The GenetiSure Cancer Research CGH+SNP Array (2x400K)

Product Note

- **Superior copy number and copy-neutral aberration detection on one array**
- **Single exon copy number detection**
- **LOH resolution validated to 2.5 Mb**
- **Easily add or remove genes to customize your array**
- **Complete workflow from a single supplier**

Detect both copy number aberrations and loss of heterozygosity in cancer samples on a single array

A new Human Comparative Genomic Hybridization (CGH) + Single Nucleotide Polymorphism (SNP) cancer research array has been developed to enable high-resolution and simultaneous detection of copy number and copy-neutral changes on the same array, thus increasing efficiency without sacrificing quality. An increased number of SNP probes provide loss of heterozygosity (LOH) detection down to 2.5 Mb, and as low as 1 Mb in some cases. Copy number resolution has been enhanced by dramatically increasing the number of CGH probes in cancer-associated genes, with an average of ≥3 probes per targeted exon.

More effective, high-resolution detection of cancer genetic variation

CGH analysis has revolutionized the field of cytogenetics by providing accurate identification of copy number variations at greater than 1,000-fold resolution, compared to traditional karyotyping. The development of the Agilent SurePrint G3 Human CGH+SNP Platform enabled rapid and reliable identification of both copy number variations and copy-neutral aberrations, such as LOH or uniparental disomy (UPD), in a single array assay. The new GenetiSure Cancer Research CGH+SNP array brings higher LOH resolution and exon-level copy number resolution to cancer research studies.

Using the identical high-throughput workflow as previous SurePrint G3 CGH+SNP arrays, the GenetiSure Cancer Research CGH+SNP array can be quickly incorporated into your cytogenetics research. CGH+SNP arrays can also be easily customized, offering maximum flexibility, while the Agilent 60-mer probes enable high-confidence characterization of copy number and copy-neutral chromosomal aberrations.

Agilent Technologies

A customizable platform for simultaneous detection of copy number and copy-neutral variation in cancer samples

The GenetiSure Cancer Research CGH+SNP array contains ~300,000 CGH probes and ~103,000 SNP probes. Many of the CGH probes are targeted to cancer regions of the genome, sourced from the COSMIC (Wellcome Trust Sanger Institute) and the Cancer Genetics Consortium (CGC) somatic cancer mutation databases (Table 1), with median CGH probe spacing of ~10 Kb in the targeted cancer regions. Copy number changes (amplifications and deletions) are measured using three or more CGH probes for almost 90 % of the covered exons, providing resolution down to the single-exon level. While the previous 4x180k cancer CGH+SNP array had a resolution of 5 Mb for copy-neutral aberrations, the lower limit detection range for the new cancer research array is 2.5 Mb, with the ability to detect 1 Mb changes in some cases, due to the increased number of SNP probes.

Custom cancer arrays can also be readily designed in many array formats, including 1x1 million, 2x400K, 4x180K, and 8x60K, using SureDesign, a free web-based application (https://earray.chem.agilent.com/suredesign/). The SureDesign database houses more than 28 million CGH probes, and approximately 118,000 probes for SNPs. Multiple array formats allow for maximum flexibility to meet sample throughput and cost requirements.

A simple, efficient sample preparation process starts from as little as 500 ng DNA, and uses restriction digestion followed by Klenow-based enzymatic labeling (Figure 1). The CGH+SNP arrays are printed on 1×3 inch glass slides, and are compatible with Agilent standard hybridization gaskets and chambers. Arrays are scanned at 3 µm using the Agilent SureScan Array Scanner (p/n G4900DA).

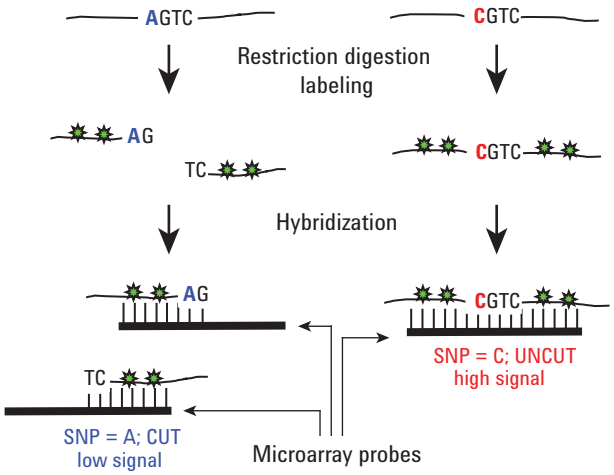

Figure 1. The Agilent CGH+SNP microarrays use the same workflow as the CGH-only arrays. Restriction digestion of genomic DNA allows genotyping of SNPs located in the enzymes' recognition sites.

