CytoSure

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Constitutional v3 & Constitutional v3 +LOH Arrays

Features

Up-to-date ID/DD gene content

- The latest research-validated genes and regions

Single exonic CNV detection in the genes that matter

- Enabling high-resolution CNV detection in up to 502 genes of interest

The best of both worlds

- Accurate identification of CNVs, LOH, UPD and consanguineous samples

Integrated sample tracking probes and optimised labelling kits

- The complete solution for reliable analysis and reporting

Streamlined data analysis and interpretation

- Straightforward and fast analysis of CNVs and LOH

CytoSure

Constitutional v3 & Constitutional v3 +LOH Arrays

Enhanced exon-level CNV coverage of developmental disorder genes and reliable detection of loss of heterozygosity, all on a single array

CytoSure® Constitutional v3 arrays offer enhanced exon-level coverage of developmental disorder genes. They combine the up-to-date and relevant developmental delay content from the recent Deciphering Developmental Disorders (DDD) study and latest updates from ClinGen*. The addition of a research-validated collection of single nucleotide polymorphism (SNP) probes with the CytoSure Constitutional v3 +LOH array facilitates the precise identification of loss of heterozygosity (LOH) and uniparental disomy (UPD) in addition to accurate copy number (CN) detection. This offers cost-effective detection of a broader range of genetic syndromes — without the requirement for further investment in equipment or training.

Single exonic CNV detection in the genes that matter

CytoSure Constitutional v3 arrays include probes for up to 502 highly-targeted developmental delay genes identified by both the DDD project and ClinGen, enabling detection of single exon aberrations. Higher probe density across the exons and introns of important developmental delay genes allows improved detection of small (<500bp) deletions and duplications that might otherwise be missed or require manual calling on other outdated constitutional cytogenetics array designs (Figure 1).

