OncoScan CNV Assay and OncoScan CNV Plus Assay

Unleash the power of copy number profiling

Approximately 80% of all cancers are affected by both somatic mutations (SM) and copy number (CN) changes [1]. Recent publications have shown that in certain types of cancers, copy number variation (CNV) plays a more important role than SM with 5 out of 10 cancers being driven by CN changes. Table 1 shows the percentage of cases in each category of certain CN-driven tumors [1].

Table 1. Examples of CN-driven tumors.

Tumor	CN	SM
Ovarian	100%	0%
Breast	90%	10%
Lung squamous cell carcinoma	85%	15%
Head and neck	75%	25%
Lung adenocarcinoma	60%	40%

It is vital to map the CNVs in cancer research samples to fully profile a tumor and identify new biomarkers. The Applied Biosystems™ OncoScan™ CNV Assay and the Applied Biosystems™ OncoScan™ CNV Plus Assay are the only tools capable of determining highly accurate CN changes and allelic imbalances, including loss of heterozygosity (LOH) and copy-neutral LOH (cnLOH) across the entire genome in solid tumors.

- **OncoScan CNV Assay**—high-density CN coverage across 900 cancer genes and standard coverage across the whole genome
- **OncoScan CNV Plus Assay**—same CN coverage as the OncoScan CNV Assay plus a somatic mutation panel covering 74 mutations in 9 genes (Figure 1)

The OncoScan assays utilize Molecular Inversion Probe (MIP) technology, proven for identifying CN alterations, LOH, cnLOH, and somatic mutations (Figure 2). This assay has been shown to perform well with highly degraded DNA, such as that derived from formalin-fixed, paraffin-embedded (FFPE) tumor samples of various ages, and with low amounts of DNA starting material, making the assay a natural choice in clinical cancer research.

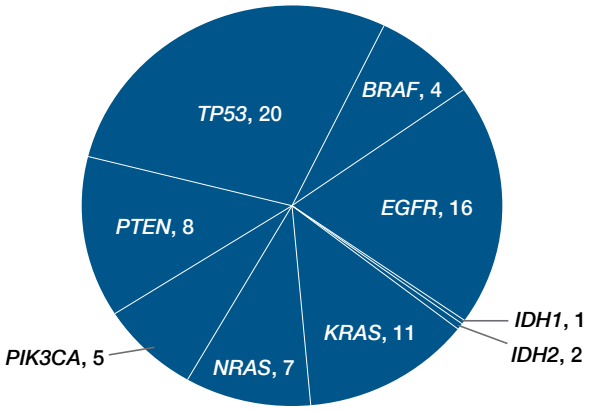

Figure 1. Somatic gene panel representing the number of somatic mutations by genes detected by the OncoScan CNV Plus Assay.

OncoScan assays provide:

- **Whole-genome CN analysis**—detect structural variants such as deletions, duplications, and unbalanced translocations that are not well characterized by short-read sequencing or targeted sequencing
- **Comprehensive coverage**—whole-genome analysis of genes with established significance as well as those with emerging evidence, helping to "future-proof" the technology investment and minimize revalidation burden
- **Complete flexibility**—detect chromosomal arm aberrations, focal changes, and LOH and cnLOH in a single assay, to help reduce costs and processing times
- **Robust performance**—detect subclones and assess clonal evolution and genetic variations that are known to have important implications in cancer
- **Low sample input and fast results**—get results in 72 hours from only 80 ng of FFPE-derived DNA
- **Rapid analysis**—free software provides intuitive data visualizations for hundreds of samples in minutes
- **High-resolution CN detection in priority cancer genes**—accurate identification of very small (50–125 kb) to large (Mb) CN variations

OncoScan CNV Assay genetic coverage

MIP probes are carefully selected and empirically tested to provide excellent performance across the genome with a higher density of SNP probes in cancer and cancer-related genes (Table 2).

The genes covered with the highest probe density were selected through collaboration with leading scientists from the Stand Up to Cancer™ consortium (SU2C); other target genes were selected following input from the Cancer Genomics Consortium and using cancer gene census lists from the Wellcome Trust Sanger Institute.

Table 2. Microarray markers coverage.