Table 1. Comparison of the new GenetiSure Cancer Research array and the Agilent SurePrint Cancer microarray.

	GenetiSure Cancer Research CGH+SNP 2x400K	Agilent SurePrint G3 Cancer CGH+SNP 4x180K
Catalog part number	G5975A	G4869A
Number of CGH probes	~ 300,000	~120,000
Number of targeted CGH probes	~123,000	~20,000
Median CGH probe spacing	~9.8 Kb overall, 20 Kb backbone	
20 Kb backbone	~25 Kb	
COSMIC/CGC genes, exon coverage	~ 89% ≥3 probes/exon	Minimum 1 probe/exon
Number of SNP probes	~103,000	~60,000
Copy-neutral LOH resolution	~ 2.5–10 Mb	~ 5–10 Mb

High-resolution copy-neutral and copy number cancer aberrations on the same array

The resolution of the GenetiSure Cancer Research CGH+SNP array for detection of LOH was validated using samples from the 1000 Genome Deep Catalog of Human Genetic Variation. Figure 2 illustrates detection of a 2-Mb LOH in the CSMD3 gene on chromosome 8 that was not found using the previous 4x180K cancer array (data not shown).

The same array enables detection of amplifications and deletions as small as single or partial exons, due to the increased number of CGH probes and their closer spacing, particularly in cancer genes. Figure 3 illustrates detection of two 1 Kb amplifications in a gene of interest (A), and a 0.47 Kb deletion in a second gene of interest (B). In both cases, the copy number changes were not detected by the previous 4x180K cancer array (data not shown).

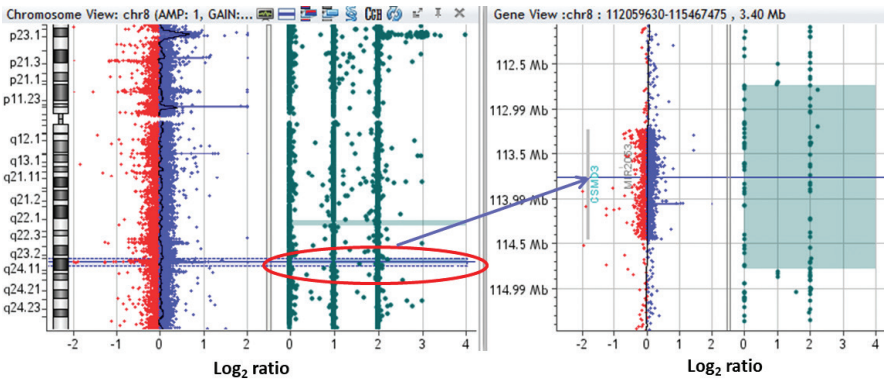

Figure 2. View in Agilent CytoGenomics software of a detected loss of heterozygosity of a 2.0 Mb region spanning a single gene of interest (CSMD3) on chromosome 8 using the GenetiSure Cancer CGH+SNP Research array. An expanded view of this region is shown in the right-hand panel.

Powerful Agilent CytoGenomics Software for both CGH and SNP detection

Agilent CytoGenomics Software for CGH+SNP array analysis enables comparative genome-wide analysis between test and reference samples hybridized to different arrays within the same slide. Copy number aberration calls are determined entirely by non-SNP oligonucleotides, maximizing signal-to-noise ratio (S/N). A SNP call is made from the $\log_2$ ratio of the signal of the sample to the signal of a genotyped internal reference. Regions of copy-neutral LOH are then located by identifying genomic regions with a statistically significant scarcity of heterozygous SNP calls.

