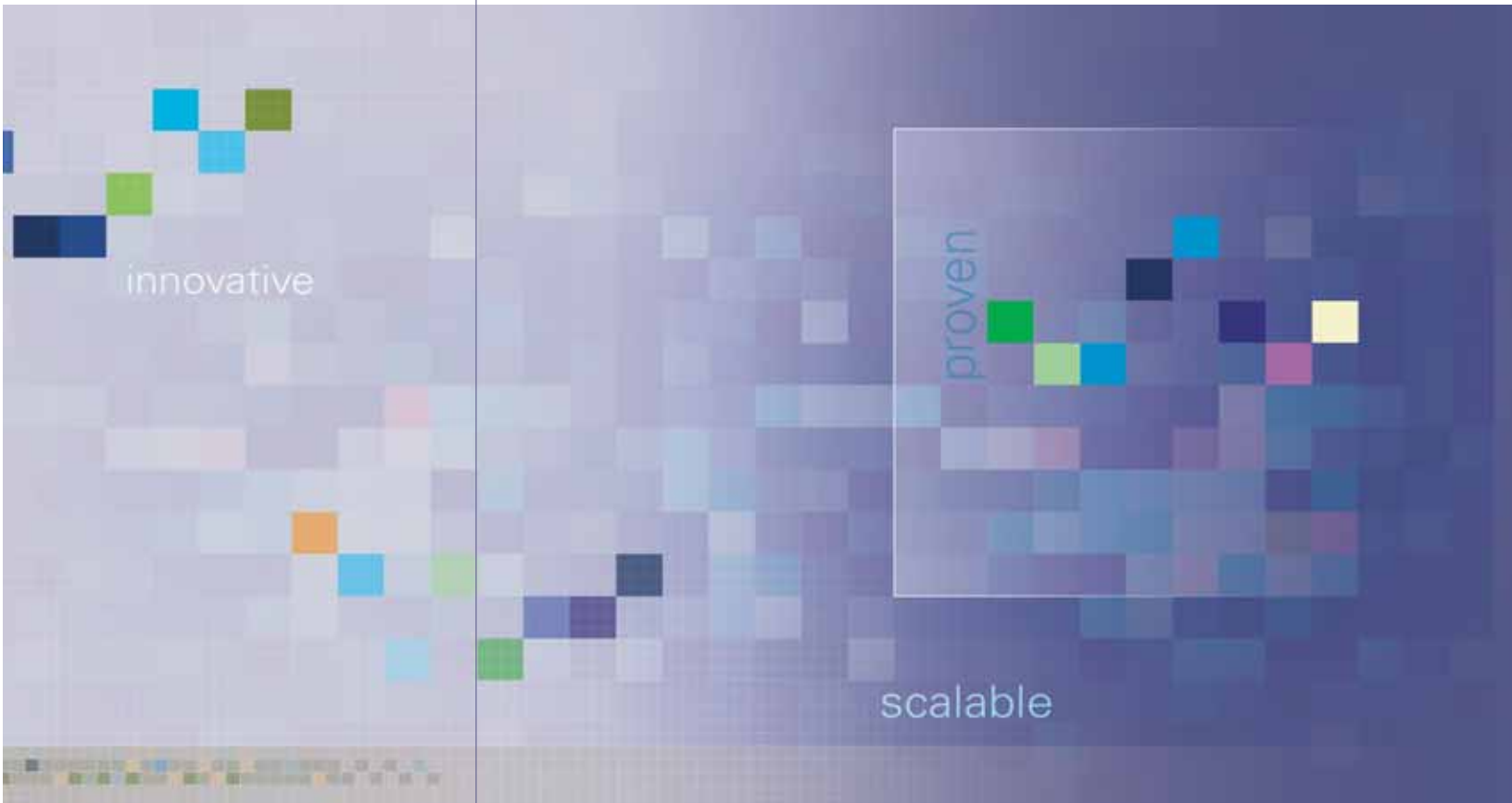


DNA Analysis with the GeneChip® System



From DNA to Discovery

Translating the genome into knowledge about human biology is a challenging task. The breathtaking speed of scientific discoveries and the current competitive research environment require **more information from every experiment**. In order to keep pace with these demands, scientists need more powerful and flexible solutions that provide a **comprehensive view of the genome**.

