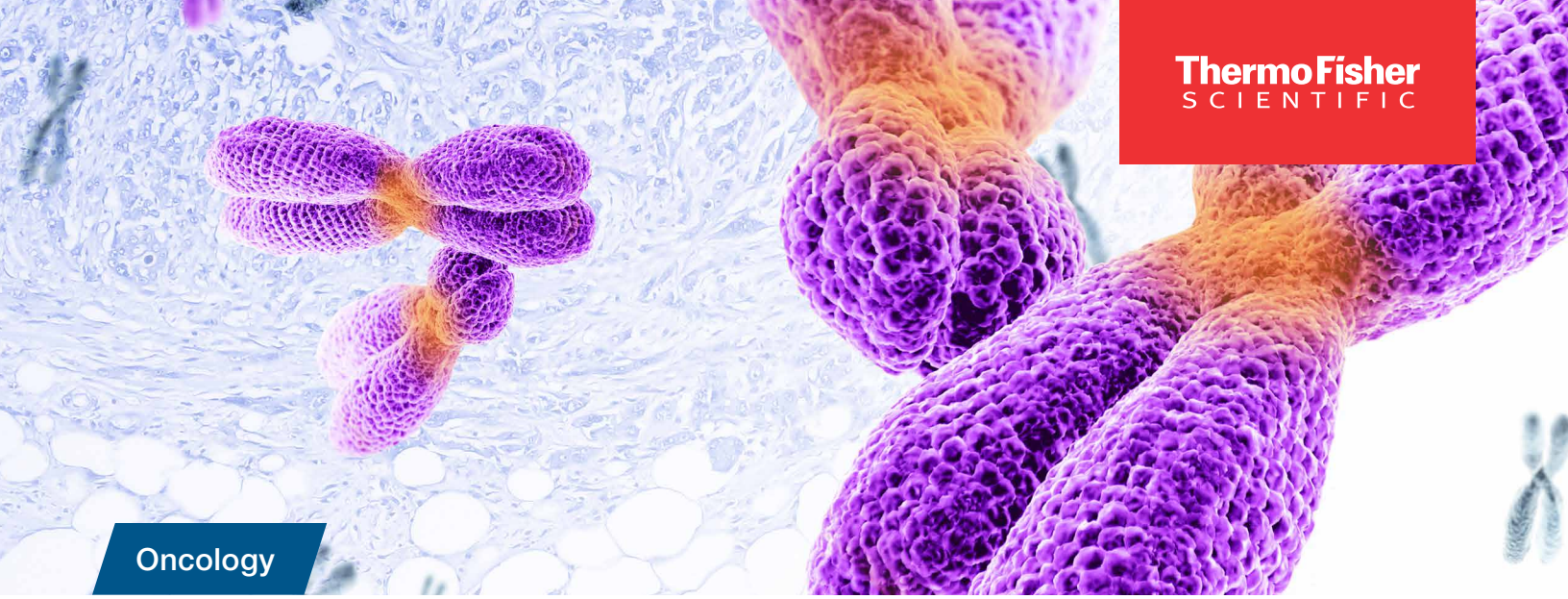


Oncology

OncoScan CNV and CNV Plus Assays

Unleash the power of copy number profiling for your research needs

The importance of copy number analysis in solid tumor research

The ability to accurately detect copy number (CN) changes such as copy number variations (CNVs) is critical to fully profile solid tumors. Approximately 80% of all cancers are affected by both somatic mutations (SMs) and CN changes [1]. Recent publications have shown that in certain types of cancers, CNs play a more important role than SMs, with 5 out of 10 cancers being driven by CN changes. Aneuploidy is used as a proxy for increased CNVs at the whole or partial chromosome level. Table 1 shows how high aneuploidy is prevalent across common tumor types [2].

Applied Biosystems™ Oncoscan™ CNV Assay and CNV Plus Assay

Table 1. High-aneuploidy tumors.