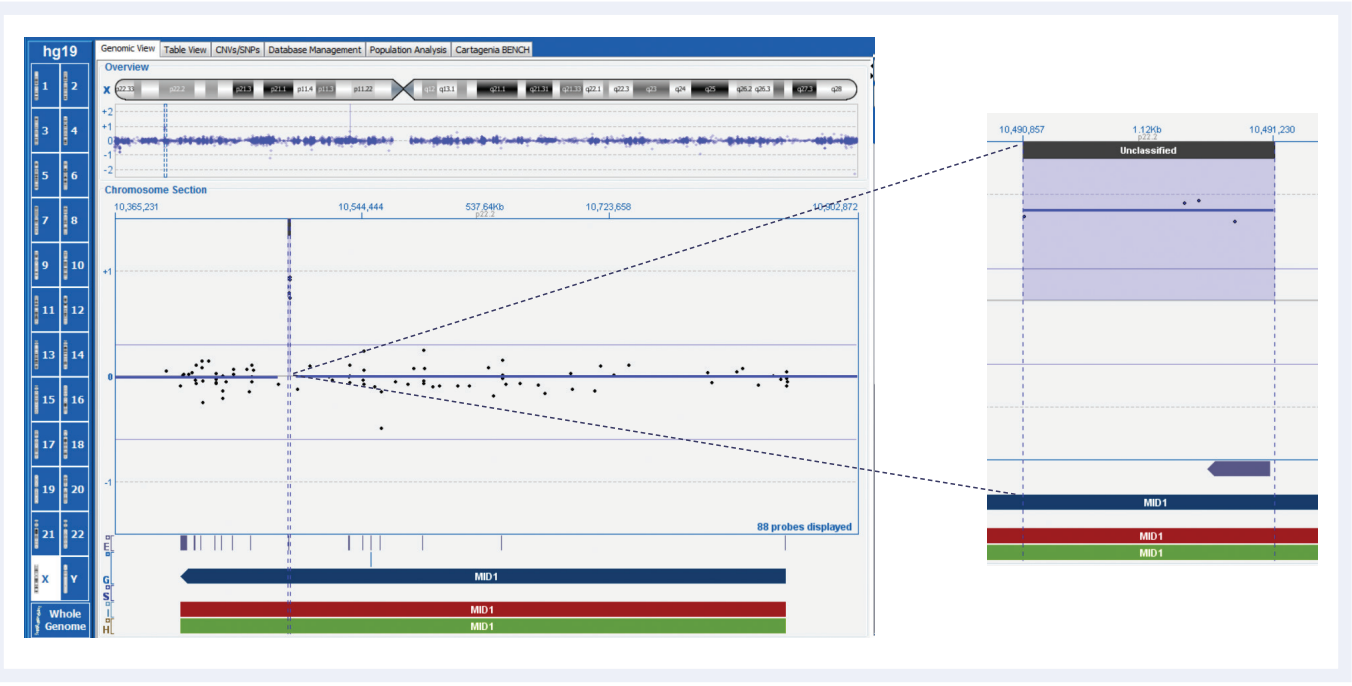

Figure 1: Accurate detection of a small, single-exon (<500bp; 4 probes) duplication in *MID1* associated with Opitz-G syndrome[1]. Data generated using the CytoSure Constitutional v3 (8x60k) array.

Optimised and targeted probes

An informed and sophisticated approach to array design has been used with CytoSure Constitutional v3 arrays, with more probes being located in regions of the genome that are most likely to detect a biologically relevant aberration. These biologically relevant regions have been identified and prioritised during the DDD study and through the ClinGen dosage sensitivity map, with the highest priority regions being covered at an exon-level resolution. In addition, a tiered backbone approach has been adopted with a greater concentration of probes in regions where novel aberrations are more likely to be uncovered, without compromising on overall backbone resolution (Table 1).

Product	Cat. No.	Top priority genes	Medium priority genes	Lower priority genes	Decipher Syndrome regions	ClinGen regions	High priority backbone resolution	Medium priority backbone resolution	Lower priority backbone resolution
CytoSure Constitutional v3 (8x60k)	020045	Exon targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	189kb (1 probe every ~63kb)	375kb (1 probe every ~125kb))	663kb (1 probe every ~221kb))
CytoSure Constitutional v3 (8x60k)	020046	Exon targeted	Exon targeted	Exon targeted	Whole-gene targeted	Whole-gene targeted	68kb (1 probe every ~22kb)	74kb (1 probe every ~ 24kb)	162kb (1 probe every ~54kb)
CytoSure Constitutional +LOH (4x180k)	020047	Exon targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	Whole-gene targeted	68kb (1 probe every ~22kb)	74kb (1 probe every ~24kb)	162kb (1 probe every ~54kb)

Table 1. Selection guide for CytoSure Constitutional v3 arrays. For a complete list of genes covered, please email contact@ogt.com.

The best of both worlds – CNVs and LOH

For a number of years, microarrays have been considered the first approach for research into CNV analysis in children with developmental delay, intellectual disability and congenital anomalies. The CytoSure Constitutional v3 +LOH array offers the detection of whole chromosome aneuploidies, submicroscopic deletions and duplications and single-exon CNV detection (Figure 1). In addition, the inclusion of empirically selected SNP probes facilitates the detection of copy-neutral events such as LOH, UPD and long-contiguous stretch of homozygosity (LCSH) of 7Mb and above, which can be associated with consanguinity (Figure 2). Additionally, SNPs can provide an internal confirmation of CNVs that may eliminate the need for follow-up investigation (Figure 3).

