AFFYMETRIX®

Data Sheet

GeneChip® Human Mapping 100K Set

The GeneChip® Mapping 100K Set is the first in a family of products for whole-genome association studies. It is comprised of a set of two arrays which enable genotyping of greater than 100,000 SNPs with a single primer. The high throughput and ease of use of the Mapping 100K Set at a cost of one cent per SNP enable whole-genome association studies at the benchtop for the first time. The Mapping 100K Set can be used for many applications, including cancer genetics, linkage disequilibrium, case-control and family-based association studies, chromosomal copy number change analysis, and population genetics.

Approximately half of the SNPs on the Mapping 100K are from public databases while half are from the SNP database created by Perlegen Sciences, Inc. SNPs on the new 100K Set are freely available in the dbSNP Database.

The proven GeneChip® Mapping Assay, which was validated in over 15 publications in the year since its launch, is also used with the Mapping 100K Set.

Introduction

The GeneChip® Mapping 100K Set is the first in a family of products for association studies. It uses the same proven technology as the GeneChip Mapping 10K Array and enables researchers to generate 100,000 genotypes with the easy-to-use, one-primer Mapping Assay, which has been validated in over 15 published studies.

The Mapping 100K Set is comprised of two arrays, each with greater than 50,000 SNPs. One array uses the XbaI restriction enzyme, while the second uses HindIII. Together, the family of GeneChip Mapping products offers researchers solutions for genotyping 10,000, 50,000, or 100,000 SNPs for a variety of applications, including linkage and association studies, as well as cancer and population genetics.

PROVEN ASSAY

The GeneChip Mapping Assay for the Mapping 100K Set builds on the proven and simple approach for reducing complexity of the genome that is employed by the GeneChip Mapping 10K Array.

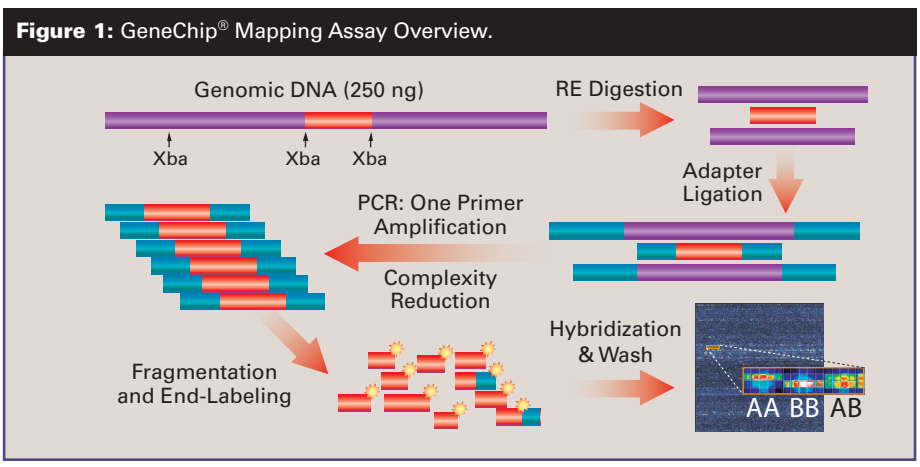
Total genomic DNA (250 ng) is digested with a restriction enzyme (XbaI or HindIII) and ligated to adapters that recognize the cohesive four basepair (bp) overhangs. All fragments resulting from restriction enzyme digestion, regardless of size, are substrates for adapter ligation. A generic primer that recognizes the adapter sequence is used to amplify adapter ligated DNA fragments. PCR conditions have been optimized to preferentially amplify fragments in the 250 to 2,000 bp size range. The amplified DNA is then fragmented, labeled, and hybridized to the GeneChip Mapping 100K Set.

SNP SELECTION AND GENOME COVERAGE

Approximately half of the SNPs on the Mapping 100K Set are from the public domain, while the other half are from the SNP database discovered by Perlegen Sciences, Inc.