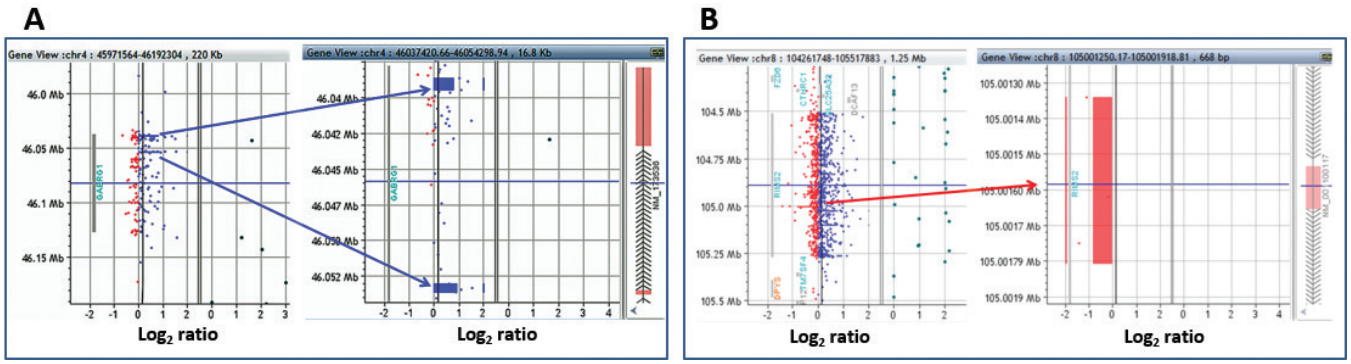

Figure 3. A) Two small amplifications (~1 kb each) in two exons (blue rectangular regions) in the GABRG1 gene are called using the new 2x400K design, but not using the previous 4x180K cancer design, which lacked probes in these regions. B) A 0.47 kb deletion was detected in a single exon (in pink on the right-hand vertical axis) of the RIMS2 gene using the new design, but not with the previous design which also lacked probes in this region. In each case, the GenetiSure Cancer Research CGH+SNP array provides increased gene focus with more probes than the previous 4x180K cancer array, as shown by the presence of many more red and blue individual probe dots.

Complete CGH microarray workflow

The Agilent array workflow is streamlined, and takes significantly less time to process samples compared with other microarray methods. Agilent offers all of the reagents and instruments needed to process your CGH+SNP data including custom and catalog arrays, labeling kits, hybridization and wash solutions, a hybridization oven, the best-in-class SureScan microarray scanner, and easy-to-use software to identify aberrations (Figure 4).

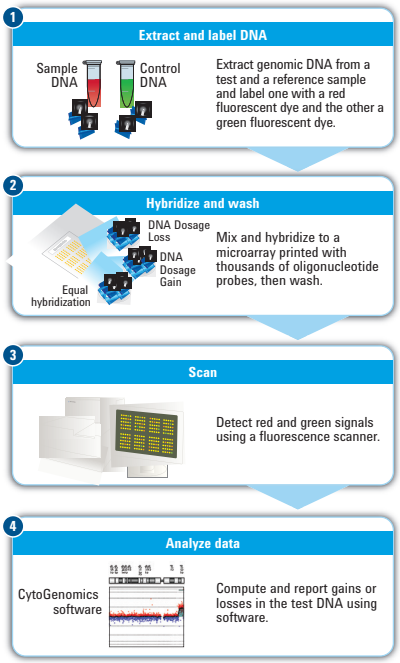

Figure 4. The complete CGH+SNP microarray workflow.

Ordering Information

Description	No. of arrays/slide	No. of slides	No. of samples	Part number	Stocked/ MTO*
GenetiSure CGH+SNP Arrays					
GenetiSure Cancer Research CGH+SNP Array, 2x400K	2	5	10	G5975A	Stocked
GenetiSure Postnatal Research CGH+SNP Array, 2x400K	2	5	10	G5974A	Stocked
Other CGH+SNP Arrays					
Agilent SurePrint G3 ISCA CGH+SNP Array, 4x180K	4	3	12	G4890A	Stocked
Agilent SurePrint G3 Human Genome CGH+SNP Array, 2x400K	2	1	2	G4825A-028081 (G4842A†)	MTO
Agilent SurePrint G3 Cancer CGH+SNP Array, 4x180K	4	1	4	G4826A-030587 (G4869A†)	MTO
Agilent SurePrint G3 Custom CGH+SNP Array, 1x1M	1	1	1	G4882A	MTO
Agilent SurePrint G3 Custom CGH+SNP Array, 2x400K	2	1	2	G4883A	MTO
Agilent SurePrint G3 Custom CGH+SNP Array, 4x180K	4	1	4	G4884A	MTO
Agilent SurePrint G3 Custom CGH+SNP Array, 8x60K	8	1	8	G4885A	MTO

*MTO= Make-to-Order

†Former catalog number

Note: Arrays are shipped with a foil seal. After breaking the foil, store microarrays at room temperature, in the dark, under a vacuum desiccator or in a nitrogen purge box. Do not expose microarrays to open air during storage.

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