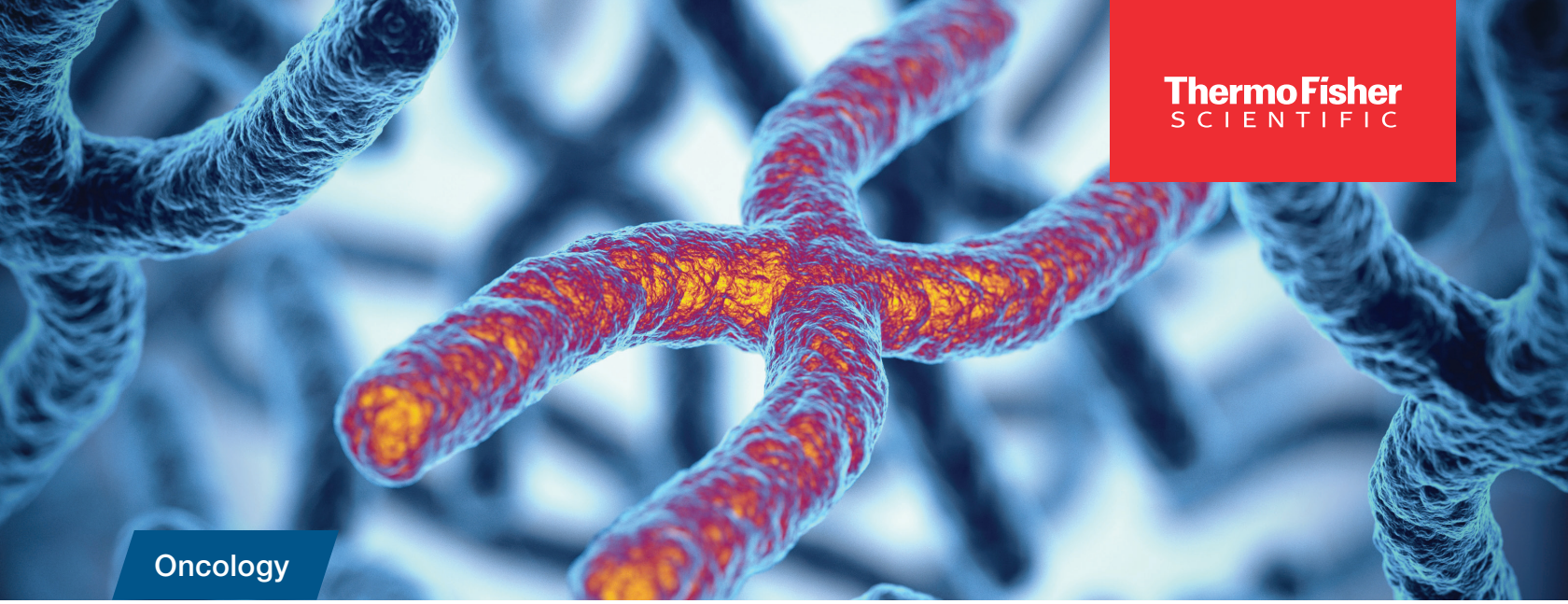

Oncology

OncoScan CNV and CNV Plus Assays for research

Catch critical copy number changes

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. 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%

Accurately identify solid tumor CN biomarkers

CN-based cancer biomarkers have important and predictive value. The Applied Biosystems™ OncoScan™ CNV and CNV Plus Assays for research are the only tools capable of accurately identifying CN changes and allelic imbalances, including loss of heterozygosity (LOH), copy-neutral LOH (cnLOH), and chromothripsis 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 64 mutations in 9 genes (Figure 1)

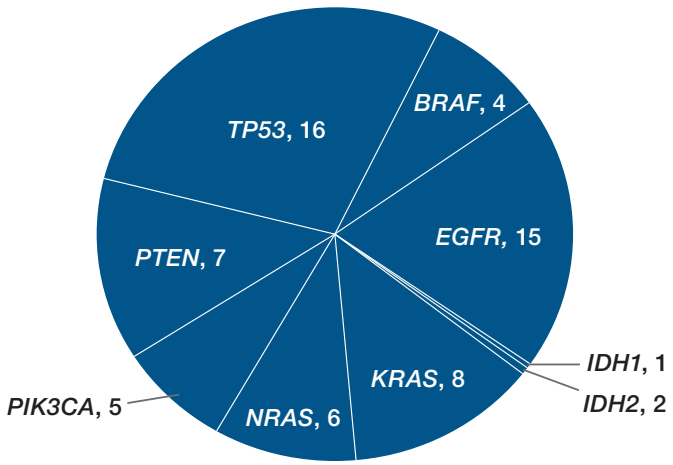

Figure 1. Somatic gene panel representing the number of somatic mutations by genes detected by the OncoScan CNV Plus Assay.

