What are the potential benefits to our family?

The WGS technology used in this research study can capture much more information than those currently offered in the clinical diagnostic laboratory. Therefore, we may be able to help you learn more about the heart problem identified in your baby, including the risks to other family members and future pregnancies.

What does the research study involve?

Should you choose to take part in this study here is what is involved:

- You will meet with the CGC team for a 30-60 minute research appointment. The study will be explained in detail and you will be asked for:
  - consent for participation
  - a detailed personal and family history (if not previously collected)
  - in some cases, cardiac assessment of parents (echo, ECG)
  - a DNA sample collected from parents (bloodwork)*
  - a DNA sample collected from the baby
- If consented, whole genome sequencing will be performed on DNA samples from you and your baby. This part does not require any additional time on your end).
- Once WGS results are available, you will have a follow up appointment for 30-60 minutes with the CGC team to review the results.

* *If bloodwork has been obtained from previous testing, another sample may not be needed*

Possible risks

WGS may show changes in a gene that predicts a risk for a person to develop another genetic condition. This is called an additional finding. These findings are unexpected and not related to why the testing was done in the first place. If an additional finding is discovered, other family members may need to be informed and offered testing. It can therefore be upsetting and stressful to learn about these additional findings.

The genetic counsellor and/or study doctor will review all possible risks of participating in this research study with you before you are asked to provide consent.

Who can participate?

If you had a pregnancy or are currently pregnant with a baby that was identified to have a congenital heart problem, and you are interested in learning more about this study, please seek further information from our Cardiac Genome Clinic genetic counsellor, Kelsey Kalbfleisch.

For more information contact:

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Clinical and Metabolic Genetics, SickKids

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In partnership with

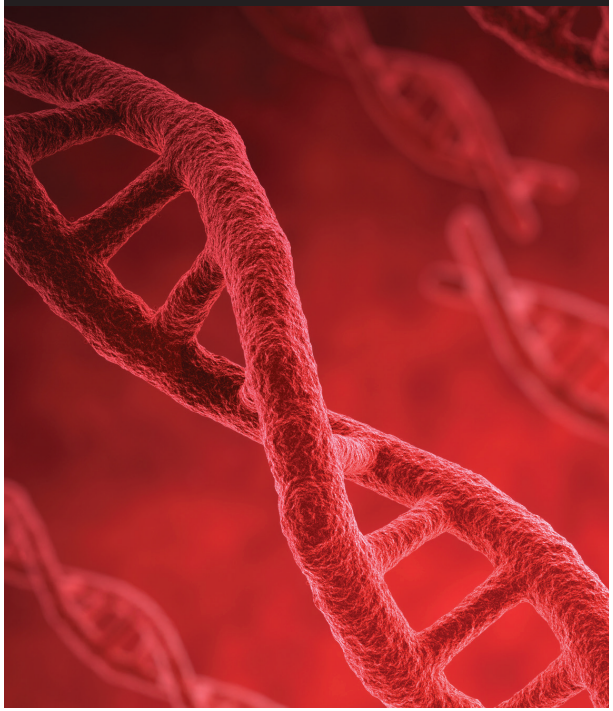
SickKids | Centre for Genetic Medicine

Sinai Health | Mount Sinai Hospital
Joseph & Wolf Lebovic Health Complex

Dec 2020 CSS# 2721

THE PROMISE OF A HEALTHY HEART.

Cardiac Genome Project

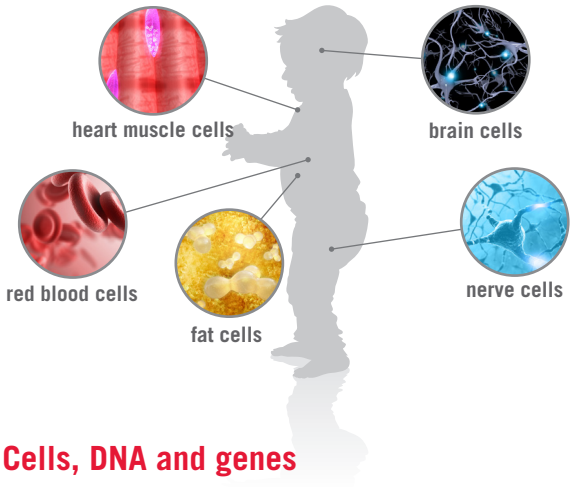


TED ROGERS CENTRE FOR HEART RESEARCH

What is the purpose of the research?