Genetic content	Resolution	Median probe density (kb/probe)
Cancer gene coverage		
232 genes	50 kb	2.5
644 genes	50–110 kb	5.0
15 genes	110–125 kb	5.6
Whole-genome coverage		
90% of genome (outside of cancer genes)	300–310 kb	16
97% of genome (outside of cancer genes)	380 kb	19

Chromosome Analysis Suite (ChAS) Software

ChAS algorithms address two major challenges associated with solid-tumor CN analysis:

- Establishing the expected normal CN state for a given locus
- Accounting for "normal cell contamination" present in most samples, which affects CN estimates

To address the first challenge, a universal reference dataset is available that includes ~400 normal and normal adjacent tissue (NAT) FFPE samples from over 20 sources covering a broad range of geographic locations, collection sites, block ages, cancer tissue types, as well as gender. These sources were chosen to capture the diversity of FFPE samples for which the normal CN at each locus was assessed.

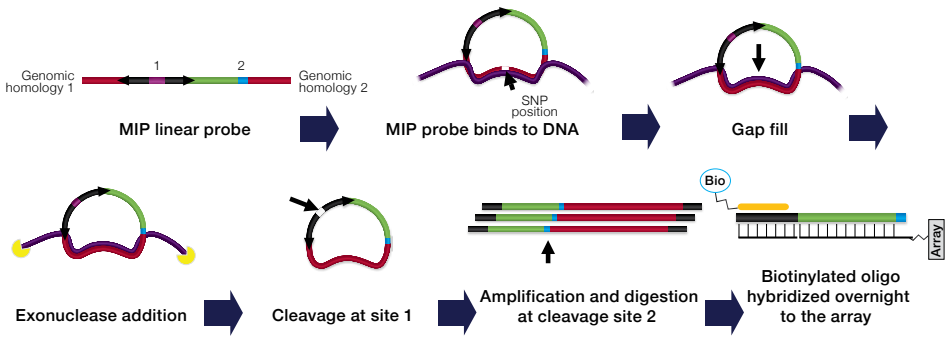

Figure 2. Overview of MIP technology.

To address the second challenge, the TuScan algorithm was developed based on a modification of the ASCAT2 algorithm to determine if a consistent percentage of aberrant cells (%AC) and ploidy are present at each CN change. The algorithm reports the linear integer CN in the cancer portion only, effectively subtracting the normal component, and thereby enabling a comparison between tumor samples with different contributions of normal cell contamination. For highly heterogeneous samples or where there is a very low percentage presence of aberrant cells, the algorithm reports the fractional, average linear CN of all cells within the sample. Figures 3–5 show example CN and somatic mutation data viewed in ChAS software.

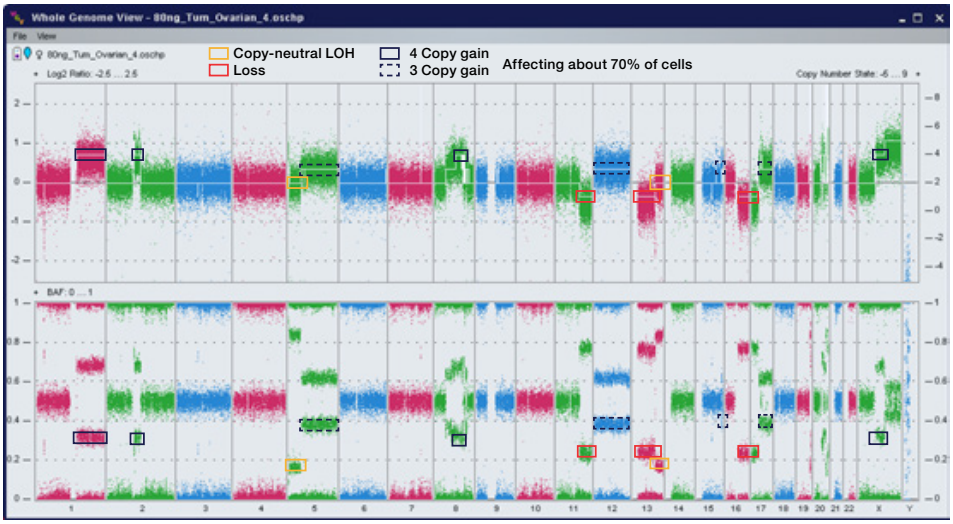

Figure 3. OncoScan CNV Assay data presented in log_2 ratio and b-allele frequency (BAF) view in ChAS software. Shown here are cnLOH (yellow squares), CN loss (red squares), and CN gain (dark purple squares with solid or dotted lines). The top view shows the log ratio and the bottom view shows the BAF that enables detection of low-level mosaic gain, loss, and LOH.