Proven GeneChip® DNA Analysis products provide the information you need today by enabling you to **access the genome at your benchtop** in ways that were **previously unimaginable**. From population genetics to disease genetics to pharmacogenomics, GeneChip DNA Analysis products provide the **throughput, accuracy, and reliability** you can count on.

Standard and custom arrays, assays, and software **address the entire genetic workflow** from whole-genome association studies to custom genotyping and resequencing. To **correlate biological function with genetic discoveries**, genotyping and resequencing data can be rapidly followed up with expression analysis on the GeneChip System.

The reliability, affordability, and ease of use of GeneChip genotyping and resequencing arrays are driving a revolution in DNA Analysis. GeneChip DNA Analysis products provide more than just highly accurate data—Be the 1 to **shorten the distance between DNA and discovery**.



Experimental Workflow for Genetic Analysis

Whole-Genome Scans

- GeneChip® Mapping 500K Array Set
- GeneChip® Human Mapping 100K Set
- GeneChip® Human Mapping 10K 2.0 Array



Applications:

- Whole-genome association studies
- Chromosomal copy number analysis
- Linkage analysis
- Population genetics

Experimental Requirements:

- Scalable solution for genotyping hundreds of thousands of markers
- Proven, easy-to-use, and reliable assay
- Smaller amounts of DNA starting material
- Cost-effective solutions that fit your budget

Custom Genotyping Solutions

- GeneChip® Universal Tag Arrays
- Custom and Application-Specific Assays
- Genotyping Services



Applications:

- Fine mapping of SNPs in candidate genes or regions
- Supplement whole-genome scans with cSNPs or custom SNPs
- SNP-typing for agricultural and other non-human applications

Experimental Requirements:

- Thousands to tens of thousands of SNPs
- Flexible SNP content
- Enables multiplex analysis of thousands of SNPs in a single assay panel
- High conversion rate



▣▣ Resequencing

- GeneChip® CustomSeq™ Resequencing Arrays



Applications:

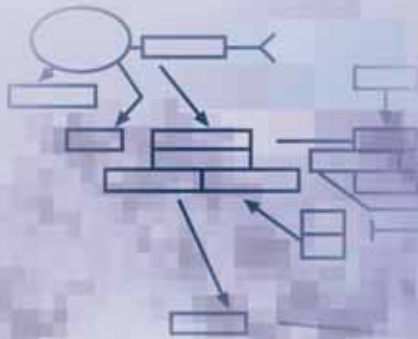
- Comprehensive resequencing of small genomes
- Identification of causative SNPs
- Comparative sequencing of candidate regions

Experimental Requirements:

- Efficient and cost-effective method for sequencing large amounts of DNA
- Data analysis solutions that reduce assembly time
- Flexibility to analyze both large contiguous and non-contiguous regions

▣▣ Functional Analysis

- GeneChip® Expression and Tiling Arrays
- NetAffx™ Analysis Center and Integrated Genome Browser



Applications:

- Correlation of molecular phenotype with genotype
- Whole-genome analysis of gene expression and splicing events
- Chromatin immunoprecipitation experiments
- Gene interactions of complex networks and pathways

Experimental Requirements:

- Visualize multiple types of genetic data together
- Genome-wide expression analysis of all known exons
- High-resolution tiling arrays to identify novel transcripts and DNA-protein interactions
- Extensive annotation of genes and markers



Enabling Genome Discovery

GeneChip® DNA Analysis Platform



- From whole-genome scans to focused genotyping and resequencing experiments, GeneChip® DNA products provide the most rapid, accurate, and cost-effective analysis.
- Access a growing suite of automated applications.
- Flexible platform configurations support benchtop studies as well as production scale research.
- Correlate genetic information with biological function using a single, integrated platform for both RNA and DNA analysis.