	Average aneuploidy score [2]
Adrenocortical carcinoma	18.3
Bladder urothelial carcinoma	13.6
Breast invasive carcinoma	12.1
Colon adenocarcinoma	11.6
Lower grade glioma	3.9
Ovarian serous cystadenocarcinoma	14.0
Prostate adenocarcinoma	2.6

applied biosystems

OncoScan CNV and CNV Plus Assays: Clinical research use cases

Unlocking HRD complexity with whole-genome profiling

Homologous recombination deficiency (HRD) is critical in the stratification and selection of cases for novel treatments using PARP inhibitors in multiple cancers. OncoScan CNV and CNV Plus Assays, due to their ability for whole-genome profiling of CN and loss of heterozygosity (LOH), are among the best tools for researching the cytogenetics of HRD.

Identifying biomarkers and tumor classifications

OncoScan CNV and CNV Plus Assays have been applied in clinical research of different types of cancer. They can detect key biomarkers important for researching tumor classification, like in pediatric brain tumor research and melanoma research, for example.

Analyzing genomic variation using circulating cell-free DNA

Liquid biopsies are rapidly becoming an alternative to invasive tissue biopsies for analyzing genomic variation associated with tumors. Cell-free DNA (cfDNA) is also a degraded DNA, which makes the molecular inversion probes (MIPs) of OncoScan CNV and CNV Plus Assays excellent tools for researching chromosomal aberrations and CNVs in this tissue type [3–5].

Accurately identify solid tumor, copy number biomarkers for research purposes

CN-based cancer biomarkers have potential diagnostic, prognostic, and predictive value. OncoScan CNV and CNV Plus Assays are the only microarrays capable of accurately identifying cytogenetic changes and allelic imbalances, such as LOH, copy-neutral LOH (cnLOH), and chromothripsis, across the entire genome in solid tumors. The utilization of MIP (molecular inversion probe) chemistry in the OncoScan CNV and CNV Plus Assays enhances analysis of degraded formalin-fixed, paraffin-embedded (FFPE) samples (Figure 1). The laboratory workflow, excluding gDNA extraction, delivers results within a mere three days (Figure 2). This efficient turnaround time positions these assays as excellent choices for clinical cancer research.

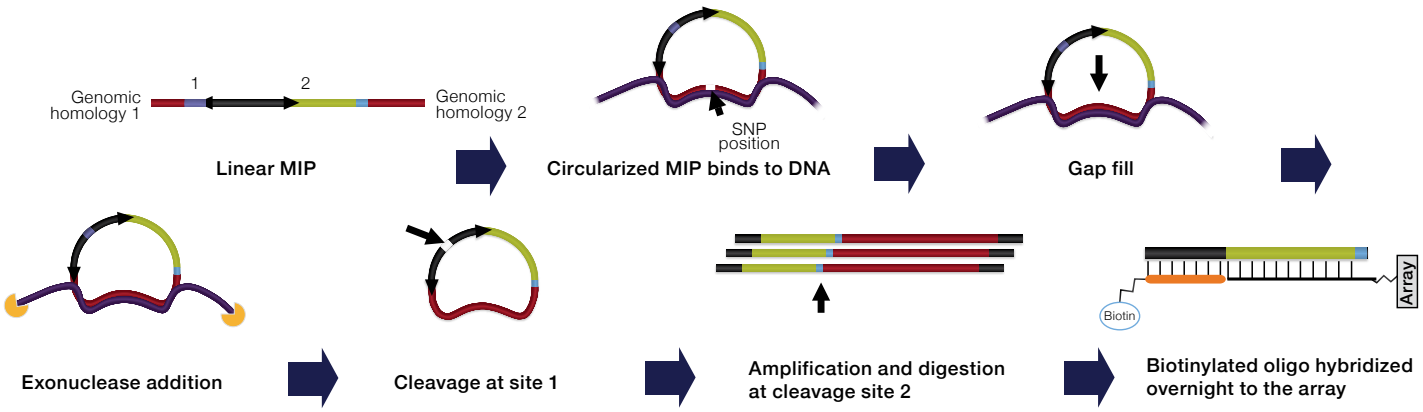
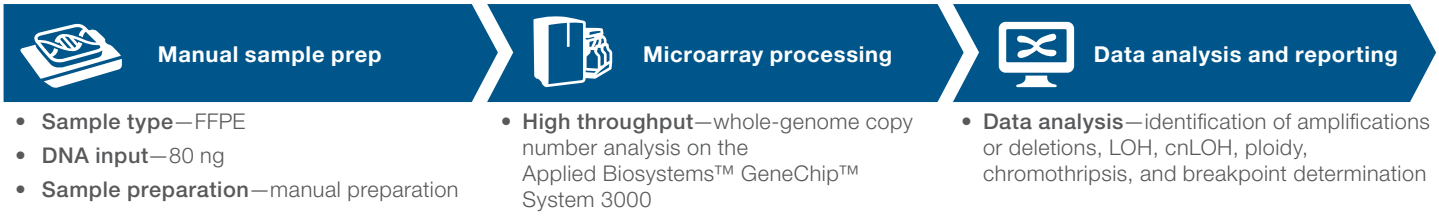


