Data Sheet

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Axiom® Genome-Wide LAT 1 Array
World Array 4

The highest available coverage of disease-associated common and rare alleles in populations with genetic contributions from West African, European, and Native American ancestries for GWAS, replication and fine mapping in one study

Highlights

- Whole-genome design with highly saturated marker density in strong disease associations and functional relevance
- Coverage-optimized for populations including West Africans, Europeans and Native Americans to enable the highest discovery with minimum marker redundancy
- GWAS, replication, and fine mapping in one experiment to save time and cost
- Intelligent, innovative SNP selection maximizes efficient imputation of millions of additional SNPs
- Fully automated array processing significantly reduces hands-on time and cost

Axiom® Genome-Wide LAT 1 Array is part of Axiom® Genotyping Solution, an innovative technology that supports the entire genotyping workflow from whole-genome to highly targeted gene and causal variant studies. Axiom® World Arrays are a family of predesigned, population specific panels that offer optimal coverage for genome-wide association, replication, and candidate gene association studies.

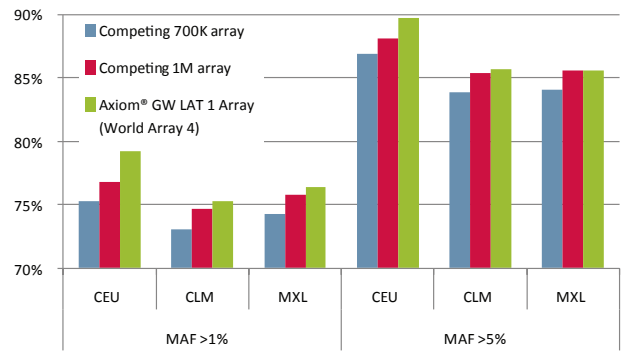
Optimized genome-wide coverage to drive discovery in complex traits and diseases

Axiom Genome-Wide LAT 1 Array was designed with the following goals:

- Provide coverage down to a minor allele frequency (MAF) of 1% in specific gene-based regions
- Saturate over 5,000 gene regions previously identified as disease-associated from prior GWAS for both replication and fine mapping applications
- Improve coverage of both common and rare variants by utilizing data from the low-pass and high-pass projects of the 1000 Genomes Project
- Incorporate redundant coverage of SNPs with known strong associations with disease or trait outcomes

The result of this design strategy is Axiom Genome-Wide LAT 1 Array, which maximizes coverage of known common and rare disease-associated alleles. Genotype imputation was applied to SNP selection for maximum genome-wide coverage. Imputed genomic coverage across five Caucasian and Hispanic populations can be seen in Figure 1.

Figure 1: Imputed genomic coverage at r^2 >0.8 as measured against common (MAF >5%) and rare (MAF >1%) alleles in three ethnic populations: Western European (CEU), Colombian from Medellin (CLM) and Mexican from Los Angeles (MXL) across two competing arrays and Axiom® Genome-Wide LAT 1 Array. Data generated using 1000 Genomes March 2012 integrated phase 1 release version 3.



SNPs were selected from disease and drug response GWAS databases including the National Human Genome Research Institute (NHGRI) Catalog of Published Associations, the Human Genome Epidemiology Navigator (HuGE), the Pharmacogenetics Knowledge Base (PharmaGKB), and the Pharmacogenetics Membrane Transporter (PMT) database. Additionally, over 4,000 disease-associated genes were selected from peer-reviewed scientific publications to be covered with SNPs with MAF as low as 1%. Table 1 classifies the genomic content of Axiom Genome-Wide LAT 1 Array by SNP type included in the design.

Table 1: Count of Axiom Genome-Wide LAT 1 Array markers by biological categories.

Category	Count
SNP	813,551
Indel	4,259
Mitochondrial SNPs	123
Chromosome Y	234
Chromosome X	25,397
Coding	23,426
ADME	6,534
Cardiovascular	8,981
Cancer	9,985
MHC	9,616
Immune and inflammation	8,256
Total markers	817,810

SNPs were prioritized during the design process based on significance for pharmacogenetic and disease-related traits and were grouped into one of four categories: primary, secondary, tertiary, and genome-wide coverage. Table 2 contains a summary of the different tiers, a description of the tier content, and the number of markers in each tier.

Table 2: Descriptions of the different tiers of markers included on the Axiom Genome-Wide LAT 1 Array design.

Tier	Description	No. of SNPs
Primary	SNPs from HuGE Database and NHGRI Catalog with strong confirmed p-value	279
Secondary	QC SNPs, tagging SNP in high LD (r2 >0.6); imputation SNP ±100 kb of 1' SNP, SNPs suggestive of association but not yet replicated p-value $<10^{-5}$ association	20,020
Tertiary	SNPs mined from a variety of sources and selected for functional significance (miRNA, splice-site SNPs)	43,398
Genome-wide coverage	Additional SNPs selected to ensure redundancy and genome-wide coverage	754,113
Total number of SNPs on the array		817,810

Axiom® Genome-Wide LAT 1 Array design history

The SNP selection criteria for Axiom® Genome-Wide LAT 1 Array was based on the design of Axiom® Genome-Wide EUR Array[1] with additional requirements to ensure high coverage of African, European, and Native American ancestries.[2] Axiom Genome-Wide LAT 1 Array was designed to target a variety of Hispanic populations. For example, rare allele coverage (MAF ≥1%) is excellent for Puerto Rican populations, who have a greater percentage of African ancestry, and Mexicans, who have a smaller degree of African ancestry.[2,3]

