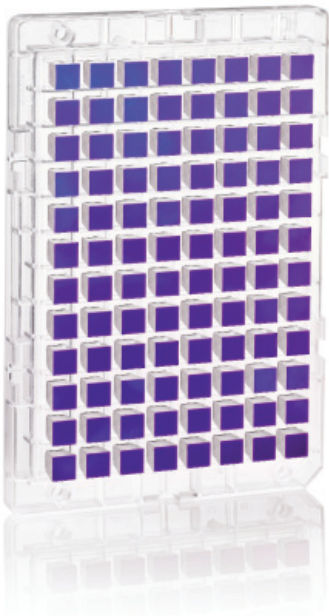


Axiom[®] Exome Genotyping Array

The most complete array to screen functional variants for disease relevance



The Axiom[®] Exome Array contains the most comprehensive panel to screen for putative functional variants in protein coding regions of the human genome. When combined with genotype data from genome-wide arrays, this panel of rare non-synonymous coding SNPs, insertion/deletion mutations and other key GWAS markers is a powerful tool to identify casual variants in complex diseases.

The Axiom[®] Exome Genotyping Array is part of the Axiom[®] Genotyping Solution, Affymetrix' innovative technology for genome-wide association, replication, and candidate gene association studies.

Introduction

The Axiom Exome Array is based on genomic content derived from a pool of novel variants discovered in over 16 major human exome sequencing initiatives, including the NHLBI Exome Project, the Genetics of Type 2 Diabetes program (GoT2D), the 1000 Genomes Project, the Cancer Genome Atlas Project, the SardiNIA exome study, the Autism Exome Sequencing Study the UK10K project, and others. The variants were ascertained by sequencing 12,000 ethnically diverse samples of European, African, Latino, and Asian ancestry at 20x coverage or higher and represent multiple disease cohorts, including type 2 diabetes, cancer, infectious disease, cardiovascular disease, and neurological/psychiatric disorders. A final "super set" of putative functional variants was selected from this pool if the SNP or indel was

discovered in at least two separate individuals. The minor allele frequency for most of these variants is greater than 0.5%.

Benefits of the Axiom Exome Genotyping Array:

Comprehensive content

- The most novel coding SNPs and indels from 1000 Genomes and other exome resequencing initiatives
- Approximately 30,000 novel single-base and complex indels from draft Phase 1 1000 Genomes Project exome calls

Informative markers

- Ancestry informative markers (AIMs), GWAS hit SNPs, identity-by-descent (IBD) markers, and more

High-quality data

- Wet-lab validated against 1,256 reference samples in the Axiom Assay to ensure high call rate and reproducibility

Flexible format

- Customize up to 100,000 additional markers for replication and fine mapping of candidate genes

Less hands-on time

- Fully automated and fast array processing significantly reduces hands-on time, saves money, and reduces errors

Flexible format

The array is configured in two formats:

Axiom[®] Exome Array

- High exon coverage
- Fits any budget
- Large set of novel indels
- Fixed format

Axiom[®] Exome Plus Array

Includes Axiom Exome Array content, plus:

- ~20,000 additional cSNPs and indels
- Flexible format up to 100,000 custom markers

Proven performance

The Axiom Exome Array is wet-lab validated in the Axiom[®] Genotyping Assay by genotyping 1,256 samples from the International HapMap Project and 1000 Genomes sample

collection, and performance has been evaluated against stringent quality control metrics including call rate, concordance, and reproducibility. The performance and genotype data will be released into the public domain in early 2012 and will be freely downloadable from the Affymetrix website.

Analysis workflow for the Axiom® Exome Genotyping Array

A two-stage analysis workflow is recommended to fully utilize the content of the array. The goal of the first stage of the analysis workflow is to identify the samples with performance metrics that meet and/or exceed the recommended QC thresholds. These QC-passing samples are then included in the second stage of the genotyping workflow, where all markers on the array will be genotyped. After completing this second stage of analysis, the advanced analysis technique is used to identify monomorphic (uninformative) markers and remove these from the analysis. The benefit of this advanced analysis is that it provides the greatest flexibility in finding the most informative content for each dataset.

For more information on how to analyze this array, please consult the *Advanced Analysis Workflow for the Axiom Exome Genotyping Arrays Technical Note*, P/N DNA01244-1.

Sample types

In addition to supporting cell line gDNA as an assay template, the Axiom® Genotyping Assay also 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)

Table 1: Axiom Exome Array product specifications.

Categories	Number of markers		
	Axiom Exome Array	Axiom Exome Plus	Competitive Exome Array
Quality	Validated	Validated	Unvalidated
Total validated markers	295,988	318,983	>250,000
Non synonymous coding	231,147	247,546	232,125
Splice and stop	15,781	17,066	12,249
Synonymous SNPs	4,120	4,367	4,651
Ancestry informative markers ¹	4,501	4,507	3,468
ESP SNPs ²	822	861	843
SNPs for DNA fingerprinting	261	263	259
Identity-by-descent SNPs	5,473	5,478	3,369
GWAS tag markers	4,997	5,053	5,325
HLA region	2,228	2,262	2,459
Indels ³	29,746	35,137	180
Chromosome X/Y	6,360/159	6,918/161	470/180
Mitochondrial DNA /miRNA	199/243	207/250	245/270
Customizable markers	N/A	<100,000	Varies

¹ Includes SNPs from the Latino Ancestry Cancer Epidemiology Consortium

² SNPs derived from the NHLBI GO Exome Sequencing Project (ESP)

³ Single-base and complex indels ascertained in the draft Phase 1 1000 Genomes Project exome calls

Table 2: Number of markers by indel size.

Size (bp)	Number of markers	
	Axiom® Exome	Axiom® Exome Plus
1 bp	14,865	17,486
2–10 bp	13,093	16,396
11–50 bp	1,076	1,237
51–140 bp	14	18

Table 3: Distribution of coding SNPs by minor allele frequency (MAF) TT (estimated over 1,256 samples).

MAF	Number of markers	
	Axiom Exome	Axiom Exome Plus
<1%	234,370	255,477
1–5%	20,670	21,335
>5%	40,948	42,171

Table 4: Performance metrics achieved by the Axiom Exome Array.

Metric	Specification	Actual performance ⁴ (n = 1,256 samples from HapMap and 1000 Genomes Projects)
Call rate	>99%	99.76%
Sample pass rate	>95%	99.8%
Reproducibility	>99.8%	99.99%
Concordance	>99.5%	99.5%

⁴Performance metrics based on wet-lab validation against 1,256 samples from the International HapMap and 1000 Genomes reference sample collections.

Ordering information

Part number	Product	Description
901861	Axiom® Exome Array Plate	Contains one 96-array plate
000838	Axiom® Exome Plus Array Plate	Contains one 96-array plate with custom markers
901758	Axiom® 2.0 Reagent Kit	Includes all reagents (except isopropanol) for processing 96 DNA samples
901606	Axiom® GeneTitan® Consumables Kit	Contains all GeneTitan® Instrument consumables required to process one Axiom Array Plate

*Reagent kits do not include Beckman plastic consumables required to run the assay on the Beckman Biomek® FXP Target Prep Express System.



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