All SNPs on the GeneChip Mapping

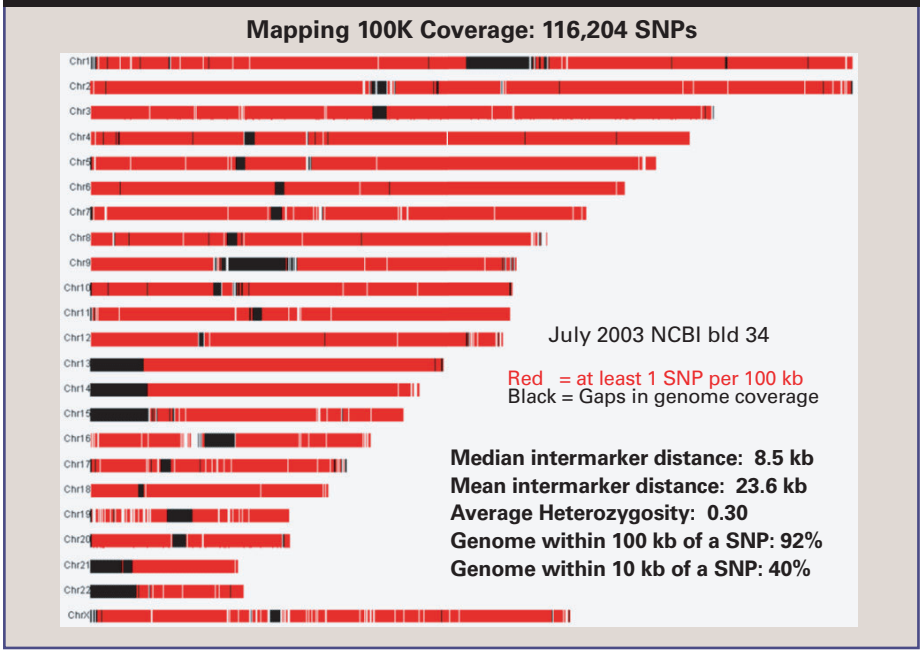
Figure 1: GeneChip® Mapping Assay Overview.



100K Set went through a rigorous screening and validation process. The optimal SNPs in this group were selected based on accuracy, call rate, and physical distribution across the genome. The median physical distance between SNPs is 8.5 kb and the average distance between SNPs is 23.6 kb. The average heterozygosity of these SNPs is 0.30.

The Mapping 100K Set provides broad coverage of the human genome: 92 percent of the genome is within 100 kb of a SNP, 83 percent of the genome is within 50 kb of a SNP, and 40 percent of the genome is within 10 kb of a SNP. For more information about the SNPs on the arrays, please visit the NetAffx™ Analysis Center.

Figure 2: Genome Coverage of Mapping 100K SNPs by chromosome. Black areas represent gaps in the human genome sequence, primarily centromeres and telomeres.



100,000 SNPS. FIRST IN A FAMILY FOR ASSOCIATION STUDIES

The Mapping 100K Set allows 100,000 genotypes in a single experiment, enabling researchers to conduct genome-wide studies pertaining to disease genetics, drug response, and linkage disequilibrium. The SNP genome coverage, ease of use of the assay, and cost of less than one cent per SNP now make it possible to begin large-scale linkage analysis and association studies. All of the SNPs used on the Mapping 100K Set have been validated across a wide range of populations and ethnicities. Future products will have complementary sets of SNPs to increase SNP density from 100,000 to over 500,000 SNPs. Customers can expect call rates greater than or equal to 95 percent. Internal validation studies had an average call rate of 99.18 percent over 354 samples.

SNPS FROM PERLEGEN SCIENCES, INC.

Approximately half of the SNP content for the Mapping 100K Set is from the public domain while the other half was acquired from Perlegen Sciences, Inc. In 2001, Perlegen discovered and validated 1.7 million SNPs, by resequencing 50 genomes from 25 people on the Affymetrix platform. Affymetrix has had full access to these SNPs since 2002 for use in Affymetrix products.

USE LESS DNA STARTING MATERIAL

Each array in the GeneChip Mapping 100K Set requires only 250 ng genomic DNA as starting material, making the most of precious sample resources.