Figure 1. Overview of MIP technology.



- **Sample type**—FFPE
- **DNA input**—80 ng
- **Sample preparation**—manual preparation

- **High throughput**—whole-genome copy number analysis on the Applied Biosystems™ GeneChip™ System 3000

- **Data analysis**—identification of amplifications or deletions, LOH, cnLOH, ploidy, chromothripsis, and breakpoint determination

Figure 2. The workflows of OncoScan CNV and CNV Plus Assays enable detection and analysis of CN changes in solid tumors in as few as 3 days.

OncoScan CNV and CNV Plus Assays:

- **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 an SM panel covering 64 mutations in 9 genes (Figure 3)

OncoScan CNV and CNV Plus Assays provide:

- **Exceptional flexibility**—detect chromosomal arm aberrations, gains, losses, focal changes, LOH, and cnLOH in a single assay, helping reduce costs and processing times
- **Comprehensive coverage**—whole-genome analysis with the latest content genes with established significance in cancer and tumor progression, as well as those with emerging evidence of significance
- **Robust performance**—obtain consistent results from lot to lot and operator to operator
- **A broad SM panel**—covering 64 mutations in 9 genes (*BRAF*, *EGFR*, *IDH1*, *IDH2*, *KRAS*, *NRAS*, *PIK3CA*, *PTEN*, and *TP53*)
- **Low sample input and fast results**—get results in as few as 2 days from only 80 ng of FFPE-derived DNA
- **Rapid analysis**—included software provides intuitive data visualization for hundreds of samples in minutes
- **Evidence-based database development**—link evidence with observations for internal database management and expansion
- **The OncoScan CNV Plus Assay offers high-resolution CN detection in priority cancer genes**—accurate identification of very small (50–125 kb) to large (Mbs) CNVs

Chromosome Analysis Suite (ChAS) software

View and analyze chromosomal aberrations across the genome, including CN gain or loss, LOH, mosaicism, and clonality. Developed with input from our customers and leading professionals, Applied Biosystems™ Chromosome Analysis Suite (ChAS) software is designed specifically for analysis and reporting in chromosomal aberration research. Enhanced, intuitive features help simplify cytogenetic investigation.

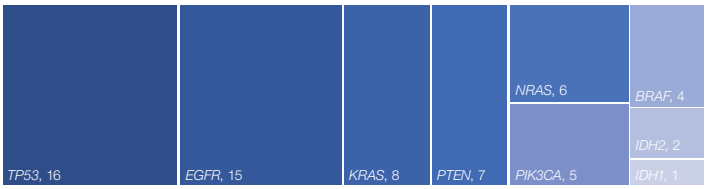


Figure 3. Somatic gene panel representing the number of SMs by genes detected by the OncoScan CNV Plus Assay.

