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Advancing clinical solutions with Chromosomal Microarray Analysis applications using CytoScan

Paula Rendeiro

Thermo Fisher Scientific

Genetic errors can occur at different levels in genetic material and can be associated with a large spectrum of clinical traits. Copy number variants (CNVs) represent one the most important type of genetic errors. They are defined as variation in number of copies in DNA segments, and they can range in size from 1kb to several Mb owing to deletions, insertions, duplications or complex recombination.

Advanced genetic assessment technologies enable cytogenetic researchers to identify significantly more copy number variations (CNVs) and other structural alterations associated with constitutional disorders and malignancies than ever before. Test methods such as karyotyping, fluorescent in situ hybridization (FISH), and low-resolution arrays have deficiencies in genomic coverage and limited resolution, limiting the number of significant variants that can be seen. Compromising on genomic coverage, content, or resolution leads to significant aberrations being missed, necessitating further analysis, which can delay results and increase costs.

Whole-genome microarrays that cover both polymorphic (e.g., single-nucleotide polymorphisms or SNPs), such as CytoScan, and nonpolymorphic regions of the genome can be used to assess DNA copy number alterations at a much higher resolution than conventional cytogenetic analysis to support the assessment of potentially causative genetic alterations such as CNVs, chromosomal imbalances, and allelic imbalance indicative of absence of heterozygosity (AOH) or loss of heterozygosity (LOH).

CNVs have been associated with development delay, intellectual disability and congenital anomalies from many years now. Already in 2010 there was a world consensus to use Chromosomal Microarray Analysis as first-tier testing in these conditions, due to its high diagnostic yield (15-20%) over conventional cytogenetic testing as karyotype and FISH.

CNVs have also a very important role in prenatal testing, due to its association with development disorders and congenital anomalies. Since 2012 many different large-scale studies showed the increased yield of use of Chromosomal Microarray Analysis in prenatal testing (5-10%).

CNVs have been shown to indirectly influence a healthy individual's susceptibility to cancer, by varying the gene dosage of tumour suppressor genes or oncogenes; and can serve as potential diagnostic, prognostic, and predictive biomarkers.

Current guidelines and recommendations from major professional societies, such as ACMG, ESHG, ACOG, SFMF and CGC, endorse the use of Chromosomal Microarray Analysis in different clinical applications: postnatal, prenatal and oncology.

CytoScan arrays have high resolution whole-genome design, with excellent coverage of constitutional genes (OMIM, RefSeq, ClinGen, ClinVar) and cancer genes. Its design ensures that most regions are represented, not just those currently identified as relevant, but future ones also, making it a “future-proof” platform.