HIGHLY ACCURATE AND REPRODUCIBLE

In order to determine the accuracy and reproducibility of the Mapping 100K Set, 30 Caucasian trios were genotyped with four different technologies as part of the HapMap Project. These reference genotypes were used to measure concordance of genotypes generated with the Mapping 100K Set. 13,056 SNPs overlapped between the HapMap public data release #4 and the Mapping 100K Set. Concordance of genotypes generated with the Mapping 100K Set with the reference data was 99.73 percent across greater than 1.1 million genotypes. Mendelian inheritance consistency was measured at 99.97 percent over ten trios. Reproducibility was measured at 99.99 percent when calculated for three different individuals with five replicates each. Genotype calls were made with a confidence score cut off of 0.25 for all of the measurements above.

AUTOMATED GENOTYPE CALLS IN SOFTWARE

The GeneChip Mapping 100K Set is used in conjunction with GeneChip® DNA Analysis Software (GDAS) 3.0, which uses an automated genotype-calling algorithm that provides a confidence score for each individual genotype.

Customers can expect a call rate of greater than or equal to 95 percent when using DNA of reasonable quality. Internal validation studies have demonstrated a call rate of over 99 percent over a variety of populations, including African-American, Asian, and Caucasian.

GDAS 3.0 SUPPORT FAMILY-BASED STUDIES

GDAS 3.0 incorporates advanced functionality that supports family-based studies. Researchers can batch import pedigree and other sample information, check for Mendelian errors, and export the data into MERLIN- or GeneHunter-compatible formats.

ADJUSTABLE ALGORITHM ALLOWS 99% CALL RATES AT 99% ACCURACY

GDAS 3.0 uses a new model based algorithm (called the Dynamic Model), which uses a *p*-value based confidence score to make genotype calls. In a study conducted at Affymetrix, the default value of 0.25 gives a call rate of 99.14 percent for 30 HapMap Trios (90 Caucasian samples). Concordance was 99.73 percent for 13,056 SNPs in common between the Mapping 100K Set and the HapMap public data release #4. The confidence score can be adjusted to allow genotyping with either greater accuracy or higher call rates, depending on what is needed for the application of interest. At a confidence score of 0.4, the experiment above has a call rate of 99.65 with 99.68 concordance. At a confidence score of 0.05, the call rate is 95.96 percent, with 99.77 percent concordance.

GENOTYPE CALLING ALGORITHM CAN DETECT RARE SNPS

The Dynamic Model has the ability to accurately genotype SNPs with minor allele frequencies below five percent, eliminating the need for a pre-existing training set of data.

SNP ANNOTATION AVAILABLE THROUGH THE NETAFFX™ ANALYSIS CENTER

Extensive annotation for each SNP is provided for both GDAS 3.0 and in the NetAffx™ Analysis Center. This annotation combines data from multiple sources within the public domain and consolidates it into a single database, providing a level of standardization that facilitates collaboration and sharing of data. Open access to SNP lists and annotations, as well as to research methods and validation studies, provides researchers with the greatest flexibility in their research, and enables them to troubleshoot results or follow-up genotyping experiments with downstream analyses.

SNP annotation includes TSC ID, dbSNP ID, nearest microsatellite markers, nearest gene, physical map location, cytoband, genetic map location, and allele frequencies in multiple populations.

ARRAY SPECIFICATIONS

Each array in the Mapping 100K Set includes more than 2.5 million features, each consisting of more than one million copies of a 25 bp oligonucleotide probe of a defined sequence, synthesized in parallel by proven photolithographic manufacturing. Each SNP is interrogated by 10 probe quartets where each probe quartet is comprised of a Perfect Match and a Mismatch probe for each allele. In total, there are 40 different 25 bp oligonucleotides per SNP.

NEW APPLICATIONS BUILT FOR THE GENECHIP® 2.0 PLATFORM

The GeneChip Mapping 100K Set runs on the GeneChip® 2.0 Platform and uses the GeneChip® Scanner 3000 with the complimentary High-Resolution Update, the GeneChip® Fluidics Station 450, and GDAS 3.0. The GeneChip Mapping 100K Set is also compatible with the previous generation GeneChip Fluidics Station 400.

REAGENT KITS VALIDATED AS PART OF THE MAPPING 100K SET

Two reagent kits are included with the GeneChip Mapping 100K Set. One kit is specific to the XbaI restriction enzyme while the other is designed for the HindIII restriction enzyme. Both kits contain validated and qualified reagents for the most critical steps in the GeneChip Mapping Assay. This includes the PCR primer and adapter necessary to selectively amplify a portion of the human genome, reagents to fragment and label the PCR products, and several control reagents. The kit was developed and validated during the process of developing the Mapping 100K Set.

