological and clinical datasets and use them to predict outcomes in disease and to predict response to treatment by using machine learning and artificial intelligence. Data from smart wearables like smart watches and textiles are further changing the way we monitor patients. These devices can monitor heart health during activities of daily living, and detect early warning signals for adverse events before they occur that can guide timely prevention and save lives. We are pleased to lead a pan-Canadian Heart Function Alliance network focussed on applying such precision medicine approaches to the care of children and young adults with heart disease to prevent, predict and personalize care and improve outcomes.

We thank the Ted Rogers Centre for Heart Research and the Canadian Heart Failure Alliance for their investment in this work.

**References**


**Infants with dilated cardiomyopathy caused by defects in VCL gene can show complete recovery of heart function**

SickKids researchers found that children with defects in the VCL gene typically present in infancy with severe dilated cardiomyopathy but surprisingly, a majority show full recovery of heart function as they grow older. This exciting finding provides hope for families with dilated cardiomyopathy caused by VCL gene defects.

**Age and sex differences in the genetics of cardiomyopathy**

Through collaboration with Genomics England, researchers at SickKids found some unique genetic differences between children and adults with cardiomyopathy. This information can help physicians provide more precise predictions of when disease may manifest in different families depending on the genetic cause.

**Advances in Cardiac precision medicine**

Our precision medicine program continues to advance the application of tailored care to children with heart disease.

**New precision child health tool inspires the vision shared in SickKids Heal the Future video**

November 21, 2023, marks a significant milestone in the Precision Child Health movement at SickKids. A new precision medicine tool developed by our team was integrated into the electronic medical records and is being used by physicians at SickKids (and internationally) to help shared decision making in patients with Hypertrophic Cardiomyopathy (HCM). HCM is the genetic condition that inspired the most recent chapter of the SickKids VS campaign: Heal the Future.

HCM is a leading cause of sudden cardiac death in adolescents and young adults. The timely insertion of an implantable cardioverter defibrillator is a crucial intervention to help prevent fatal outcomes. The short film portrays the promise of Precision Child Health, a transformative approach to providing individualized care at SickKids. The film shows the potentially life-altering impact of a medical device in a boy who collapsed at school due to HCM, inspired by the real story of a SickKids patient, tragically passed at 10-years-old.

**Did you know?**

20% of children with dilated cardiomyopathy show complete recovery of heart function.

**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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**Read more here:** [https://tedrogersresearch.ca/2024/01/primacy-risk-calculator-goes-live-in-epic/](https://tedrogersresearch.ca/2024/01/primacy-risk-calculator-goes-live-in-epic/)

**Short film:** [https://www.youtube.com/watch?v=AxAJn7KfKsg](https://www.youtube.com/watch?v=AxAJn7KfKsg)