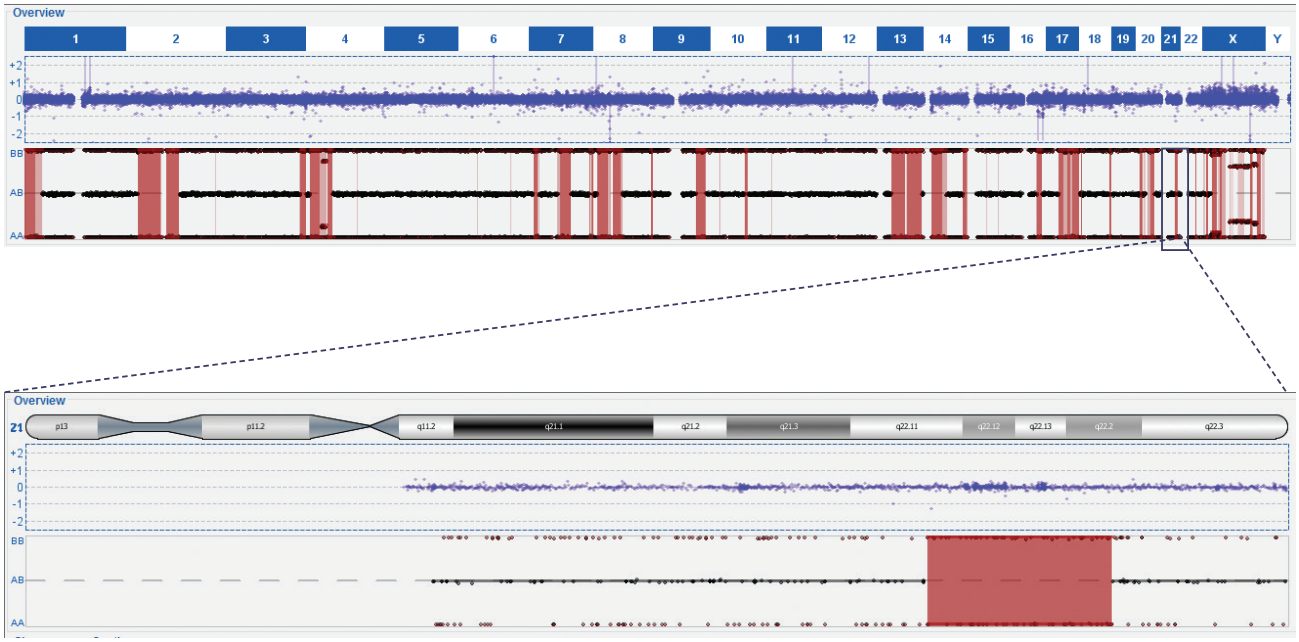

Figure 2: Multiple regions of homozygosity associated with parental consanguinity detected using the CytoSure Constitutional v3 +LOH array. The close-up view illustrates a section of LOH of 7.05Mb on 21q[1].

