

## Paediatric Microarrays for Neurodevelopmental Genetic Testing

**Microarray testing is available at Mater Pathology for the diagnosis of patients with intellectual disability, developmental delay, autism or congenital abnormalities.**

Microarray testing has been recommended by the American College of Medical Genetics (ACMG) as the first tier test<sup>1</sup> for the investigation of individuals with unexplained developmental delay/intellectual disability, autism spectrum disorders or two or more congenital anomalies.

### **Why do a microarray instead of a karyotype?**

Aneuploidy or large unbalanced chromosome rearrangements are often found in the above patients by karyotype, however many pathogenic rearrangements are below the resolution of this test. Microarrays offer a high resolution and genome wide method for detecting copy number changes (such as deletions and duplications).

### **What array type does Mater Pathology use?**

Mater Pathology uses the Affymetrix 750K SNP array which has a total of 750,000 probes consisting of approximately 550,000 probes to allow for the detection of copy number changes at an effective resolution of approximately 100 kb. The Affymetrix SNP array has an added benefit over CGH-arrays used by some other providers in also having 200,000 SNP probes which detects regions of long contiguous stretches of homozygosity (LCSH) which can be an indicator of uniparental disomy (UPD) or regions which are identical-by-descent (IBD).

### **What type of results can you expect?**

1. No copy number changes (CNC) detected.

Many results will have no changes detected and the cause of the patient's illness remains unexplained. Microarrays can NOT detect single gene mutations, disorders such as Fragile X syndrome, CNC's below the array resolution or cases where there is low level mosaicism. Microarrays also do NOT detect balanced rearrangements however this is unlikely to be associated with an abnormal phenotype.

2. A copy number change is detected.

Different types of CNC's may be detected including:

a) A pathogenic CNC

- A deletion or duplication of known clinical significance with a recognised phenotype.

b) A variant of uncertain significance

- A region which has been described in individuals with developmental delay/intellectual impairment, but is also been found in unaffected individuals and family members. Genes within these regions may show incomplete penetrance or variable expressivity and the clinical significance of these regions has not been fully elucidated.

c) A variant of unknown significance

- A region which has not been well described in the literature or in relevant databases and the significance of which is unknown.

d) Incidental finding

- A copy number change that is unrelated to the clinical presentation of the individual but has clinical significance.

### 3. A region/s of LCSH has been detected.

Large regions of LCSH on a single chromosome may be an indicator of UPD. This is of potential clinical significance when the chromosome involved is imprinted, such as chromosome 15 in association with Prader-Willi/Angelman syndrome. Multiple regions of LCSH on several chromosomes may be an indicator of consanguinity. Such individuals are at risk of a recessively inherited single gene disorder which may require further assessment via a clinical genetics service.

## Practical Information

**Specimen requirements:** 5mls of peripheral blood in an EDTA tube and a Mater Pathology request form for microarray testing with any relevant clinical information noted. Such information is essential when trying to interpret copy number changes.

**Billing:** A Medicare item number is available for this test. No out of pocket fees apply.

**Further Information:** If you would like to find out more about microarray testing, please contact the Cytogenetics Department at Mater Pathology on 07 3163 8498 or 07 3163 5988.

## Further Neurodevelopmental Genetic Testing at Mater Pathology

In addition to microarray testing, Mater Pathology offers a range of genetic tests for single-gene ('Mendelian') causes of neurodevelopmental abnormalities.

These can be carried out on the sample used for microarray analysis (5mls of peripheral blood in an EDTA tube) if required, or on a separate EDTA sample.

### The available tests include:

Test	Billing
<i>FMR1 screening PCR for Fragile X syndrome</i>	A Medicare item number is available for this test. No out of pocket fees apply.
MS-MLPA analysis for Prader-Willi/Angelman syndromes	No specific Medicare item number*
UBE3A sequencing for Angelman syndrome with normal MS-MLPA results	No specific Medicare item number*
MECP2 sequencing and MLPA for Rett syndrome	No specific Medicare item number*
Sequencing panel for 23 genes involved in Noonan syndrome and related RASopathies (panel includes: A2ML1, BRAF, CBL, CDC42, HRAS KAT6B, KRAS, LZTR1, MAP2K1, MAP2K2, MRAS, NF1, NRAS, PPP1CB, PTPN11, RAF1, RASA2, RIT1, RRAS, SHOC2, SOS1, SOS2 and SPRED1).	No specific Medicare item number*

\*There is no specific Medicare item number for these disorders. There is a general Medicare item for targeted genetic investigation of developmental delay (73291) which may cover part of the cost of testing. Note that item 73291 cannot be applied if the specific test is requested on the same sample as a microarray test.

**Further Information:** If you would like to find out more about genetic testing for Mendelian disorders, please contact the Molecular Genetics Department at Mater Pathology on 07 3163 8996.

Mater Pathology has created an itemised price list to provide doctors and their patients with an assurance of the total costs for the most commonly requested non-rebatable pathology tests.

To view a list of these tests, **visit [pathology.mater.org.au/for-doctors/price-list](http://pathology.mater.org.au/for-doctors/price-list)**