

The Affymetrix® Solution for Molecular Cytogenetics



CONFIDENCE
ACCURACY
PRECISION

**The SNP Array 6.0, the Cytogenetics Copy
Number Assay and Genotyping Console**



The Affymetrix® Solution for Cytogenetics

The Affymetrix® solution for cytogenetics enables cytogeneticists to achieve the highest “diagnostic potential” with a simple solution and rapid results. The solution—which includes the Affymetrix® Genome-Wide Human SNP Array 6.0, an optimized assay and state-of-the-art software—is the preferred microarray platform for cytogenetics labs.

The Affymetrix solution enables you to see chromosomal aberrations at an unprecedented resolution and detect uniparental disomies (UPDs) on a single array.

Power your cytogenetics study with the most comprehensive solution currently available, and the technology that’s revolutionizing the field of cytogenetics.

The Affymetrix Solution for Cytogenetics Includes:

- The high-density SNP Array 6.0, with 1.8 million markers evenly distributed across the whole genome
- Simple cytogenetics copy number assay
- Intuitive Genotyping Console software

Benefits of the Affymetrix Solution for Cytogenetics:

- Whole-genome coverage, including subtelomeric regions and pericentromeres
- Confident and accurate detection of small gains and losses
- Precise determination of breakpoints to unequivocally determine which genes are affected
- Identification of UPDs (copy number-neutral LOH)
- Easy, three-day assay
- Simple software tool that summarizes all aberrations detected



■ Applying Microarrays to Cytogenetics

The Affymetrix solution for cytogenetics is easy, even if you're new to microarray-based studies. The process requires only two primary steps: preparing the DNA for the microarray using the cytogenetics copy number assay, and analyzing the data using Genotyping Console.

As little as 500 ng of genomic DNA is required, and a clearly marked, pictorial manual will take you through the three-day assay from purified DNA to array data. Genotyping Console then makes it easy to move from data to results. All detected copy number changes are summarized in a Segment Report and displayed visually in a familiar Karyoview.

Genotyping Console's Chromosome View provides a closer view of these aberrations, by aligning copy number and LOH with annotated genes, CNVs, FISH clones and any customized tracks. Within this single view, you'll be able to determine which genes are affected by the aberration, whether or not this region overlaps known CNVs and which FISH clones may be used for confirmation if desired.



Figure1a: Illustration of a 419 kb deletion on Xp21.1 containing 372 markers.

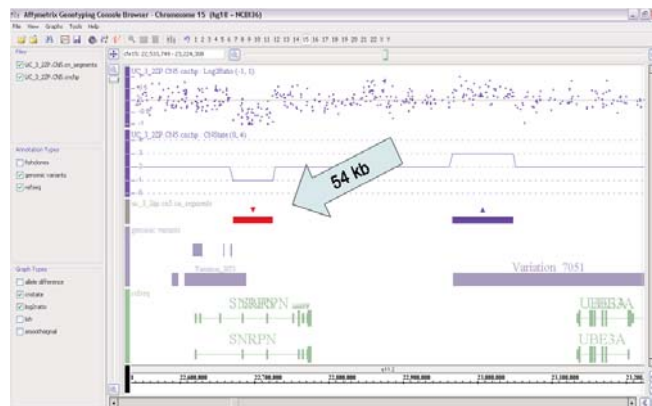


Figure1b: Illustration of a 54 kb deletion (on SNP Array 6.0) which was previously FISH confirmed. This example shows the high resolution of the Affymetrix platform and the benefit of providing the segment and annotation tracks in the same view.

The SNP Array 6.0: Ideal for Cytogenetic Studies

One Array, Multiple Applications

The SNP Array 6.0 measures copy number, allele-specific copy number and copy number-neutral LOH. The array contains more than 1.8 million markers evenly distributed across the entire genome, allowing the detection of small gains and losses. Of these probes, 906,600 target SNPs, and the remaining 945,826 target non-polymorphic sequences. Both types of probes are used to detect copy number changes, and the probes targeting SNPs are also used for measuring UPDs and consanguinity.

Copy Number Resolution

With an intermarker spacing of 696 base pairs, the SNP Array 6.0 offers the highest resolution of copy number changes. This array will enable you to detect even the smallest changes with confidence and fine-map the breakpoints of observed aberrations.

Copy Number-neutral LOH

Copy number-neutral LOH can expose important recessive mutations and regions affected by imprinting. The SNP Array 6.0 measures sequence within the polymorphic regions to derive allelic information. Even if the copy number within a chromosomal region is normal, the sequences could still be severely abnormal. This can only be determined by also looking at the sequence, which the SNP Array 6.0 is uniquely able to measure. This information is then used to uncover UPDs.

