Information on Prenatal Exome Sequencing for Parents

As part of your care, your doctor may offer you various tests to try and identify a genetic cause for the unexpected findings detected in your pregnancy. Your doctor will discuss this with you in more detail at your appointment. One of these tests is called Prenatal Exome Sequencing.

What is exome sequencing?

To answer this, it's helpful to first understand that the genome is the body's 'instruction manual', containing nearly all the information needed to create, run and repair the human body. The genome is made up of a chemical code called DNA, consisting of a series of nucleotides or 'letters' that can be 'read' using a technique called sequencing. There are over 3 billion letters in the entire genome but only a small percentage of these (~2%) directly translate into proteins, which are the main building blocks and tools within the body. This ~2% is called the exome and it is the portion of the DNA where we most frequently find the changes that cause genetic conditions.

Exome sequencing reads through all of the DNA letters within the exome, allowing us to look at a person's genes in great detail. This is one of the tests you may be offered to see if we can find a change in your unborn baby's DNA that might be the cause of the unexpected findings that have been noticed on ultrasound scanning. We will need to compare your unborn baby's exome with yours (both parents if possible) to help us tell the difference between harmless changes which can run in families and those changes which may be causing a genetic condition.

In this test we analyse the sequencing results using a targeted approach. This means we only examine the genes that we currently think may affect how the baby develops in the womb. In addition, as prenatal imaging does not allow us to examine the baby in as much detail as we can after birth, sometimes information after delivery may prompt further tests that may enable a diagnosis.

What results might you get from exome sequencing?

- **No relevant result** - This means that we have not identified a cause for the unexpected findings in your pregnancy. In the future, as knowledge and technology improves, we may be able to find the cause and we will discuss when you should seek further advice, for example if you are planning another pregnancy.
- **Relevant result** – This means we have identified a DNA change which clearly explains the unexpected findings in your pregnancy. This may give you more information about the condition affecting your unborn baby and play a part in your decisions about how to proceed with your pregnancy. It may also inform you about the risk of the same condition happening again in any future pregnancies. Sometimes this information may guide your medical team as to how best to manage your pregnancy, delivery and treatment in the newborn period.
- **Uncertain result** – This means that we have found a DNA change which *could* explain the findings in your pregnancy, but more tests or research may be needed to determine if this is relevant or not. In some cases, we cannot be sure whether a change is the cause of your unborn baby's condition or just part of normal variation. This might become clearer with time and as our knowledge of the genome improves.
- **Incidental finding** – Very rarely, the test may reveal an unexpected change in your unborn baby's DNA which may not be not related to the features seen on ultrasound scanning but could have other health implications for the baby, for you, your family or future pregnancies.

As with all health data, the data from your genomic test will be stored securely within the NHS so that we can reanalyse it in light of new knowledge and understanding.

What will happen if I am offered exome sequencing?

Your doctor will explain the test in more detail, why you are being offered it and how you will get your results. You will be asked to sign a consent form if you agree to the test, understand what results you might get and when. You will be able to ask any questions you have. If you agree to have the test, you will be asked to have a procedure called amniocentesis or chorionic villus sampling (CVS) to obtain a sample of the baby's DNA. If you have already had one of these procedures, you will simply be asked to agree to some of this sample being used for exome sequencing. Both parents will also be asked to provide a blood sample. Results are usually available after 2-3 weeks and your doctor will discuss these with you.

Evaluating the new service

As this is a new test in the NHS it is important to for us to monitor how the test is performing. To do this it may be necessary for healthcare professionals to collect relevant information from your medical record after your test result, or to look at information about your test. This will be done in a way that does not personally identify you. This may help us improve the service we are offering.

Contributing to research

In many cases, once we understand the underlying genetic cause of a condition we can work with researchers in our universities and industry to develop new treatments in future. We will also ask your permission for us to contact you should any relevant research studies become available, so these can be discussed with you in more detail.

Your doctor will discuss all this with you and answer any questions you may have and then ask you to sign a form to say whether you consent to exome sequencing or not, and if you agree to being contacted about any new research. If you decide not to have exome sequencing or not to be re-contacted, you will still receive the best possible care from your healthcare team. The same applies no matter what the result of your exome sequencing may be, should you choose to have the test.

If you want to discuss this further Antenatal Results and Choices (ARC) is a national charity providing impartial information and support around prenatal screening and diagnosis.
Helpline: 020 7713 7356 Email: info@arc-uk.org web: www.arc-uk.org