applied biosystems

OncoScan CNV assays not only provide whole-genome coverage, but also have enriched SNP and CN content for over 900 cancer-related genes—the molecular cytogenetic changes that are most commonly seen in cancers. Because these assays use molecular inversion probe (MIP) technology (Figure 2), they 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. Results are provided in just three days (Figure 3), which makes the assay a natural choice in cancer research.

OncoScan CNV 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 and those with emerging evidence, thus helping to reduce future re-verification burden
- **All-in-one assay**—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**—go from sample to answer, including data analysis, in just 3 days, using only 80 ng of FFPE-derived DNA

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.

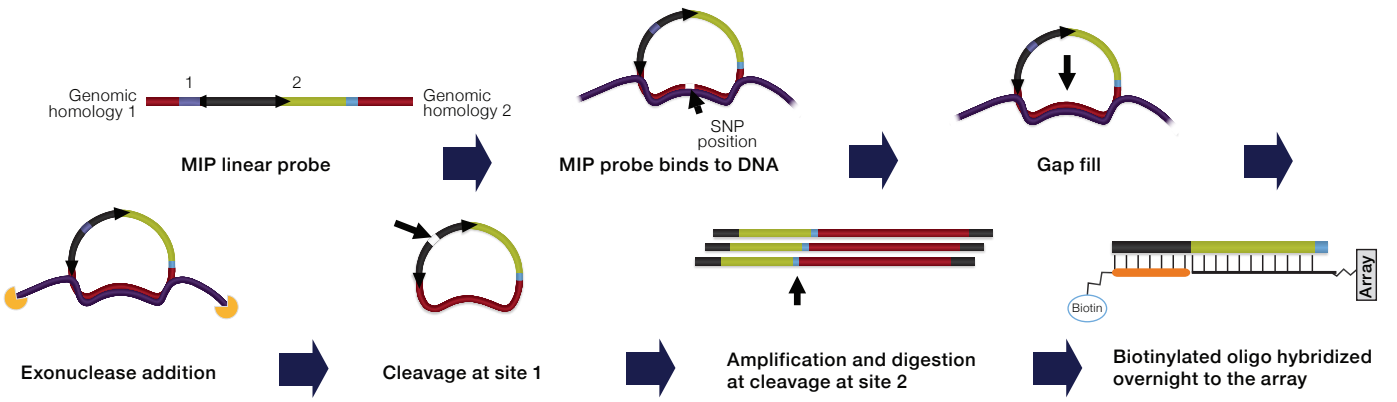

Figure 2. Overview of MIP technology.

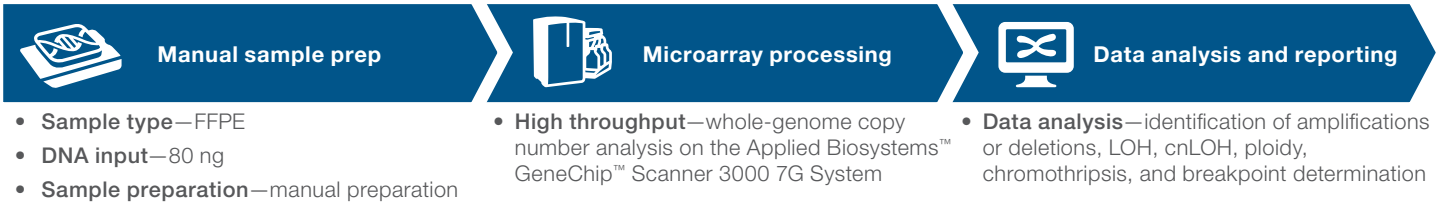

Figure 3. The OncoScan CNV and CNV Plus Assay workflows enable detection and analysis of copy number changes in solid tumors in as little as 3 days.