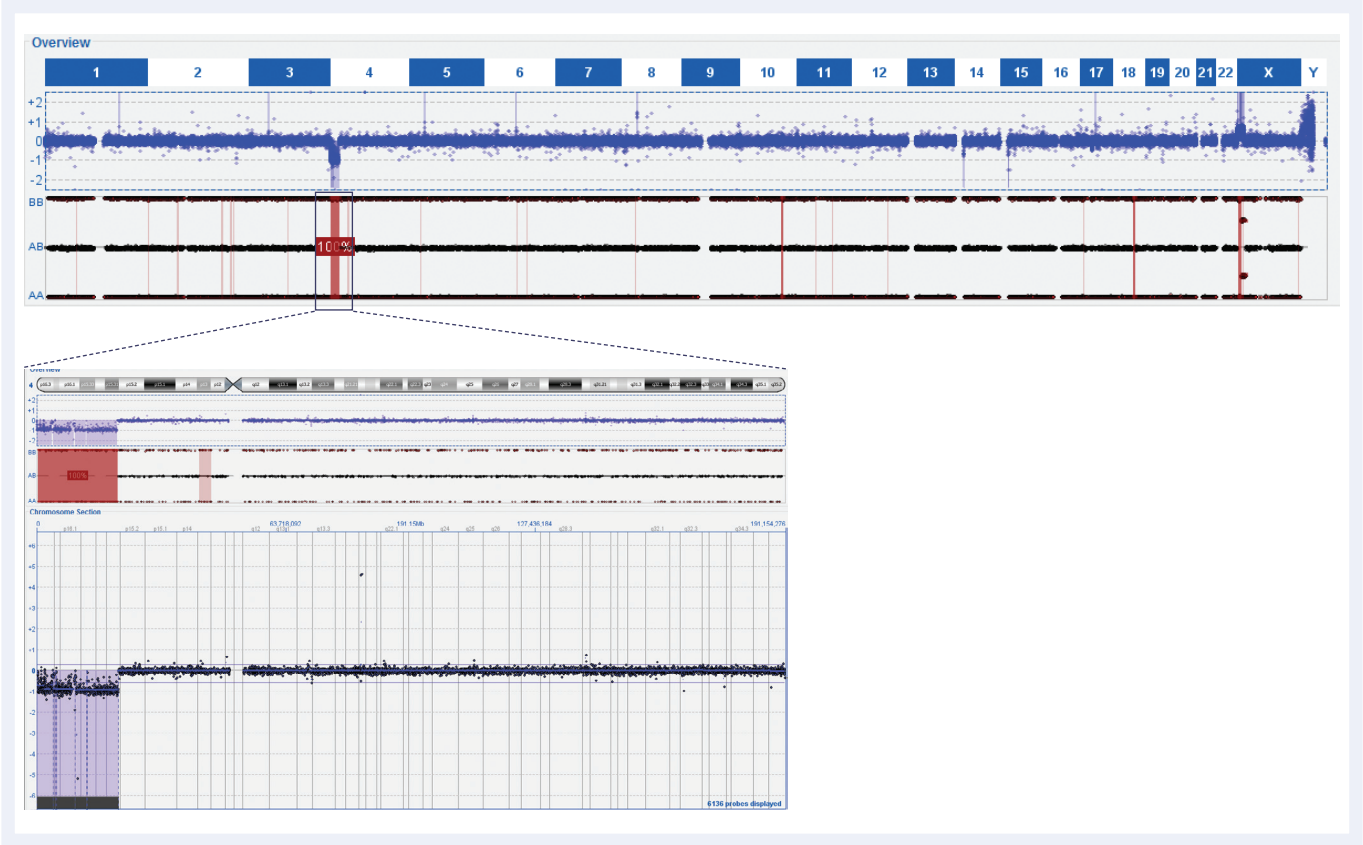

Figure 3: A t(X;4) unbalanced translocation detected using the CytoSure Constitutional v3 +LOH array. The close-up view of the loss on Chromosome 4 clearly illustrates how the SNP probes act as an independent verification of the copy number change[5].

A range of array formats to suit your requirements

CytoSure Constitutional v3 arrays are available in a range of formats to match your resolution and throughput requirements. All CytoSure arrays have been research-validated using CytoSure Genomic DNA Labelling Kits, which have been uniquely developed and optimised to enable rapid delivery of high-quality results with excellent signal-to noise ratios and superior DLRs. Two formats are available: the CytoSure Genomic DNA Labelling Kit is sufficient for 24 samples and is ideal for labs running one or two arrays a week, and for high-throughput labs, the CytoSure HT Genomic DNA Labelling Kit is recommended as its plate-based protocol allows simultaneous labelling of 96 samples. To achieve the best quality data possible, it is recommended that CytoSure arrays are used in conjunction with CytoSure Genomic DNA Labelling Kits.

Easy identification of sample mix-up via spike-in controls

As laboratories scale up their processes to increase throughput and reduce costs, parallel processing of higher numbers of samples increases the possibility of sample mix-up. Even automated workflows contain several steps where sample identity can be lost (e.g. pipetting samples into gasket slides). CytoSure Constitutional v3 arrays contain sample tracking probes which, when used in conjunction with CytoSure Sample Tracking Spike-ins, enable researchers to quickly and easily identify any erroneous samples, ensuring only accurate data is reported.

Streamlined data analysis and interpretation

CytoSure Interpret Software, which accompanies all CytoSure arrays, is a powerful, easy-to-use package for the analysis of CNV and SNP data with the ability to analyse data in both hg19 and hg38. Innovative features such as the Accelerate Workflow and automatic aberration classification functionality enable the automation of data analysis workflows, minimising the need for user intervention and maximising the consistency and speed of data interpretation.

The unique database enables easy back-up of data, simplified searching and user tracking. CytoSure Interpret Software also includes extensive annotation tracks covering syndromes, genes, exons, benign and pathogenic CNVs. These link to publicly available databases such as ClinGen, Ensembl and the Database of Genomic Variants, providing results in context.

Understanding the complex genetic composition of consanguineous samples, samples with UPD and samples with long stretches of LOH is also simplified using CytoSure Interpret Software. Regions of LOH can be identified by viewing the B-allele frequency (BAF) plot or the Allele Status Plot. CytoSure Interpret Software further simplifies the analysis of LOH using a proprietary 'LOH Score' whereby, continuous stretches of homozygous SNPs are scored and those regions with a score above a recommended threshold are considered to be significant (Figure 4).

It is easy to get started as the software is provided with full on-site training. If necessary, legacy array data can also be converted and loaded into CytoSure Interpret Software allowing seamless transfer of aberration information for more powerful analysis.