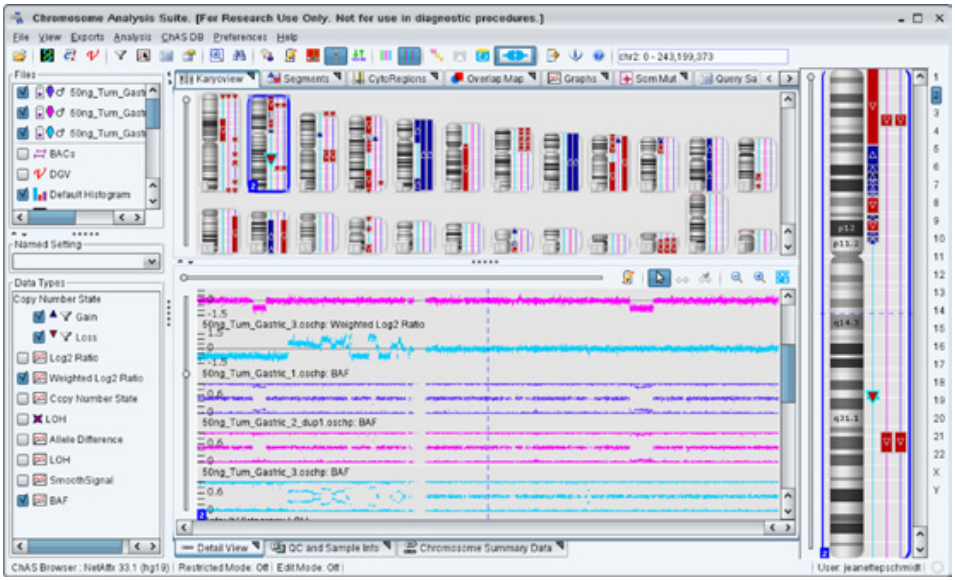

Figure 4. OncoScan CNV Assay data presented in karyoview in ChAS software. Shown here is the whole-genome visualization and ability to compare data from three samples (where each vertical line next to the chromosome represents one sample). CN gains are shown in blue and CN losses are shown in red.

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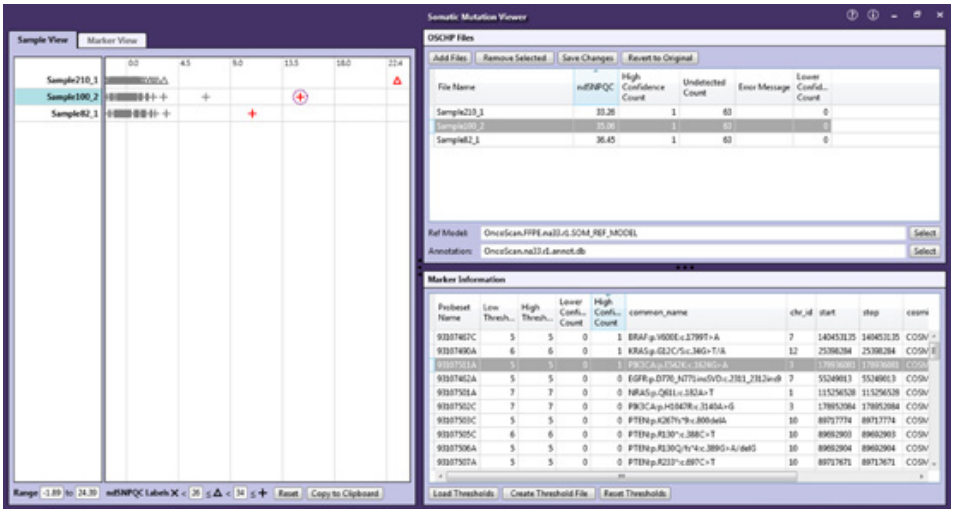

Figure 5. OncoScan CNV Plus Assay data presented in somatic mutation view in ChAS software. Shown here is the somatic mutation sample view.

Ordering information

Product	Description	Cat. No.
OncoScan CNV Assay	Contains OncoScan CNV Reagent Kit and 48 OncoScan CNV Arrays. Sufficient for 24 samples.	902695
OncoScan CNV Plus Assay	Contains OncoScan CNV Plus Reagent Kit and 48 OncoScan CNV Plus Arrays. Sufficient for 24 samples.	902293

Reference

1. Ciriello G et al. (2013) Emerging landscape of oncogenic signatures across human cancers. *Nature Genetics* 45(10):1127–1133.

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