Fact sheet **16**

CHROMOSOME MICROARRAY (CMA) TESTING IN CHILDREN & ADULTS

This fact sheet is about a test called chromosome microarray (CMA). This test checks for extra or missing pieces of genetic material (DNA) in the cells of the body.

IN SUMMARY

- Chromosome microarray (CMA) testing is a detailed genetic test that can look for extra or missing pieces of genetic material or DNA
- The test can be done on a blood, saliva or other tissue sample (in adults and children)
- Refer to the fact sheet on CMA in pregnancy for how this test can be applied on a sample taken from a pregnancy.

OUR DNA

In all the cells of our body our genetic material, or DNA, is packaged on string-like structures called chromosomes (see *Figure 16.1*). There are 46 chromosomes in each of our cells, made up of 23 pairs. Half of the chromosomes come from our mother in the egg and the other half from our father in the sperm.

Our DNA contains information (our genes) that is used by the cells to make our bodies grow and work properly. It is important that there is the right amount of DNA in each cell of our body. Too much or too little DNA can cause a condition affecting health, learning or development.

WHAT IS CMA TESTING?

Chromosome microarray (CMA) testing is a genetic test that can find extra or missing pieces of chromosome material or DNA. As there are usually two copies of each chromosome, there are generally also two copies of each piece of DNA along each of the chromosomes.

Using a small sample of blood or tissue, a CMA test will look for changes in the number of copies of DNA segments. These are known as **copy number variants**.

If the test finds a copy number variant involving a section of DNA, the laboratory will check which genes it contains. Understanding the genes that are present in extra copies, or are missing, can tell us about what the result means for that person such as:

- The cause of the developmental or health concern
- How symptoms might develop over time
- The possibility of the condition affecting children or other relatives

WHAT INFORMATION WILL THE CMA TEST PROVIDE?

There is a CMA Testing Guide for doctors and patients available to support the information in this fact sheet.

As part of looking for a cause for a developmental or health condition about you, your child or family member, a doctor or genetics specialist may suggest a chromosome microarray (CMA) test. The information below will help you understand how this test works and possible results.

1. No copy number variant or chromosome imbalance is found

The cause of the health or developmental concern remains unexplained.

This is the most common result.

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Figure 16.1:
Diagram showing structure of chromosomes and genes within the chromosomes.

Our DNA: In all the cells of your body our genetic material, or DNA, is packaged on string-like structures called chromosomes. Our DNA contains important coded information or genes.

Cells
Cells contains our DNA packaged on chromosomes

Chromosomes
Each chromosome is made of DNA and contains many genes

Some genetic conditions occur when there is an extra or missing copy of an entire chromosome

DNA codes our genes
Each gene gives a specific message to the cells

Some genetic conditions occur when there is an extra or missing copy of a small section of DNA interrupting an important gene message

2. A copy number variant is found that is unlikely to cause any health or developmental concern

These are sometimes called **benign copy number variants**. Most often, copy number variants found on CMA are harmless and may not be reported.

The cause of the health or developmental concern remains unexplained.

3. A copy number variant or chromosome imbalance is found that explains the health or developmental concern

Testing of parents or relatives may be suggested to see if the variant is only present in the person with the condition, or if it may have been inherited. You will receive more information about the result from your health professionals and genetics team. The information may include recommendations for additional health checks.

4. A copy number variant or chromosome imbalance is found but its impact on health or development is unclear

This type of result is called a **variant of uncertain significance**. There are a number of steps needed to further check what this result might mean. For example, testing of parents or other relatives may be offered to see if the variant is only present in the person with a health condition, or if it was inherited from a parent.

For example, the results might tell us:

- **One of the parents also has the copy number variant**
  - If the parent has the same condition as their child, the variant is more likely to be the cause of the health or developmental concern
  - If the parent does not have the same condition as the child, the variant is less likely to be the cause of the health or developmental concern. Further testing of other family members or waiting for more studies and data, may be needed to confirm our understanding of this. A local genetics service may assist.

  As a general guide variants of uncertain significance that do not contain any genes are likely to be benign (not harmful). If parents do not have any signs or symptoms of the condition, testing them for the variant may have less value.

  For certain conditions such as mild developmental delay or autism, if there are other members of the family who also have this (sometimes both sides of the family), it may have been caused by environmental factors and/or a combination of genetic causes. Until there is further information available, testing other family members may have limited value.

- **Neither of the parents has the copy number variant**

  This means the variant must have happened during or soon after the child's conception (a **de novo variant**). Even if present, the effect that this variant may have on the person's health and development may be uncertain until there is more evidence to say otherwise.

  – The variant may, or may not be the cause of the developmental or health concerns and this is unclear. Therefore the result remains of uncertain significance unless there is more evidence to say otherwise.

5. A copy number variant is found in your family that contains a gene or genes unrelated to the developmental or health concerns, but may cause other health problems in the future.

This will be a rare result. One or more genes located in the extra or missing DNA section are known to be linked with other health or developmental concerns. This is also known as an incidental finding. This information could be significant for your child's, or your future health.

HOW TO REQUEST TESTING OF A PARENT OR RELATIVE

If a person with a health condition has been previously found to have a variant of uncertain significance on CMA, testing a parent or relative is covered by Medicare.

For example:

1. If a parent does not have clinical signs of the health or developmental condition in their child, indicate on the test request:
   - Targeted report CMA for [e.g. del 15q11.2] VUS
   - Parent of [FULL NAME] with [e.g. del 15q11.2] VUS. Parent has no clinical features
   - Describe any other relevant family history

This is covered by Medicare Item 73292.

This test will help clarify our understanding of the known copy number variant in the family, without identifying additional potentially uncertain information about the parent.

2. If a parent has a health or developmental condition consistent with their child's, indicate on the test request:
   - Full report CMA
   - Parent of [FULL NAME] with [DETAILS] VUS; parent has [DESCRIBE CLINICAL FEATURES]
   - Describe any other relevant family history

This may be covered by Medicare Item 73291.

The reason for doing a full CMA in this instance rather than a targeted option, is that there may be different reasons for similar health conditions occurring more than once in the same family.

It is important to talk about what type of information you will receive from this test with your health professional or genetics clinic.