

## From Karyotyping to Microarrays – improved diagnostics with cost savings

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**Leading researchers have recommended that for many genetic imbalances, microarray-based analysis should be the first cytogenetic test performed; it provides improved diagnostics, and also holds the potential for cost savings in comparison with karyotyping.**

**Let AROS assist you in implementing microarray testing in your clinic.**

With 40 to > 1000 times higher resolution, microarrays offer significantly higher diagnostic yields (15%-20%) than karyotyping; this includes, among others diagnoses such as unexplained developmental delay/intellectual disability, autism spectrum disorder and multiple congenital anomalies.

In addition to a much higher resolution, microarray analyses are not based on the subjective assessment of gains and losses, and thus there is less interpersonal and interlaboratory variation in detection rates. This has led leading researchers to recommend workflows, where microarray based analysis is the first test performed\*.

*AROS Applied Biotechnology has many years of experience in microarray-based analysis on different platforms, incl. experience with a range of cytogenetic microarray based analyses.*

*We would be pleased to assist you in identifying how to optimally apply microarray data in your department.*

### **Available microarray technologies for Cytogenetic microarray-based analysis:**

In principle, all microarrays that can be used for copy number variation analysis may be used for cytogenetics testing. The most commonly used from Affymetrix and Illumina are:

#### **1. Affymetrix Genome-Wide Human SNP Array 6.0**

The Human SNP 6.0 Array has already been used for several years as second-tier testing in cytogenetics. It provides 950,000 markers for CNV, including 202,000 probes targeting 5,677 CNV regions from the Toronto Database of Genomic Variants, and 744,000 probes evenly spaced along the genome. In addition it contains 900,000 SNP markers that, as with the 2.7M Array, enable you to detect loss of heterozygosity (LOH), uniparental disomies (UPD), and regions of the genome that are identical-by-descent.

*Affymetrix' arrays come with a specially develop Chromosomal Analysis Suite free of charge. Among others the software summarizes chromosomal aberrations across the genome, provides focus analysis on specific regions of known significance, analyzes the genome at different levels of resolution and has direct access to e.g. NCBI, UCSC Genome Browser, Ensembl, and OMIM. Also you can customize and load your own annotations and regions for focused analysis.*

2. **Illumina's HumanOmni2.5-Quad BeadChip** with 2.5 million markers, **HumanOmniExpress-12 BeadChip** with 700,000 markers, and **HumanCytoSNP-12 BeadChip** with 300,000 markers all belongs to the Infinium Array series. As with other Illumina Infinium Arrays, these simultaneously measure intensity differences and allelic ratios, enabling the profiling of intercellular mosaicism and copy-neutral LOH events such as uniparental disomy (UPD), mitotic recombination, or gene conversion events, all of which cannot be detected on array-CGH platforms.

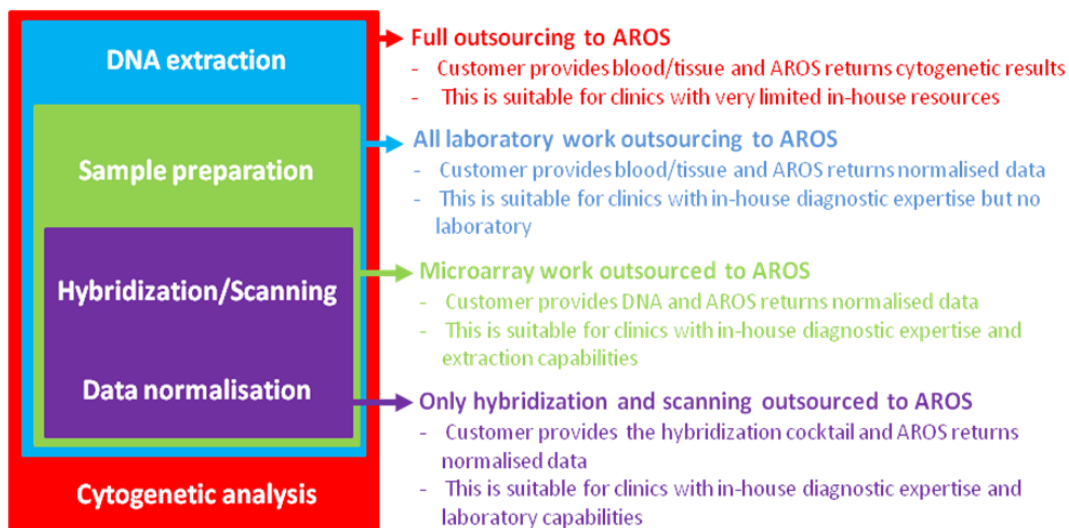
*Analysis of Infinium HD BeadChip data is supported by Illumina's general BeadStudio Genotyping Module, and the standalone KaryoStudio data analysis software package. The integrated chromosomal browser displays gene information, found regions, and regions previously associated with phenotypes. It enables use of standard region list, or customer-selected regions and phenotypes for cross-matching, and links to databases such as the Database of Genomic Variants, UCSC genome browser, and DECIPHER.*

