What are the potential benefits?

The WGS technology used in this research study can capture much more information than other genetic tests currently offered in the clinical diagnostic laboratory. Therefore, we may be able to help you learn more about your heart, including the risks to other family members and what screening or treatment may be appropriate.

What does the research study involve?

Our study involves working with individuals at risk of heart failure. In genetics, it is helpful to think in the context of the family, so the CGP team may ask to involve additional biological relatives. Should you choose to take part in this study, here is what is involved:

- You will meet with the CGP team in person or over the phone for about 60-minutes. The study will be explained in detail and you will be asked for:
  - consent for participation
  - a detailed personal and family history
  - a physical exam with a geneticist (if it has not been previously done)
  - If possible, cardiac assessment of parents (echo, ECG)
  - sample collection (bloodwork)*
- If consented, you and in some cases other family members, will undergo WGS. This part does not require any additional time on your end.
- Once the WGS results are available, the CGP team +/- your cardiologist will review the results with you in person or over the phone.

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

Possible risks

It may be stressful or upsetting to learn that the cause of your heart condition was inherited and that other family members may be at risk.

WGS may show changes in a gene that predicts a risk of developing another genetic condition. This is called a "secondary" finding. These findings are unexpected and not related to why the testing was done in the first place. If a secondary 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.

Who can participate?

If you have, or are at risk of heart failure, please seek further information from your cardiologist or from our Cardiac Genome Clinic study staff.

For more information contact:

Cardiac Genome Clinic
Ted Rogers Centre for Heart Research
Clinical and Metabolic Genetics, SickKids

Tel: 416-813-7654 ext 404875
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www.tedrogersresearch.ca

In partnership with

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab Michener Institute

SickKids®

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THE PROMISE OF A HEALTHY HEART.

Cardiac Genome Project

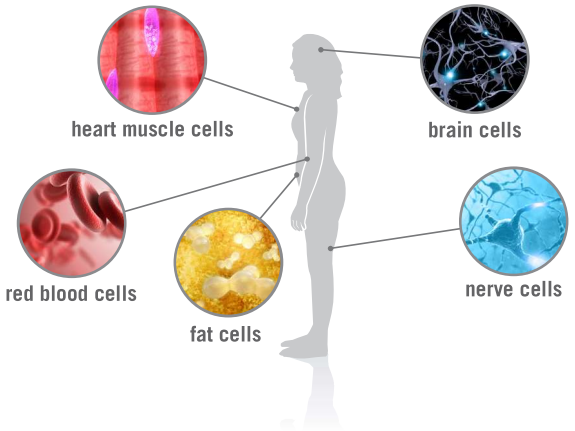


TED ROGERS CENTRE FOR HEART RESEARCH

What is the purpose of the research?

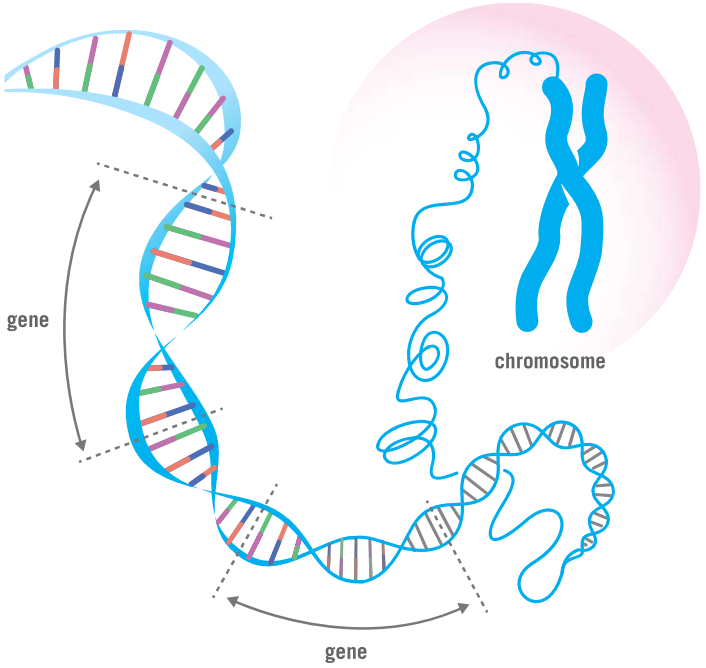
The Cardiac Genome Project (CGP) study aims to identify genetic changes associated with the risk of heart failure using a new technology called whole genome sequencing (WGS). This will help us understand how heart failure develops and how we can provide earlier diagnosis and treatment. Our project aims to study the following:

1) The genetic basis of heart failure
2) The challenges of using WGS in routine clinical cardiac care
3) The best approach for improving medical care using genomic data



Cells, DNA and genes

In order to understand WGS, it helps to understand how our cells, DNA and genes work. Our bodies are made up of trillions of cells, each of which contain DNA. DNA is like a large instruction book that tells our body how to grow, develop and function. This book contains many individual instructions called genes. There are approximately 20,000 genes in our cells, most of which tell our bodies how to make proteins. The type of proteins made determine what kind of cell it will be, such as a heart muscle cell or a brain cell. Sometimes the DNA code can vary from person to person. These genetic variants determine our characteristics and make each of us unique. Genetic variants are usually harmless; however, some can lead to the development of serious medical conditions such as heart failure. WGS can be used to identify these harmful variants.



What is WGS?

Standard of care clinical genetic testing for heart failure is limited and typically only looks at some of your genetic information. WGS has the power to look for harmful variants in all of your genes at once. Testing can take 12-18 months to complete.

Your doctor along with the CGP 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 – Secondary findings

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

Possible results	What this means	Next step(s)
1. Positive	A gene change is found that is likely causing the health problem. OR A gene change is found that is not causing your heart problem but may provide important information. For example, the use of certain medications may not be recommended based on this result.	Genetic counselling and/or talking about this result with your doctor would be important to learn more about what this means.
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 your 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. Secondary 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 are at risk for developing other health problems.	If you decide that you want to know about secondary findings, talking with your doctor and/or genetic counsellor would be important to learn more about what this means. Secondary findings might lead to recommendations for you to see other doctors, have other tests or avoid some medications.