SNPs polymorphic in Yorubans from Nigeria (YRI) with a MAF ≥10% and SNPs polymorphic in Western European (CEU) with a MAF ≥3% were selected. Coverage of polymorphic Native American SNPs that are absent or infrequent in other populations were included on the array by referencing HapMap Mexicans from LA (MXL) data and by screening 92 Latinos across 5 million SNPs.[2] Only the SNPs with MAF >5% in both MXL and Latino populations and with MAF <2% in CEU and YRI populations were selected for placement on the array.[2]

All SNPs were selected to facilitate imputation to the complete HapMap and 1000 Genomes maps and provide the highest coverage of alleles in populations with Hispanic heritage.

Superior performance

Table 3 summarizes the performance metrics achieved in studies using two sample types.

Table 3: Performance metrics achieved by the Axiom Genome-Wide LAT 1 Array.

Metric	Sample set 1	Sample set 2
Sample type	Cell line	Saliva
Number of samples attempted	90	575
Percent of samples that passed DQC and call rate cutoffs	100%	94.96%
Average sample call rate	99.62%	99.52%
Average HapMap concordance	99.70%	N/A

Sample types

Axiom® Genotyping Assay supports the following sample types as starting material in the target preparation assay:

- gDNA derived from fresh blood
- gDNA derived from saliva (collected using Oragene® DNA collection kits from DNA Genotek)
- Whole-genome amplified DNA (amplified from gDNA using QIAGEN® REPLI-g® kits).

Analysis workflow for the Axiom® Genotyping Array

An analysis workflow is recommended to utilize the content of the array. The following guides detail the use of Genotyping Console™ Software or Affymetrix Power Tools to perform quality control analysis and sample or SNP filtering prior to downstream analysis: *Axiom Genotyping Solution Data Analysis Guide* (P/N 702961) and the *Best Practices Supplement to Axiom Genotyping Solution Data Analysis User Guide for Axiom Genome-Wide EUR 1, EAS 1, LAT 1, and AFR 1 Arrays* (P/N 703106). The benefit of the advanced analysis workflow is that it provides the greatest flexibility in finding the most informative content in each dataset.

Genomics journal publications

For more information about this array (including design strategy and performance), please refer to the following publications:

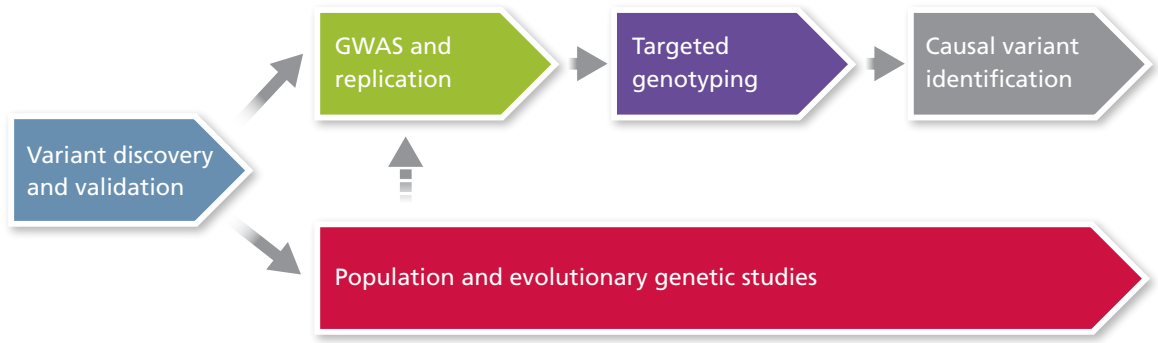
[1]Hoffmann T. J., *et al.* Next generation genome-wide association tool: design and coverage of a high-throughput European-optimized SNP array. *Genomics* **98**(2):79-89 (2011). PMID: 21565264

[2]Burchard E. G., *et al.* Latino populations: a unique opportunity for the study of race, genetics, and social environment in epidemiological research. *American Journal of Public Health* **95**(12):2161-2168. PMID: 16257940

[3]Hoffmann T. J., *et al.* Design and coverage of high throughput genotyping arrays optimized for individuals of East Asian, African American, and Latino race/ethnicity using imputation and a novel hybrid SNP selection algorithm. *Genomics* **98**(6):422-430 (2011). PMID: 21903159

Altshuler D., *et al.* A map of human genome variation from population-scale sequencing. *Nature* **467**(7319):1061-1073 (2010). PMID: 20981092

Figure 2: Axiom Genotyping Solutions can help you discover more. Affymetrix offers cost-effective high-coverage arrays enabling a wide range of human genetic research workflows.



Ordering information

Part number	Product name	Description
901849	Axiom® Genome-Wide LAT 1 Array Plate	Includes one 96-array Axiom Genome-Wide LAT 1 Plate (World Array 4)
901606	Axiom® GeneTitan® Consumables Kit	Contains all GeneTitan® Instrument consumables required to process one Axiom® Array Plate
901758	Axiom® 2.0 Reagent Kit	Includes all reagents (except isopropanol) for processing 96 DNA samples

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