Data Sheet

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Axiom® Genome-Wide Human Origins 1 Array

The first and only genotyping array optimized for studying population and evolutionary genetics

Axiom® Genome-Wide Human Origins 1 Array is a powerful tool for human population geneticists to learn about human history, migration, and natural selection. Designed specifically for studies of human population and evolutionary genetics, the array includes SNPs selected using a simple and clean ascertainment strategy that permits evolutionary hypotheses to be studied in a straightforward and quantitative way, thus enabling valuable inferences about human history.

Population genetics and GWAS arrays

Population geneticists have, historically, conducted studies using commercially available genome-wide association study (GWAS) arrays. This compromise was necessary because of the absence of SNP arrays optimized for population and evolutionary genetics. However, SNP ascertainment methods appropriate to GWAS array design confound statistical analysis and allele frequency estimation in population genetic studies, leading to potential for bias. This occurs because ancestry of samples used for GWAS SNP selection is not well-documented. GWAS SNPs are also picked and thinned on the basis of population-specific linkage disequilibrium and haplotype structure. These limitations necessitate the design of an array with cleanly ascertained and well-documented SNPs from samples of known ancestry.

Axiom Genome-Wide Human Origins 1 Array for population genetics contains 629,443 SNPs from modern human populations and ancient hominids with:

- Content for 11 modern human populations
- Coverage in Neanderthal, Denisova, and chimpanzee genomes for comparison in ancient hominids and apes
- Compatibility SNPs in mitochondria, Y chromosome, and overlapping with other commercial arrays for joint analysis with legacy datasets

Axiom Genome-Wide Human Origins 1 Array is part of the Axiom family of Genome-Wide Arrays, which also includes Axiom® Genome-Wide Human Array Plates that offer the best genetic coverage of rare and common variants for population-optimized GWAS studies.

Array design

Axiom Genome-Wide Human Origins 1 Array was designed to meet the needs of population geneticists:

- Establish a common set of ~629,000 SNPs that can be typed in diverse populations
- Provide cleanly ascertained, well-documented SNPs for population inference
- Assure minimal error rate

The SNP ascertainment strategy that enabled design of Axiom Human Origins 1 Array is described in the research paper by Keinan A., *et al., Nature Genetics* (2007). SNPs were discovered by comparing two chromosomes from the same individual of known ancestry and then genotyped in a larger panel of samples from the same population. An important feature of this strategy is that false-negative SNPs should not bias inferences and false-positive SNPs that result from sequencing errors, mapping errors, segmental duplications or copy number variations are not expected to substantially bias inferences.

Axiom Human Origins 1 Array is a union of 13 different discovery panels, shown in Table 1. The first 12 panels contain tens of thousands of SNPs per population, enabling allele frequency spectrum analysis in each population. The 13th panel is based on alignment of three different genomes:

- **Chimpanzee:** the closest living evolutionary relative to humans
- **Denisova:** an archaic hominid from southern Siberia for whom there is 1.9× genome sequence coverage
- **San Bushmen:** a population that appears to be symmetrically related to most present-day humans. SNPs were selected that aligned between Denisova and chimpanzee and likely arose due to mutations in the last million years of human history. The 13th panel is also the only panel containing SNPs from chromosome X for X-autosome comparisons.

There are a total of 629,443 novel variants on the array. 542,399 of these SNPs were discovered using the clean ascertainment strategy described above. An additional 87,044 SNPs were selected from the Axiom® Genomic Database and include mitochondrial SNPs, Y chromosome SNPs, and SNPs present in Affymetrix® Genome-Wide Human SNP Array 6.0. These SNPs empower users to infer mitochondrial DNA and the Y chromosome haplotypes and to carry out joint analysis with other datasets that have been collected on diverse populations.

Table 1: Summary of SNP count within populations targeted by the Axiom Genome-Wide Human Origins 1 Array design.

Panel no.	Population	Sample ID	No. SNPs per population
1	French	HGDP00521	111,970
2	Han Chinese	HGDP00778	78,253
3	Papuan1	HGDP00542	48,531
4	San Bushman	HGDP01029	163,313
5	Yoruba	HGDP00927	124,115
6	Mbuti Pygmies	HGDP00456	12,162
7	Karitiana	HGDP00998	2,635
8	Sardinian	HGDP00665	12,922
9	Melanesian	HGDP00491	14,988
10	Cambodian	HGDP00711	16,987
11	Mongolian	HGDP01224	10,757
12	Papuan2	HGDP00551	12,117
13	Denisova-San	Den-HGDP01029	151,435
Total number of unique SNPs			629,443

Note: The total number of unique SNPs is less than the sum of the SNPs in the 13 panels because of overlap of SNPs across panels.

Validation of the array

Axiom® Human Origins 1 Array Plates were processed on the GeneTitan® MC Instrument with the Axiom® Genotyping Solution. All 629,443 markers on the array were successfully genotyped using samples from the HGDP-CEPH Human Genome Diversity Panel and passed rigorous quality metric thresholds. The genotype dataset (Harvard HGDP-CEPH Genotypes) and the detailed technical document are publicly available at the CEPH website (http://www.cephb.fr/en/hgdp/). The performance specifications and results for 996 samples (952 HGDP-CEPH samples and 44 HapMap samples) are summarized in Table 2.

Analyzing Axiom Genome-wide Human Origins 1 Array

Please consult the Analysis Workflow for the *Axiom Genome-Wide Human Origins 1 Array Technical Note** for information on genotyping analysis using Genotyping Console™ Software.

*Part number DNA01149 Rev. 1

Sample types

Axiom® Genotyping Assay supports the following sample types:

- Cell line gDNA
- 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 2: Performance metrics achieved by Axiom Genome-Wide Human Origins 1 Array.

Metric	Specification	Results on CEPH Human Genome Diversity Panel
Sample pass rate DQC and call rate cutoffs	≥95%	98.90%
Average sample SNP call rate	≥99%	99.56%
Average sample SNP concordance	≥99.5%	99.83%
Mendelian inheritance error	<0.3%	0.06%
Gender calls	–	333 females 652 males
Gender calling accuracy	–	100%
Average reproducibility	>99.8%	99.86%

Publications

Keinan A., *et.al.* Measurement of the human allele frequency spectrum demonstrates greater genetic drift in East Asians than Europeans. *Nature Genetics* **39**(10):1251-5 (2007).

Rosenberg N. A., *et.al.* Clines, clusters, and the effect of study design on the inference of human population structure. *PLoS Genetics* **1**(6):e70 (2005).

Wang S., *et al.* Genetic variation and population structure in Native Americans. *PLoS Genetics* **3**(11):e185 (2007).

Tishkoff S. A., *et al.* The genetic structure and history of Africans and African Americans. *Science* **324**(5930):1035-44 (2009).

Reich D., *et al.* Genetic history of an archaic hominin group from Denisova cave in Siberia. *Nature* **468**:1053-60 (2010).

Cann H. M., *et al.* A human genome diversity cell line panel. *Science* **296**(5566):261-2 (2002).

Ordering information

Part number	Product	Description
901853	Axiom® Genome-Wide Human Origins 1 Array	Contains one 96-array plate
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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