



Data Sheet

Affymetrix GeneChip® Human MALD 3K SNP Kit

Admixture mapping, or mapping by admixture linkage disequilibrium (MALD), provides a method for localizing genes that cause disease in an admixed ethnic population. It can be a powerful method for performing a whole genome linkage disequilibrium (LD)-based association scan at a fraction of the cost of haplotypic or direct association mapping. The Affymetrix GeneChip® Human MALD 3K SNP Kit contains approximately 3,000 MALD SNPs that are multiplexed in a single assay. The panel is designed for the study of those diseases that differ in incidence between parental African and European populations.

Features and Benefits

- Whereas whole-genome haplotype studies require 10^5 - 10^6 markers (Ref. 1) the 3,000 MALD markers (substantially fewer) can be used for genotyping an admixed population cohort, resulting in genome wide ancestry information.
- The MALD panel is reported to be particularly useful for the study of genes in the etiology of diseases that have large differences in frequency across ethnic populations, e.g., multiple sclerosis, prostate cancer, end stage renal disease, etc. (Refs. 1, 3).
- Admixture mapping using this panel has the potential to localize disease variants that have large differences in frequency across populations, to within 5-10 CM.

Approximately 90 percent of the SNPs for this panel were validated by the National Cancer Institute's Laboratory of Genomic Diversity, Maryland and the Broad Institute, Cambridge, MA. These were published (Ref. 2) and made publicly available online (www.journals.uchicago.edu/AJHG/journal/issues/v74n5/40977/Tab_Delimited_Supptable1_Rev.txt). The remaining 10 percent of SNPs were selected for this panel using the Shannon Information Content (SIC) method. SNPs were selected with a spacing of an average of 1.2 CM, from a combination of public and private databases totaling almost 450,000 SNPs.

Key Specifications

- Accuracy \geq 99.3 percent
- Data completeness \geq 98 percent
- Repeatability \geq 99.25 percent
- Quantity of unamplified genomic DNA is 2.0 μ g
- Quantity of genomic DNA required with recommended amplification is 50 \pm 10ng
- Throughput of 48 samples/day (including two controls) in your lab

Panel Design

The MALD panel is a high-density marker map shown to have large allele frequency differences between African and Caucasian populations.

Table 1.

Lower relative risk in African-Americans

Hepatitis C clearance	0.19
HIV vertical transmission	0.30
Multiple sclerosis	0.50
Atrial fibrillation	0.51
Carotid artery disease	0.62

Higher relative risk in African-Americans

Lupus nephritis with systemic lupus erythematosus	3.13
Myeloma	3.14
Dementia	3.21
Prostate cancer	2.73
Hypertensive heart disease	2.80
Pregnancy-related death	2.65
Hypertension	2.49
Focal segmental glomerulosclerosis	2.61
Interacranial hemorrhage	2.10
Non-insulin dependent diabetes	1.99

MALD Strategy for Disease Studies

The SNPs chosen for inclusion in this panel (approximately one SNP every 300-350 kb) were shown to be highly differentiated SNPs that are five times more informative, on average, than randomly chosen micro-satellites. The panel can be used to screen the genomes of patients that have chromosomal segments of different ethnic origins. There is a reasonable expectation that the population with the highest disease incidence will have the causative genes located in the genomic regions that contribute to the ancestry of the population.

A recent review publication (Ref. 3) identified twenty-five potential disease studies that a MALD-based genes approach

to discovery has the highest a priori chance of success and adds that the list is not exhaustive (see abbreviated table, Table 1.) The authors also estimates that sample sizes of 440 or fewer are required for 80 percent statistical power in MALD analysis, where there is strong allelic relative risk (ARR greater than or equal to 2.5).

REFERENCES

1. Gabriel, *et al.* The Structure of Haplotype Blocks In The Human Genome. *Science* **296**:2225-2229 (2002).
2. Smith, *et al.* A High-Density Admixture Map for Disease Gene Discovery in African Americans. *Am. J. Hum. Genet.* **74**:1001-1013 (2004).
3. Smith, O'Brien, *et al.* Mapping by Admixture Linkage Disequilibrium: Advances, Limitations and Guidelines. *Nature Reviews Genetics*, Sug, **6** (8) : 623-632 (2005).

AFFYMETRIX, INC.

3420 Central Expressway
Santa Clara, CA 95051 USA
Tel: 1-888-DNA-CHIP (1-888-362-2447)
Fax: 1-408-731-5441
sales@affymetrix.com
support@affymetrix.com

AFFYMETRIX UK Ltd

Voyager, Mercury Park,
Wycombe Lane, Wooburn Green,
High Wycombe HP10 0HH
United Kingdom
UK and Others Tel: +44 (0) 1628 552550
France Tel: 0800919505
Germany Tel: 01803001334
Fax: +44 (0) 1628 552585
saleseurope@affymetrix.com
supporteurope@affymetrix.com

Ordering Information

Affymetrix GeneChip® Human MALD 3K SNP Kit

900871 *Kit contains enough reagents to process a total of 24 assays (including one control)*

Affymetrix GeneChip® Universal 3K Tag Array

900602 *Arrays have approximately 3K features on each array that can detect 3K SNPs using the Affymetrix GeneChip DNA Analysis System incorporating MIP technology. (6 pack)*

900578 *(96 pack)*

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North America

888-DNA-CHIP 888-362-2447

Europe

+44 (0) 1628 552550

Japan

+81-(0)3-5730-8200


AFFYMETRIX JAPAN K.K.

Mita NN Bldg., 16 F
4-1-23 Shiba, Minato-ku,
Tokyo 108-0014 Japan
Tel: +81-(0)3-5730-8200
Fax: +81-(0)3-5730-8201
salesjapan@affymetrix.com
supportjapan@affymetrix.com

www.affymetrix.com Please visit our web site for international distributor contact information.

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