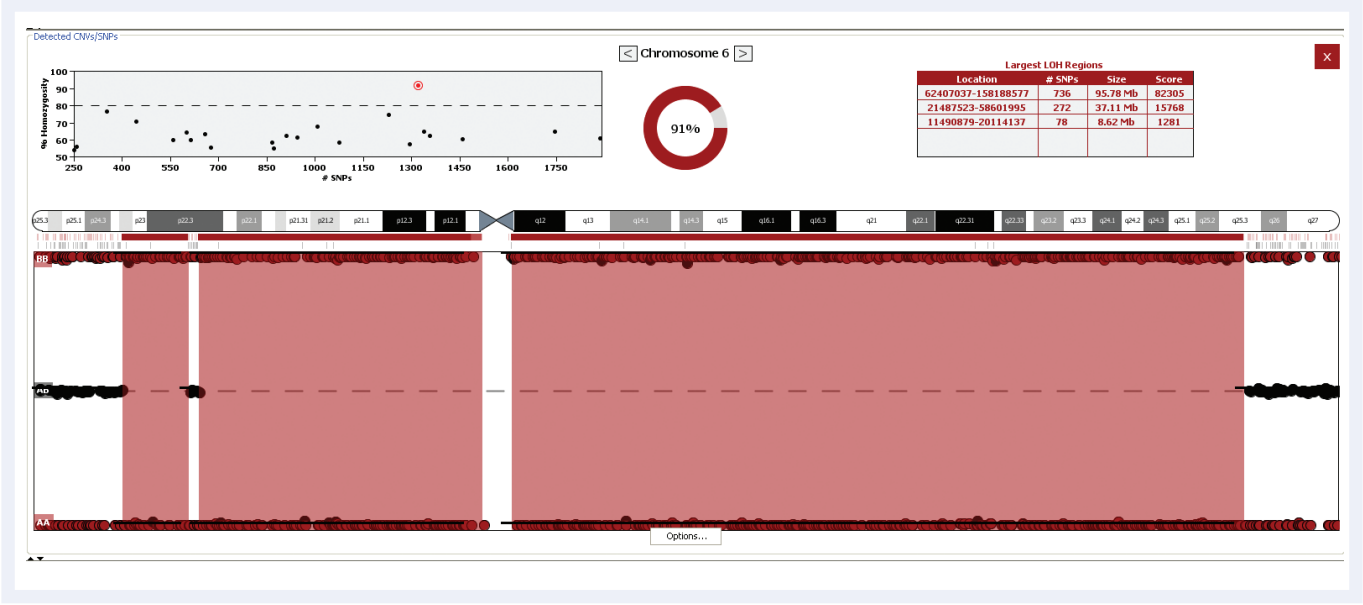

Figure 4: Chromosome 6 data from a sample where extensive regions of LOH have been detected using the CytoSure Constitutional v3 +LOH array. CytoSure Interpret Software clearly displays the percentage of homozygous alleles.

Ordering information

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Product	Contents	Cat. No.
CytoSure Constitutional v3 (8x60k)	Microarray with four arrays of 60,000 spots; CytoSure Interpret Software	020045
CytoSure Constitutional v3 (4x180k)	Microarray with four arrays of 180,000 spots; CytoSure Interpret Software	020046
CytoSure Constitutional v3 +LOH (4x180k)	Microarray with four arrays of 180,000 spots; CytoSure Interpret Software	020047
CytoSure Genomic DNA Labelling Kit	24 reactions, clean-up columns, dyes, nucleotide mix random primers, enzyme, collection tubes	020020
CytoSure HT Genomic DNA Labelling Kit	96 reactions, 2 purification plates, dyes, nucleotide mix, random primers, enzyme	500040
CytoSure Sample Tracking Spike-ins A – H	Sample Tracking Probes sufficient for 12 reactions supplied in three aliquots	500066

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* Formerly known as ISCA/ICCG.
ǂ Data kindly provided by WMRGL Birmingham UK.
ǂ Data kindly provided by the University of Louisville, Kentucky, USA.
§ Data kindly provided by the University of Illinois, Chicago, USA.

References

1. NCBI (2015) *ClinGen Dosage Sensitivity Map* [online] Available from: http://ncbi.nlm.nih.gov/projects/dbvar/clingen [Accessed 28 May 2015].

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What binds us, makes us.

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