GeneChip® Human Mapping Arrays and Assays



- Proven assay with over 50 publications in 2 years, scales from tens to hundreds of thousands of SNPs.
- GeneChip® Mapping 500K Array Set – highly powered whole-genome association today.
- Mapping 100K Set – copy number and allele-specific information from a single experiment.
- Mapping 10K 2.0 Array – identify genes without fine mapping in linkage studies.
- Only 250 ng of DNA are required per array.



Custom Genotyping Products and Services

GeneChip® CustomSeq™ Resequencing Arrays



- Highly multiplexed assays based on MIP technology detected on GeneChip® Universal Tag Arrays.
- 1,500 to 20,000 SNP custom genotyping assays provide a robust and cost-effective method for genotyping SNPs.
- Disease/application-specific SNP panels such as Immune-Inflammation & non-synonymous cSNPs.
- For researchers interested in outsourcing, Affymetrix provides custom services for a wide range of genetic analysis applications.

- Efficient and cost-effective large-scale resequencing of haploid organisms.
- Completed sequence with minimal PCR and sequence alignment in 48 hours.
- Flexible custom options containing up to 300 kb of unique sequence.
- Whole-genome variation analysis of small genomes or targeted resequencing of genic regions.



■ ■ The Proof is in the Publication

Many systems claim to provide accurate results, but the **true test** of a DNA analysis platform is whether it delivers **biologically meaningful results** that stand up to scientific rigor and scrutiny. When it comes to choosing a system that will advance your research, **the proof is in the publication.**

■ Genotyping Technology

Large-scale genotyping of complex DNA Kennedy G.C., *et al. Nature Biotechnology* **21**: 1233–1237, 2003.

Algorithms for large-scale genotyping microarrays Liu W.M., *et al. Bioinformatics* **19**: 2397–2403, 2003.

Genotyping over 100,000 SNPs on a Pair of Oligonucleotide Arrays Matsuzaki H., *et al. Nature Methods* **1**: 109–1110, 2004.

Highly multiplexed molecular inversion probe genotyping: Over 10,000 targeted SNPs genotyped in a single tube assay Hardenbol, *et al. Genome Research* **15**: 269–275, 2005.

Multiplexed genotyping with sequence-tagged molecular inversion probes Hardenbol P., *et al. Nature Biotechnology* **21**(6): 673–8, 2003.

■ Linkage Analysis

Genome wide linkage analysis of bipolar disorder using high-density single nucleotide polymorphism (SNP) genotyping assay: A comparison with microsatellite markers and the finding of significant linkage to chromosome 6q22 Middleton F.A., *et al. American Journal of Human Genetics* **5**: 886–97, 2004.

Mapping of sudden infant death with dysgenesis of the testes syndrome (SIDDT) by a high-density SNP genome scan and identification of TSPYL loss of function Puffenberger E., *et al. PNAS* **101**(32): 11689–94, 2004.

Mutations in VPS33B, encoding a regulator of SNARE-dependent membrane fusion, cause arthrogryposis-renal dysfunction-cholestasis (ARC) syndrome Gissen P., *et al. Nat Genet* **36**(4):400–4, 2004. (Epub 2004 Mar 28).

Mutations in RDH12 encoding a photoreceptor cell retinol dehydrogenase cause childhood-onset severe retinal dystrophy Janecke A., *et al. Nature Genetics* **36**(8): 850–4, 2004.

■ Whole-Genome Association

Complement factor H polymorphism in age-related macular degeneration Klein, *et al. Science* **308**(5720): 385–9, 2005 Apr 15.

Localization of cancer susceptibility genes by genome-wide single-nucleotide polymorphism linkage-disequilibrium mapping Mitra, *et al. Cancer Res* **64**(21): 8116–25, 2004 Nov 1.

