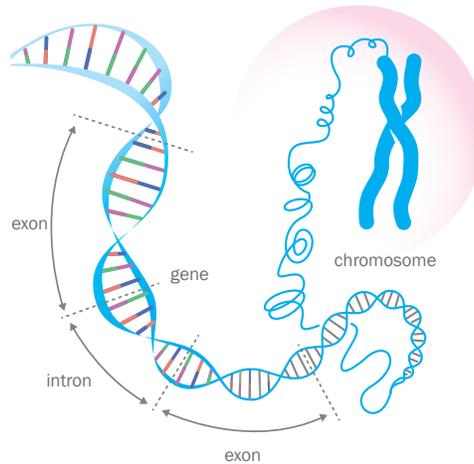
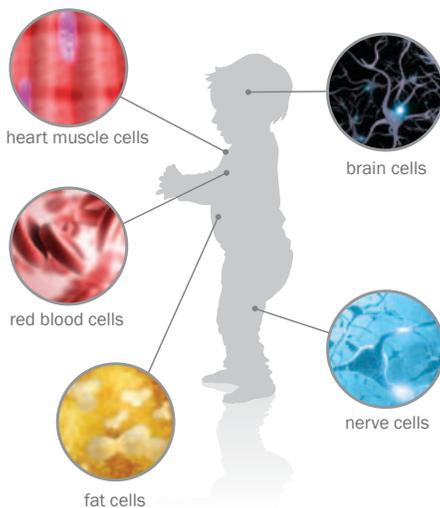


Whole Exome Sequencing

THINGS YOU SHOULD KNOW

Cells and DNA

Our bodies are made up of cells, which contain our DNA. DNA (also known as the genome) is like a large book that has all the instructions for how we are to grow. This information is in the form of genes. There are about 25,000 genes in the cells of our body. Genes affect things like the colour of our hair and our eyes, but changes or mutations in our genes can cause health problems or increase our chance to have a health problem. We do not always know why these changes occur, sometimes the change is passed down in a family and sometimes the gene change just happens by chance.



Whole Exome Sequencing (WES)

Your doctor may suggest your child have WES if other testing has not provided a reason for your child's health problems. WES is not perfect and does not always give an answer, so other testing may still be recommended.

Samples

A small blood sample (1-2 teaspoons) is necessary to perform the testing.



Whole Exome Sequencing Results

Testing may take several weeks to complete. Your doctor or 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, and **4** - additional findings. The table explains what each of these mean and what next steps may be suggested.

Possible Risks

WES 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 being 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.

Results of WES testing will be stored in your child's medical record. Therefore, these results will be available to your insurance company and may affect coverage and/or premiums (cost).

Information about a person's family history is used to interpret test results for genetic testing, including WES. If the family history is wrong or not accurate, it can cause problems interpreting the test result. In addition, any time a genetic test is done, information about non-paternity can be revealed. Non-paternity means that the biological father of a child is different from the apparent father.

Genes

Genes are made up of introns and **exons**. Exons tell our body how to make proteins. Proteins tell the cell what kind of cell it will be, such as a muscle cell, a brain cell, a skin cell etc., and how that cell should act. All the exons of our genes combined together are called the exome. Most of the changes in genes that cause medical problems are found in the exome.

Testing

In the past, it was only possible to look at 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, cost a lot of money, and still may not provide an explanation. Today, one test can be done to look at all the genes in the exome. This testing is called **whole exome sequencing** or **WES**.

Whole Exome Sequencing Possible Results

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 child's health problem but may provide important information. For example, the use of certain medication may not be recommended based 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 it cannot be determined if this change is the cause of your child's health problems.	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 your child is at risk for developing other health problems.	If you decide that you want to know about additional gene changes in your child, 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 your child to see other doctors, have other tests, or avoid some medications.

This is a simple overview of the benefits, risks and limitations of WES. We suggest that you speak with your doctor or genetic counsellor for more information or contact us at:

Centre for Genetic Medicine, SickKids
Tel: 416-813-7654 ext. 202054
email: nasim.monfared@sickkids.ca
www.sickkids.ca/Centres/Centre-Genetic-Medicine