Table 2. One assay, many powerful data types. Enable genome-wide CN and LOH analysis at high resolution on cancer genes, all with a single assay.

	OncoScan CNV and CNV Plus* Assays
Research application	High resolution analysis, up to 50 kb in ~900 cancer genes and 300 kb across the whole genome in FFPE and fresh frozen tissues
Sample types	FFPE, fresh and frozen tissue
Size of aberration (analytical claims)**	• Gains: 50 kb • Losses: 50 kb • LOH/absence of heterozygosity (AOH): 10 Mb • Mosaicism (% aberrant cells): 15% • High dynamic range of 10-plus copies
Input DNA	80 ng
Probe structure	• 220,000 MIPs for whole-genome coverage • 5,700 nonpolymorphic probes • 216,000 SNP probes
Protocol	2–3 days

* The OncoScan CNV Plus Assay includes an SM panel covering 64 mutations in 9 genes (*BRAF*, *EGFR*, *IDH1*, *IDH2*, *KRAS*, *NRAS*, *PIK3CA*, *PTEN*, and *TP53*).
** Size of aberration—the size of the segment call depends on the average marker spacing in the region. The best performance can be achieved in regions with higher marker coverage. Mosaicism detection may depend on the size of the altered segment and the type of aberration involved.

ChAS software:

- Provides CN in $\log_2$ and in linear scale
- Identifies diploid regions algorithmically, then uses the data to center $\log_2$ ratios
- Identifies LOH regions, including regions of cnLOH
- Estimates for the percentage of aberrant cells in a sample and estimates the CN change in just the aberrant cell population
- B-allele frequency (BAF) view visualizes CN gains and losses, and detects LOH, including cnLOH (Figure 4)
- Karyoview is a whole genome view, where you can compare samples (Figure 5)
- Uses the chromosome to zoom in to probe-level information
- Evaluates CN aberrations in $\log_2$ scale, plus CN calls
- Accesses external data sources such as NCBI, UCSC Genome Browser, and Ensembl™ databases
- Simplifies laboratory information management system (LIMS) management using application programming interfaces (APIs)
- Finds segment coordinates; coordinates can be exported and imported using APIs to accompany ChAS software
- Automates file generation for results with zero manual setup required

Multi-sample viewer (MSV)

Load samples from ChAS software into multi-sample viewer (MSV) software to visualize cohorts of samples simultaneously (Figure 6).

MSV software:

- Visualizes aggregate CN gains and losses across a sample cohort
- Compares samples in groups, enabling the analysis of differences and similarities in gains and losses between groups (e.g., tumor/normal)

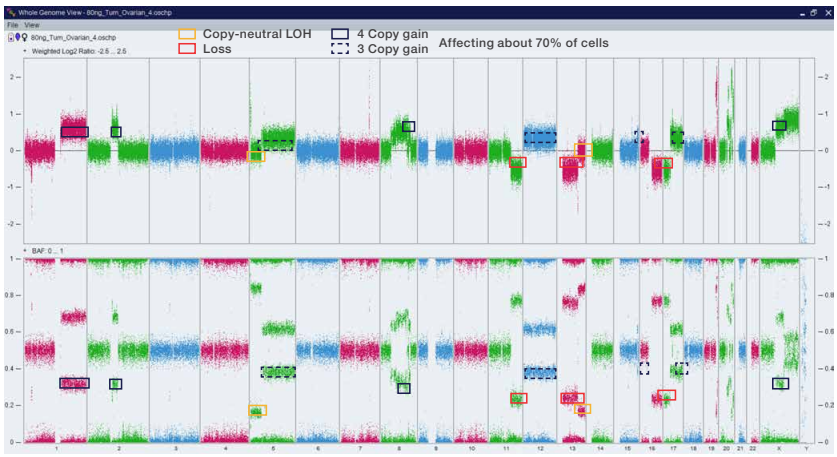


Figure 4. OncoScan CNV Assay data presented in $\log_2$ ratio and BAF view in ChAS software. Shown here are cnLOH (yellow squares), CN loss (red squares), and CN gain (dark purple squares with solid or dotted lines). The top view shows the log ratio and the bottom view shows the BAF that enables detection of low-level mosaic gain, loss, and LOH.