Allele-specific Copy Number

Imprinting leads to the differential expression of genes. Depending on whether they were inherited maternally or paternally, allele-specific copy number can determine the parent of origin and indicate if the gain is associated with allelic loss or retention.

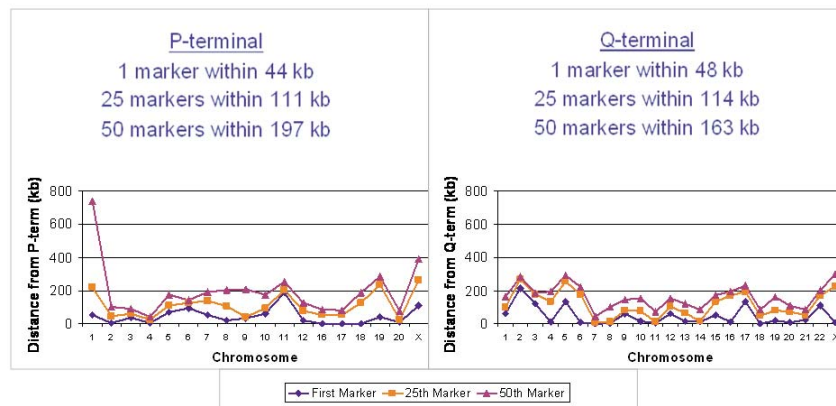


Figure 2: Subtelomeric coverage of SNP Array 6.0 markers across all chromosomes.

Two Experiments in One

Affymetrix SNP arrays provide genotype and allow the detection of copy number-neutral LOH, which enables:

- Detection of UPD
- Paternity confirmation
- Parent-of-origin analysis (for UPD and deletions)
- Homozygosity mapping
- Determination of consanguinity

The following events cannot be detected when looking at copy number alone:

- 30% of Prader-Willi = pUPD of 15q
- 2-3% of Angelman Syndrome = mUPD of 15q
- 10-30% of Beckwith-Wiedemann Syndrome = mUPD of 11p15
- 5% of Silver-Russell Syndrome = mUPD of chr7
- UPD of chromosome 14 is known to cause distinct disorders

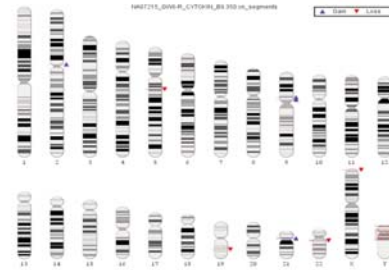


Figure 3: This figure highlights the SNP Array 6.0's ability to measure structural changes (copy number) and sequence variations (UPD) across the entire genome. Regions of LOH greater than 3 Mb are summarized in the red block. The LOH region is copy number neutral, as illustrated by the blue data points of \log_2 ratios and copy number state. This entire chromosome would be considered structurally normal, yet it is severely abnormal from a sequence perspective.

■ Highlights of Genotyping Console

Whole-genome View

- Software Karyoview designed for intuitive visualization
- High-level view of chromosomal aberrations, sizes and locations across the genome



Chromosome View

- Displays copy number, LOH and allelic differences and annotations in one view
- Enables you to visualize single or multiple samples at the same time
- Annotation tracks for genes, CNVs, BAC/FISH, custom tracks, etc.
- Link directly from Genotyping Console to UCSC, Ensembl and Toronto databases



Segment Report

- Summary of all regions exhibiting copy number change or LOH
- User-defined threshold for size and number of markers required to report segment
- Report includes location, copy number, size, number of markers and overlap with known CNVs

Custom Region Functionality

- Complete segment summarization is provided for user defined regions
- Allows for focused analysis and reporting only on the selected regions of interest
- Enables unlimited customization of cytogenetics relevant regions

■ Taking the Path to Diagnostics

Affymetrix is working to create products for cytogenetics that can be used in diagnostic settings. Affymetrix has already manufactured FDA-approved arrays and equipment, and all Affymetrix arrays are manufactured in a GMP-compliant facility and packaged in individual cartridges. In addition, the Affymetrix Clinical Services Lab (ACSL) is CLIA certified to support the development of diagnostic products, clinical trials and more.

For your cytogenetics projects, use the platform that has demonstrated its commitment to providing diagnostic tools. Use the Affymetrix solution for cytogenetics—created with you and your needs in mind.

Ordering Information

| Description | Part Number |
|--|-------------|
| Affymetrix® Genome-Wide Human SNP Array 6.0 | |
| 5 arrays | 901182 |
| 50 arrays | 901153 |
| 100 arrays | 901150 |
| Affymetrix® Genome-Wide Human SNP Nsp/Sty Assay Kit 5.0/6.0 | |
| 30 reactions | 901013 |
| User's Guide, Affymetrix® Cytogenetics Copy Number | 702607 |

Please visit our web site, www.affymetrix.com, for additional ordering information.

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