# Cholestasis genetic testing patient information

**It is important that you discuss the benefits and limitations of genetic testing with your physician, a medical geneticist or a genetic counsellor before you have genetic testing.**

What is cholestasis?

Cholestasis occurs when there is reduced or a blocked flow of bile from the liver. There are several mechanisms how this may occur. External factors may physically block the flow of bile such as gall stones or pancreatitis (due to inflammation). There are many internal factors that result in cholestasis including an underlying genetic condition. Your physician is ordering genetic testing to determine if the source of your child's cholestasis is due to a genetic condition. Genetic changes are a common cause of cholestasis and it is estimated that genetic factors account for approximately 25 – 30% of all cases of neonatal cholestasis. An accurate diagnosis can lead to early intervention and can be rapidly achieved by genetic testing.

To further understand how genetics impacts our health, it is important to understand the basics of genetics.

What is DNA?

DNA is the basic unit of genetics. It is the genetic material that we inherit from our parents and pass to our children. DNA is comprised of four separate molecules (chemicals) that are called bases. Each base is assigned a different letter. These letters are A (adenine), T (thymine), G (guanine), and C (cytosine). These four bases are joined together in very long strings of DNA within our cells. These long strings of DNA are called DNA sequences (also called the DNA code or the genetic code). DNA is what genes are composed of.

What is a gene?

A gene is a specific pattern of DNA bases; this pattern is called a DNA sequence. We have approximately 20,000 genes and each gene has a specific function within our body. Each gene creates a different protein, which are the building blocks for our body. Our genes determine how our bodies develop and function from hair and eye colour to how our brain cells communicate and how we develop during pregnancy. The genes responsible for PCD are important for the creation and functioning of the cilia.

Why pursue genetic testing?

It is important to have an accurate diagnosis as it can it can help with finding the correct therapies for your child and prevent further complications before they happen. Genetic testing can help find the cause of a patient's cholestasis. Identification of the genetic basis for cholestasis can help determine if there is a risk for future pregnancies. Cholestasis can be caused by many genes. When genetic testing is ordered, all the known genes associated with cholestasis are analysed for changes within the genes that may stop them from functioning properly. We still do not know all of the genes that can cause cholestasis, therefore it is possible that we will not identify the genetic basis for this condition in your child.

How is testing performed?

In general, DNA testing is done from a blood sample, although less frequently other samples can be obtained from other sources such as saliva. DNA is extracted from the sample and is then analysed via sequencing machines.

How long before the results are ready?

The results of genetic testing are generally ready between 3-4 weeks. Depending on what you have agreed with you healthcare provider, results may be delivered over the phone or in person

Possible results –

There are three possible results that could be reported on your whole exome sequencing test report.

Positive – Genetic changes are identified which confirms the genetic diagnosis for cholestasis

Negative – No variants were identified which could explain the patient's condition. *A negative result does not always rule out a genetic basis for cholestasis.*

Uncertain – A variant is classified as uncertain when there is insufficient evidence to determine if the variant is either disease causing (pathogenic) or has no effect (benign). *As more research is conducted, it is possible that uncertain variants may be reclassified in the future.*

Limitations of genetic testing

The genetic basis for all cases of cholestasis is still not known, therefore it is possible that your child may have cholestasis but the genetic testing will be negative. A negative result does not rule out the possibility of a genetic basis for your child's condition.

However, research is ongoing in this area so it is possible that we will know the genetic basis for all patients with cholestasis in the future, when there is no other explanation for the condition.

**It is important to follow up with your physician, a medical geneticist or a genetic counsellor to discuss the results of your genetic testing.**