Genome-wide association study in esophageal cancer using GeneChip® Mapping 10K Array Hu, *et al. Cancer Res* **65**(7): 2542–6, 2005 Apr 1.

Association of the HLA region with multiple sclerosis as confirmed by a genome screen using >10,000 SNPs on DNA chips Godde, *et al. J Mol Med* **83**(6): 486–94, 2005 Jun.



■ Resequencing Technology

Microarray-based resequencing of multiple *Bacillus anthracis* isolates Zwick, *et al. Genome Biol* **6**(1): R10, 2005. Epub 2004 Dec 17.

Sequencing arrays for screening multiple genes associated with early-onset human retinal degenerations on a high-throughput platform Mandal MN, *et al. Invest Ophthalmol Vis Sci* **46**(9): 3355-62, 2005 Sep.

The Human MitoChip: A high-throughput sequencing microarray for mitochondrial mutation detection Maitra A., *et al. Genomic Research* **14**(5): 812-9, 2004.

The MLH1 D132H variant is associated with susceptibility to sporadic colorectal cancer Lipkin S., *et al. Nature Genetics* **36**(7): 694-699, 2004.

High-throughput variation detection and genotyping using microarrays Cutler D.J., *et al. Genome Research* **11**(11): 1913-25, 2001.

■ Copy Number Analysis

Homozygous Deletions and Chromosome Amplifications in Human Lung Carcinomas Revealed by Single Nucleotide Polymorphism Array Analysis Zhao X., *et al. Cancer Res* **65**(13): July 1, 2005.

Integrative genomic analyses identify MITF as a lineage survival oncogene amplified in malignant melanoma Garraway, *et al. Nature* **436**(7047): 117-22, 2005 Jul 7.

Genomic Alterations in Cultured Human Embryonic Stem Cells Maitra, *et al. Nature Genetics* 2005 Sep 4.

Whole genome SNP arrays using DNA derived from formalin-fixed, paraffin-embedded ovarian tumor tissue Thompson ER, *et al. Hum Mutat* **26**(4): 384-9, 2005 Oct.

Genome-wide loss of heterozygosity analysis from laser capture micro-dissected prostate cancer using single nucleotide polymorphic allele (SNP) arrays and a novel bioinformatics platform dChipSNP Lieberfarb M.E., *et al. Cancer Research* **63**: 4781-4785, 2003.

Loss of heterozygosity and its correlation with expression profiles in subclasses of invasive breast cancers Wang Z.C., *et al. Cancer Research* **64**: 64-71, 2004.

High-resolution single nucleotide polymorphism array and clustering analysis of loss of heterozygosity in human lung cancer cell lines Janne P.A., *et al. Oncogene* **23**(15):2716-26, 2004 April 8.

■ Population Genetics

Large-scale SNP analysis reveals clustered and continuous patterns of human genetic variation Shriver, *et al. Hum Genomics* **2**(2):81-89, 2005.



■ ■ Be the 1

The future of genomics promises to deliver better therapies, provide early intervention, and create personalized treatments based on DNA sequence and gene expression data. By enabling you to **find things you could never find before in places you could never look before**, GeneChip DNA Analysis products provide the precise information you need to translate genomic information into a **functional understanding of health and disease**. This process of integrating data from genotyping, resequencing, and expression studies can identify important genetic **mechanisms that drive biological events**.

In the short time since the introduction of its first mapping array, Affymetrix has increased the number of SNPs on array sets from 10,000 to more than 500,000, enabling researchers to open the freezer and **conduct large-scale association studies**. Furthermore, this scaling up of the number of SNPs that can be analyzed in a single experiment is just the beginning. Affymetrix is committed to advancing translational medicine by validating ever increasing numbers of SNPs coupled with varied content for **higher power association studies**. Affymetrix' merger with ParAllele and partnership with Perlegen are resulting in flexible genotyping options and novel genetic applications that will advance our understanding of the code of life. **Be the 1 to turn yesterday's vision into today's discovery.**



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