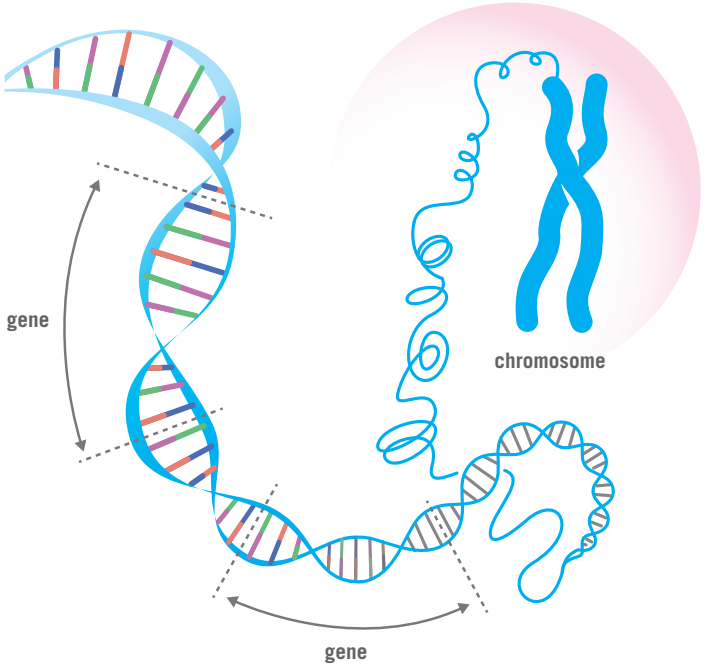
You have been asked to take part in this research study because you had a pregnancy or are currently pregnant with a baby that was identified to have a congenital heart problem.

The primary goal of this study is to better understand the genetic causes of these kinds of heart problems or "congenital disorders" by using a new kind of genetic test called whole genome sequencing (WGS).



Cells, DNA and genes

In order to understand WGS better, we need to understand how our cells, DNA and genes work. Our bodies are made up of many cells, each of which contain our DNA. DNA is like a large book that has all the instructions for how our body works. This information is structured into genes that are like the chapters in a book. There are about 25,000 genes in our cells most of which contain the instructions for making proteins. Proteins are the functional and structural parts of a cell. The type of proteins made tell the cell what kind of cell it will be, such as a heart muscle cell, a brain cell, etc., and how that cell should act. Sometimes the DNA code can vary from person to person. These genetic variants help make each of us a unique individual. Genetic variants are usually harmless. Sometimes they affect minor things like hair colour but, occasionally, they can cause or put us at risk for serious health problems.



What is WGS?

In the past, it was only possible to test one gene at a time. This is called single gene testing. For certain health conditions, single gene testing is still done, but it can take a long time and still may not provide an explanation. Today, one test can look for harmful variants in all of your genes at once. This test is called whole genome sequencing (WGS).

Your doctor along with the CGC genetic counsellor will report the results to you. There are four possible result outcomes:

1 – positive result
2 – negative result
3 – results of unclear significance
4 – additional findings

The table explains what each of these outcomes mean and the next steps which may be suggested.

Whole genome sequencing possible results

Possible results	What this means	Next step(s)
1. Positive	A gene change is found that is likely causing the congenital heart problem.	Genetic counselling and/or talking about this result with your doctor would be important to learn more about what this means. A positive result may provide information to you about the risk for other family members or future pregnancies to also have a congenital heart problem. The genetic counsellor or study doctor will talk to you about if genetic testing for the gene change is available for other family members or future pregnancies.
2. Negative	No gene changes were identified.	Your doctor can talk with you about this, and may or may not suggest other testing.
3. Results of Unclear Significance	A change in a gene is found, but with current scientific knowledge it cannot be determined if this change is the cause of the congenital heart problem.	Genetic counselling and/or talking with your doctor would be important to learn more about what this means. More testing may be suggested to understand this finding.
4. Additional Findings	A change in a disease-causing gene is found that is not related to why testing was ordered in the first place. This may mean you or your family members are at risk for developing other health problems.	If you decide that you want to know about additional gene changes in your DNA or your baby's DNA, talking with your doctor and/or genetic counsellor would be important to learn more about what this means. Additional findings might lead to recommendations for you/your family to see other doctors or have other tests.