AWMGS
All Wales Medical Genomics Service

Genomic array testing is changing across Wales

Array testing in Wales currently uses an array Comparative Genomic Hybridisation (CGH) platform. From 16th May 2022 all samples received across Wales for array studies will be processed using a new **Single Nucleotide Polymorphism (SNP) array platform**. This change will have some **important implications for your clinical practice**. The changes to the service were presented at a series of meetings during May 2022; links to the recordings of these meetings can be obtained by contacting our Education and Training team: EducationandTrainingAWMGS.cav@wales.nhs.uk, in your e-mail please specify whether you wish to receive the prenatal or postnatal samples link.

Why is the array service changing?

Essentially a SNP array is a better test!

The benefits of the new array platform include:

- ✓ Better resolution compared to the current array CGH, potentially identifying more clinically significant copy number changes.
- ✓ Better detection of mosaicism than array CGH.
- ✓ Detection of triploidy (69,XXX; 69,XXY; 69,XYY).
- ✓ Detection of ~66% of patients with clinically significant uniparental disomy (UPD).
- ✓ More streamlined working practices in the laboratory which will improve efficiency and decrease sample failure rates.

All array studies have their limitations

Limitations of SNP array technology are:

- × Although more reliable than array CGH for detection of mosaicism, SNP arrays may not detect low level mosaic imbalances (<20%).
- × SNP arrays are not able to detect UPD in ~33% of patients with a condition caused by UPD. *If UPD is suspected, further testing may be helpful before a SNP array. This can be discussed by contacting the laboratory.*
- × SNP arrays are more sensitive to the presence of maternal cell contamination (MCC). This is important for prenatal diagnostic samples (amniocentesis/chorionic villus sampling).

Limitations of both CGH array and SNP array technology:

- × Chromosomal arrays lack the resolution to check for alterations within individual genes.
- × Chromosomal arrays cannot identify balanced chromosomal rearrangements.

Will this change the way I consent for an array?

Yes, but many things are still the same. The possible outcomes of SNP array testing are:

- No significant changes are found. This means the test did not find a significant chromosome change. This result does not exclude a genetic diagnosis. Further testing might be helpful.
- The test may identify variants unrelated to the condition under investigation (incidental findings). These can have significant implications for the patient and their family.
- There is the possibility of finding variants which may not have a clear clinical phenotype. This might include:
    - Variants involving 'neurosusceptibility' loci
    - Those that display variable expressivity and/or incomplete penetrance
- The test may result in detection of variants of uncertain significance.
- Because SNPs are inherited, a SNP array might reveal the biological parents are first degree relatives (incestual relationships). This can have significant ongoing safeguarding implications which need to be managed appropriately. In this scenario, the laboratory will contact the requesting clinical team prior to a report being issued. The Clinical Genetics team can be contacted for additional support in these cases.

Can the test detect non-paternity or non-maternity?

Sometimes we might suggest testing parents too. This might help our understanding. If parents are tested, and depending upon the testing method used, it is possible the test might reveal whether the individual is biologically related to one or both of their parents. This is unlikely to occur when only testing one parent in the family, unless a first-degree relationship has been indicated in the patient by the test.

Will you report all changes which might indicate UPD?

No, UPD will only routinely be reported when the result involves an imprinted chromosome with a clinically recognised disorder associated with the UPD.

Will all cases of possible consanguinity be reported?

It is important to indicate on the request form if you suspect a patient's parents are closely related. However, only results which indicate the biological parents are first degree relatives will be reported back to the clinical team.

What will happen to array tests received by the laboratory before 16th May 2022?

These patients will still receive an array CGH test.

What will the turnaround time be for a SNP array?

We aim to report within 42 days for routine samples and 14 days for urgent and prenatal samples.

Are the array eligibility criteria changing?

No, they will still be the same and the array request form for postnatal blood samples will still need to be completed for outpatient testing:
https://medicalgenomicswales.co.uk/images/awmgsdownload/PD-GEN-DevDelReq5.pdf

Are the sample requirements staying the same?

Yes. Please send at least 1ml of blood for paediatric patients and 4ml for adult patients in an **EDTA tube**.

The sample requirements for prenatal and post-mortem tissue samples remain the same.

What about the current backlog of postnatal array CGH results?

Due to the COVID "catch up" phenomenon in 2021, we have experienced an increased rate of postnatal array CGH test requests. This has led to a backlog and the wait for these results is approximately 6-8 months from the time of request. We hope to have processed and reported all samples undergoing array CGH by the end of December 2022.

Does this mean I might get some postnatal SNP array results before I receive results for a previously requested postnatal array CGH?

Yes. To deal with the postnatal array CGH backlog separate teams will be working in parallel. One team will be working on the new postnatal SNP arrays and another will be working on the postnatal array CGH backlog. This is to minimise the risk there will be a delay in reporting postnatal SNP arrays going forward.

If you have any questions or would like to contact us:

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AWMGS
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