 瑪麗醫院 QUEEN MARY HOSPITAL	Department of Obstetrics and Gynaecology	Document No.	OGPD0035(I)-E
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	Subject Information on Prenatal Exome Sequencing	Review Date	Apr 2027
		Approved by	Prenatal Diagnosis and Counselling Team, TYH
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Information on 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 changes that cause genetic conditions.
- Exome sequencing reads through all 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 abnormal 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 believe that 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.

Why has exome sequencing been offered to you?

- Abnormal ultrasound findings (multiple fetal anomalies) of current pregnancy suggesting a monogenic etiology but for which a specific diagnosis is not suspected.
- No pathogenic finding was identified by chromosomal microarray analysis to explain the cause of fetal abnormality. At present, studies have shown that exome sequencing for single/isolated fetal anomaly has a lower yield compared to those with multisystem anomalies, with approximately 6% yield for cases with isolated anomaly and up to around 20% yields for multisystem anomalies.

What types of samples are required for this test?


- Amniotic fluid or chorionic villi obtained at amniocentesis or chorionic villus sampling (CVS), fetal blood obtained at cordocentesis, placental tissue or skin biopsy from stillbirth.
- 3 mL EDTA blood from both biological parents

When will the results be available?

- Results are usually available in 4 calendar weeks for 'rapid' analyses, where a decision regarding continuation or termination of pregnancy will be based on the result.
- If the decision on termination of pregnancy is made based on abnormal ultrasound findings, results are available 4 calendar weeks after further investigation results (for example, post-mortem, babygram) provided to the laboratory for genotype-phenotype correlation.

How do I get to know the results?

- The test result will be reported to your doctor, who will explain the result to you.
- You and your family members may be referred to a clinical geneticist for further counselling if there are pathogenic or uncertain results.

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What are the possible test results and implication?

1. No relevant result: we have not identified a cause for the ultrasound findings in your pregnancy. In the future, as knowledge and technology improve, 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.
2. Relevant result: we have identified a DNA change (pathogenic or likely pathogenic variant) which clearly explains the ultrasound 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.
3. Uncertain result: we have found a DNA change (variant of uncertain significance) which may 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 variations. This might become clearer with time and as our knowledge of the genome improves.
4. Incidental finding: Very rarely, the test may reveal an unexpected change in your unborn baby's DNA which may not be related to the features seen on ultrasound scanning but could have other health implications for the baby, for you, your family or future pregnancies.

What are the limitations of exome sequencing?

- This test does not detect copy number variants, structural variants, trinucleotide repeats, mitochondria genome and imprinting disorders.
- This test includes genes with current evidence for a causal link with structural anomaly in a baby that can be detected by imaging. It does not include genes linked to conditions that only present after birth, for example developmental delay or autism.
- Prenatal imaging does not allow us to examine the baby in as much detail as we can after birth. In some cases, more information after delivery will prompt further tests that may enable a genetic diagnosis.

I acknowledge that the above information have been discussed with me by medical staff and I fully understand it. I have been given the opportunities to ask questions pertinent to the test and satisfactory answers have been provided by medical staff.

GUM LABEL

Signature: _____

Date: _____