Figure 5. 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.

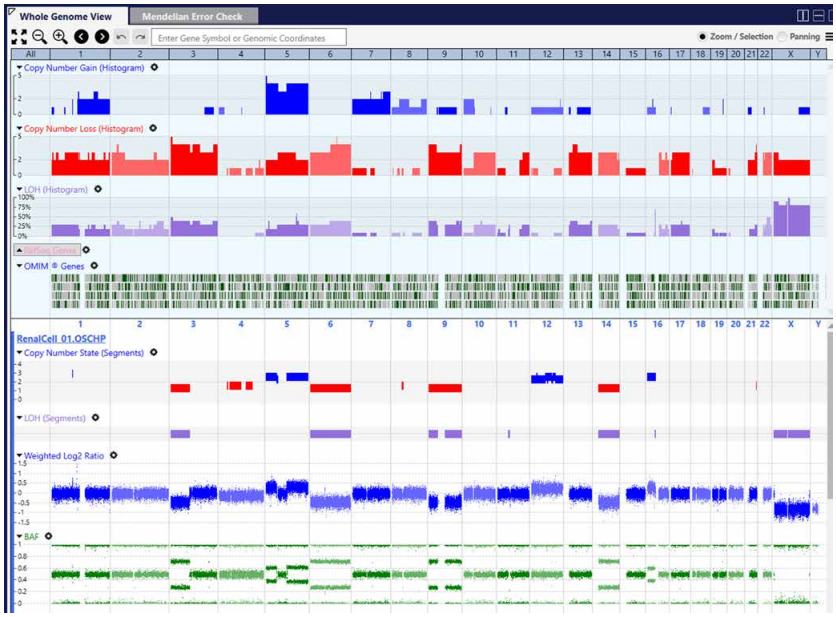


Figure 6. OncoScan CNV Assay data presented in MSV software. Shown here is the detailed karyoview of the genome segments by coordinate in a multi-sample view.

Ordering information

Product	Description	Cat. No.
OncoScan CNV and CNV Plus Assays		
OncoScan CNV Assay	Contains OncoScan CNV Reagent Kit and 48 OncoScan CNV Arrays; sufficient for 24 samples	902695
OncoScan CNV Training Kit	Arrays and reagents sufficient for 18 reactions plus training materials	902693
OncoScan CNV Plus Assay	Contains OncoScan CNV Plus Reagent Kit and 48 OncoScan CNV Plus Arrays; sufficient for 24 samples	902293
OncoScan CNV Plus Training Kit	Arrays and reagents sufficient for 18 reactions plus training materials	902305
GCS3000 OncoScan Training (3 days)	3 days of training; covers instrument operation, assay technique, and data analysis	000.878
Analysis software		
ChAS software	Available as a free download from thermofisher.com/chas	NA
Instrumentation		
GeneChip System 3000	Includes: • GeneChip Scanner 3000 with AutoLoader • GeneChip Fluidics Station 450 • GeneChip Hybridization Oven 645i • Workstation with GeneChip Data Collection Software	00-0218
GeneChip Fluidics Station 450	Single station available for purchase separately from the GeneChip System 3000	00-0079
GeneChip Hybridization Oven 645i	Single unit available for purchase separately from the GeneChip System 3000	00-0331

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5. Togneri FS et al. (2016) Genomic complexity of urothelial bladder cancer revealed in urinary cfDNA. *Eur J Hum Genet* 24(8):1167-74.

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