REFERENCE GENOMIC DNA SERVES AS A PROCESS CONTROL

Each Assay Kit contains a sample of human genomic DNA to serve as a control for the entire process from DNA to data, as well as for troubleshooting. In addition, Affymetrix provides the consensus genotypes for this sample from nine independent replicates.

BUILT-IN CONTROLS TO CROSS-CHECK FOR CONSISTENCY

Thirty-one SNPs on both the XbaI and HindIII arrays serve as built-in controls for the array set. These controls allow researchers to cross-check genotypes from the same sample on each array to verify that both arrays remain together through array preparation protocols and data analysis.

REAGENT KIT PACKAGING DESIGNED TO MINIMIZE DNA CROSS CONTAMINATION

As with all PCR applications, DNA contamination is a concern, as it can lead to genotyping errors and, therefore, a reduction in genetic power. Each GeneChip Mapping 100K Assay Kit is subdivided into three boxes to support a recommended workflow designed to minimize the possibility of DNA contamination. Additionally, the GDAS 3.0 software provides a report to help identify samples that may have otherwise undetected DNA contamination.

SAMPLE THROUGHPUT

With a standard instrument configuration of one scanner and four fluidics stations with four runs per day, a user can process 3.2 million genotypes per day. The modular GeneChip System can be easily expanded to accommodate high-throughput needs enabling tens of thousands of samples per year. For example, fluidics stations can be daisy-chained together, and GeneChip Scanner 3000s and AutoLoaders can be added to accommodate higher levels of throughput. While the fluidics stations and scanners are centrally controlled by the GeneChip® Operating Software (GCOS) platform, the GCOS Server is also available for moderate- to high-throughput analysis capabilities.

Critical Specifications

Number of SNPs	116,204
Number of Array	2
DNA Required/Array	250 ng
Call Rate	≥95%
Reproducibility	99.96%
Observed HapMap Concordance	99.73%
Average MAF	0.22
Average Heterozygosity	0.30
PCR Primers	1 per sample
PCR Reactions/Array	3 per sample
Percent of Genome Within 100 kb of a SNP	92%
Instrumentation	GeneChip® 2.0 Instrument Platform
Throughput	3.2 million genotypes per day with four GeneChip® Fluidics Stations 450

GeneChip® Mapping 100K Set Components

Adapter, Xba, or Adapter, Hind	Two annealed oligonucleotides specific for ligation to the XbaI or HindIII restriction site.
PCR Primer 001	PCR primer to amplify ligated genomic DNA
Reference Genomic DNA, 103	Human genomic DNA control, with consensus genotypes
GeneChip® Fragmentation Reagent	DNaseI enzyme, formulated to fragment purified PCR amplicons
10X Fragmentation Buffer	Buffer for fragmentation reaction
GeneChip® DNA Labeling Reagent (7.5 mm)	Proprietary biotin-labeled reagent for end-labeling fragmented PCR amplicons
Terminal Deoxynucleotidyl Transferase	Enzyme used to end-label fragmented PCR amplicons with the GeneChip® DNA Labeling Reagent
5X Terminal Deoxynucleotidyl Transferase Buffer	Buffer for labeling reaction
Oligo Control Reagent, 0100	Mixture of five biotin-labeled oligonucleotides, which hybridize to control regions (gridding and array controls) on the GeneChip® Mapping 50K Arrays

Ordering Information

GeneChip® Human Mapping 100K Set and Assay Kit

GeneChip® Human Mapping 50K Array Xba 240

900518 *Contains 30 Mapping 50K Xba Arrays*

GeneChip® Human Mapping 50K Array Hind 240

900523 *Contains 30 Mapping 50K Hind Arrays*

Supporting Products

GeneChip® Mapping 50K Xba Assay Kit

900520 *Sufficient for 30 reactions*

GeneChip® Mapping 50K Hind Assay Kit

900521 *Sufficient for 30 reactions*

GeneChip® DNA Analysis Software (GDAS)

690030 *GDAS provides data analysis for Affymetrix GeneChip DNA Arrays, including automated SNP and sequence analysis with quality scores.*

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