### Set-up:

AROS provides flexible out-sourcing to match the specific needs of your clinic.

AROS can assist you tailor-make the set-up to match your needs, your budget and your organisation.

You may outsource the process in its entirety, including DNA extraction and data analysis, or you may outsource parts of it.



### AROS training program for your staff members.

In collaboration with Affymetrix, AROS has developed dedicated protocols and a training program that enables a setup, whereby the Cytogenetics function carries out the sample preparation for microarray analysis in-house using its existing personnel and passes on the hybridization cocktail to

AROS for scanning. There are two modules in the training program: 1) A hands-on training in sample preparation and 2) A thorough training in using the analytic software.

## **Costs**

In these many situations, microarrays provide not just higher diagnostic yields, it is also less expensive.

On a single test level the average cost of karyotyping is app. ¼ of the cost of a microarray. However, most often G-banded karyotyping has to be complemented by e.g. a customized subtelomeric fluorescence in situ hybridization. When the cost hereof is included, the total cost of microarray-based analysis is on average less than the cost of the traditional analytic approach (research shows that it can be less than 65% of the average total cost of karyotyping\*\*).

## **Good laboratory practice and good clinical practice ensure the highest quality**

Good laboratory practice (GLP) and Good clinical practice (GCP) are the internationally recognized rules ensuring that highest levels of quality, reproducibility and patient integrity. GLP and GCP are important in assuring regulatory authorities that the data submitted are a true reflection of the results obtained during the study, and can therefore be relied upon when making risk/safety assessments.

AROS has been GLP certified since 2005 and has in 2010 fully adopted the GCP guidelines.

Using a laboratory that is certified under GLP and working according to GCP, demonstrates your due diligences and your devotion to quality, patient integrity and accountability.

\*) Wordsworth, S, Buchanan, J, Regan, R, Davison, V, Smith, K, Dyer, S, Campbell, C, Blair, E, Maher, E, Taylor, J, and Knight, SJ (2007). Diagnosing ideopathic learning disability: A cost-effectiveness analysis of microarray technology in the National Health Service of the United Kingdom. *Genomic Medicine*, 1:35-45

\*\*\*) Miller DT, Adam MP, Aradhya S, Biesecker LG, Brothman AR, Carter NP, Church DM, Crolla JA, Eichler EE, Epstein CJ, Faucett WA, Feuk L, Friedman JM, Hamosh A, Jackson L, Kaminsky EB, Kok K, Krantz ID, Kuhn RM, Lee C, Ostell JM, Rosenberg C, Scherer SW, Spinner NB, Stavropoulos DJ, Tepperberg JH, Thorland EC, Vermeesch JR, Waggoner DJ, Watson MS, Martin CL, Ledbetter DH, (2010). Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies, *Am J Hum Genet*. 2010 May 14;86(5):749-64.