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. Thus, ChAS software facilitates analysis of CN changes and SMs in low- to high-throughput studies that utilize OncoScan CNV assays, in a single software package. Figures 4 and 5 show example data viewed in ChAS software.

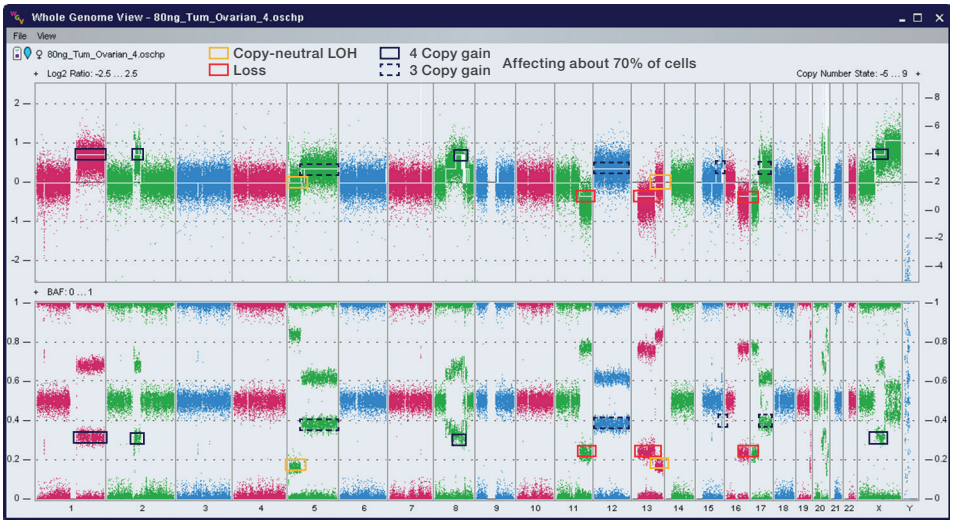

Figure 4. OncoScan CNV Assay data presented in log_2 ratio and b-allele frequency (BAF) view in ChAS software. Shown here are cnLOH (yellow squares), CN loss (red squares), and CN gain (dark purple squares with solid or dotted lines). The top view shows the log ratio and the bottom view shows the BAF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

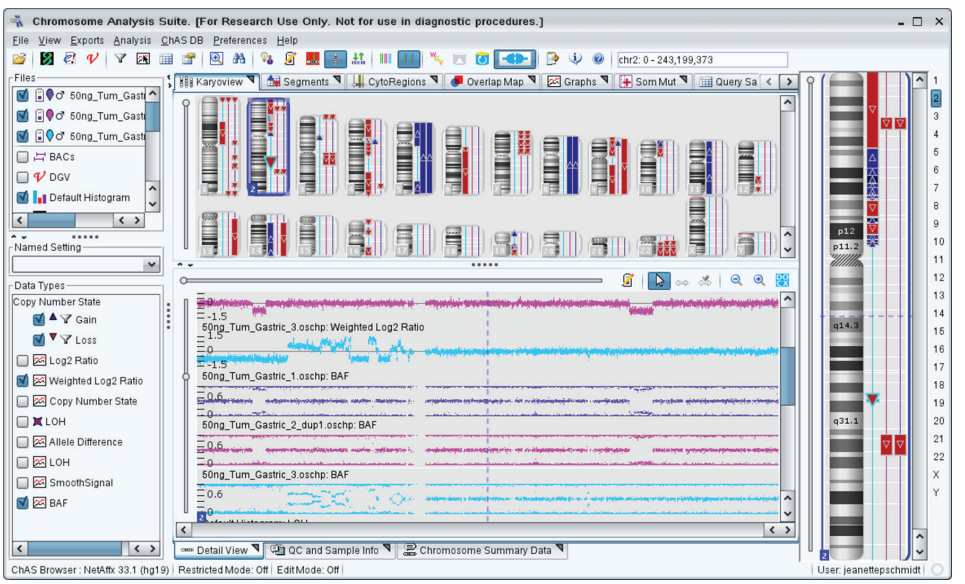

Figure 5. OncoScan CNV Assay data presented in karyoview in ChAS software. Shown here is the whole-genome visualization and ability to compare data from three samples (where each vertical line next to the chromosome represents one sample). CN gains are shown in blue and CN losses are shown in red.

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

* For Research Use Only. Not for diagnostic use.

Reference

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

Learn more at **thermofisher.com/oncoscan**