



Molecular Karyotyping/ Microarray Testing

Insight – February 2014

- Microarray testing offers a significantly increased diagnostic return for individuals with indicated clinical phenotypes, compared to traditional karyotyping.
- This testing allows detection of duplications and deletions of 0.2Mb in size in comparison to traditional cytogenetics which has a typical resolution of 5 – 10Mb in blood specimens.
- Traditional karyotyping is still the most appropriate test for patients with recurrent miscarriages, infertility, premature menopause, delayed puberty or other sexual development disorders.

Introduction

Melbourne Pathology offers molecular karyotyping or single nucleotide polymorphism (SNP) microarray testing for investigation of patients with developmental delay (DD), intellectual disability (ID), autism spectrum disorder (ASD) or multiple congenital abnormalities (MCA).

The microarray test uses 300,000 SNP markers to look for imbalances across the genome. The SNP genotyping array simultaneously measures intensity differences and allelic ratios allowing detection of aneuploidy, duplications, deletions, mosaicism and copy-neutral loss of heterozygosity (CNLOH).

Microarray testing offers a significantly increased diagnostic return for individuals with these clinical phenotypes, compared to traditional karyotyping, largely because of its higher sensitivity for submicroscopic deletions and duplications. It is now recommended as the first-tier genetic test, in place of traditional karyotyping, for patients with unexplained DD, ID, ASD or MCA. (Miller et al, 2010 PMID: 20466091). Microarray testing may also be used for testing of microdeletion or microduplication syndromes, traditionally investigated using FISH (fluorescent in situ hybridisation) probes, and has a much broader application than any individual probe.

This testing allows detection of duplications and deletions of 0.2Mb in size in comparison to traditional cytogenetics which has a typical resolution of 5 - 10Mb in blood specimens. CNLOH also allows detection of allele homozygosity associated with uniparental disomy (UPD) although heterodisomic UPD will not be detected. It will not detect balanced chromosomal rearrangements and some low level mosaicism, although low level mosaicism may also not be detected by traditional cytogenetics.

Results

Results of the microarray will be reported to the referring doctor in one of the following ways:

- No clinically significant genomic imbalance detected – a normal microarray result
- Clearly or likely pathogenic
- A duplication or deletion of unknown significance – these are usually novel copy number changes that have not been reported previously in any of the clinical databases. Follow up parental testing will be requested in these cases

- A duplication or deletion of uncertain significance – these are copy number changes that have been found in increased numbers in populations of affected patients but may be inherited from an unaffected or mildly affected parent. Follow up parental testing will be requested in these cases.

Copy number changes less than 0.2Mb in size will not be reported unless associated with a gene of known clinical significance. Copy number changes that do not contain genes or are considered benign copy number variants will also not be reported.

Long continuous stretches of homozygosity (LCSH) greater than 5Mb in length will be reported. These are generally indicative of "identity by descent" and may be associated with an increased risk of recessive Mendelian disease. Coincidental findings, unrelated to the investigation being undertaken, may occasionally be evident. These results will be discussed with the referring doctor prior to reporting.

Genetic counselling is recommended following any result that may be considered clinically significant. Results for this test will be available 3 – 4 weeks from collection.

Traditional karyotyping is still the most appropriate test for patients with recurrent miscarriages, infertility, premature menopause, delayed puberty or other sexual development disorders.

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Amanda completed her Bachelor of Science with honours at La Trobe University in 1985, and became a Fellow of the Human Genetics Society of Australasia (Cytogenetics) in 1990.

Amanda has worked as a Scientist in Cytogenetics at various hospitals including the Queen Victoria and Royal Women's Hospitals. In 1993, she was appointed Grade 3 Scientist in Cytogenetics at Melbourne Pathology, and in April 2004 became the Cytogenetics Department Manager.

Amanda is a member of the Australasian Society of Cytogeneticists, the Association of Genetic Technologists, the Human Genetics Society of Australasia, and the International Society for Prenatal Diagnosis.

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