Axiom Pan-African Cancer Research Array

Driving deeper insights into genetic factors associated with cancer

Array content summary

The Applied Biosystems™ Axiom™ Pan-African Cancer Research Array was developed with the Men of African Descent and Carcinoma of the Prostate (MADCaP) Consortium to enable better association of genetic variants with prostate and other cancers in African populations. The Axiom Pan-African Cancer Research Array provides high coverage of common as well as low-frequency whole-genome variants across diverse African populations [1], and high coverage across all 1000 Genomes phase 3 super populations. As part of the design strategy, the array was enriched for comprehensive coverage of variants that are polymorphic in African populations, including 18 ethno-linguistic groups from Sub-Saharan Africa [2,3].

Carcinoma of the prostate (CaP) disproportionately affects men of African descent and is a leading cause of death among them. Genome-wide association studies (GWAS) have identified over 200 loci relevant to CaP, but underrepresentation of African populations means that many relevant genetic variations are not captured [3-5]. The Axiom Pan-African Cancer Research Array addresses this gap by offering over 1.5 million markers across two arrays and an imputation-aware GWAS grid that tags over 94% variants commonly found in African populations.

Highlights

- Optimized for coverage of African populations by including markers tagging African polymorphisms and markers with an African minor allele frequency (MAF) of >5% located within 50 kb of a known CaP hit or within 5 kb of other cancer associations
- 1,513,172 markers selected for genomic, disease, and functional allele coverage, with emphasis on prostate and other cancers
- Offers a high density of markers in genomic regions associated with cancer susceptibility, including the 8q24 region, which has been associated with CaP and other cancers [4-6]
- 24,595 prostate expression quantitative trait loci (eQTLs)
- 38,649 markers from the National Human Genome Research Institute (NHGRI) database associated with a variety of diseases and traits
- Two-array design: array 1 offers 801,275 markers and array 2 offers 790,170 markers covering common variants (MAF >5%) and rare variants (MAF >1%) in African populations

Table 1. Key marker groups of the Axiom Pan-African Cancer Research Array.

Category	Number of markers	Description of content category
Content: Men of African Descent and Carcinoma of the Prostate (MADCaP) Consortium		
GWAS grid total provided by Thermo Fisher	>1.3M variants >526K on array 1 >789K on array 2	Markers to maximize coverage of African populations, for both common variants (MAF >5%) and rare variants (MAF >1%)
NHGRI-EBI GWAS catalog variants	38,649	NHGRI-EBI GWAS catalog variants accessed end of February 2018
Cancer-associated region variants	81,221	Markers in genomic regions that are within 5 kb of GWAS hits
CaP region variants	78,989	Markers in genomic regions that are within 50 kb of GWAS hits in study of prostate cancer
Prostate eQTL variants	27,670	Markers that affect gene expression in the prostate
Total variants contributed by collaborators	274,162	
Content: markers of significance in prostate cancer		
Somatic mutation variants in CaP	28	Markers associated with somatic mutations in CaP tumors, from The Cancer Genome Atlas
Loss-of-function variants in DNA repair genes	5	Markers in common between DNA pathways* and exonic loss-of-function mutations**
Prostate-specific antigen variants	40	Markers obtained from Hofmann et al. (2017) [8]
Circadian rhythm variants	240	Markers associated with circadian rhythm sleep disorders†
Variants from the Epidemiology of Burkitt lymphoma in East African children and minors (EMBLEM) study	227	Markers associated with malaria‡
Variants associated with baldness	283	Makers associated with baldness from Hagenaars et al. (2017) [9]
Aldehyde dehydrogenase (ALDH) genetic variants	126	Markers associated with alcohol drinking habits, biomarkers of alcohol exposure, and risk factors for cardiovascular disease†

* https://www.mdanderson.org/documents/Labs/Wood-Laboratory/human-dna-repair-genes.html

** https://macarthurlab.org/lof/

† Supplied by Ann Hsing's group at Stanford University.

‡ EMBLEM study: https://emblem.cancer.gov/

GWAS grid

The Axiom Pan-African Cancer Research Array includes over 1.3 million markers in the GWAS grid module. Common variants are intelligently selected to optimize genome-wide coverage of sub-Saharan African populations via a proprietary imputation-based marker selection strategy using the African Genome Resource reference panel and the 1000 Genomes phase 3 reference panel. This process allows access to a vast number of common markers (MAF >5%) and rare markers (MAF >1%) through imputation and helps ensure that the selection of markers offers the highest imputation accuracy across all sub-Saharan African populations. Array 1 contains over 526K GWAS grid markers and array 2 has over 789K GWAS markers, and together they achieve high imputation performance for both common (MAF >5%) and rare (MAF >1%) variants.

Imputation performance of the Axiom Pan-African Cancer Research Array in all 1000 Genomes super populations and each African sub-population across common and rare variants evaluated using the 1000 Genomes phase 3 reference panel is shown in Table 2 and Figures 1 and 2.

Table 2. Number of imputed markers with r^2 >0.8 and MAF >1% for the Axiom Pan-African Cancer Research Array, Array 1 and Array 2, across 1000 Genomes phase 3 super populations and African subpopulations.

	Number of imputed markers	
	MAF >1%	
1000 Genomes phase 3 population	Array 1	Array 2
African (AFR)	12.3M	10.2M
African Caribbeans in Barbados (ACB)	13.0M	11.2M
Americans of African Ancestry in SW USA (ASW)	12.0M	10.4M
Esan in Nigeria (ESN)	13.3M	12.0M
Gambian in Western Divisions in the Gambia (GWD)	11.3M	8.9M
Luhya in Webuye, Kenya (LWK)	12.2M	9.9M
Mende in Sierra Leone (MSL)	12.2M	9.9M
Yoruba in Ibadan, Nigeria (YRI)	12.1M	10.8M
Ad Mixed American (AMR)	8.4M	7.4M
East Asian(EAS)	6.0M	4.6M
East Asian (EUR)	7.1M	6.3M
South Asian (SAS)	7.1M	5.7M

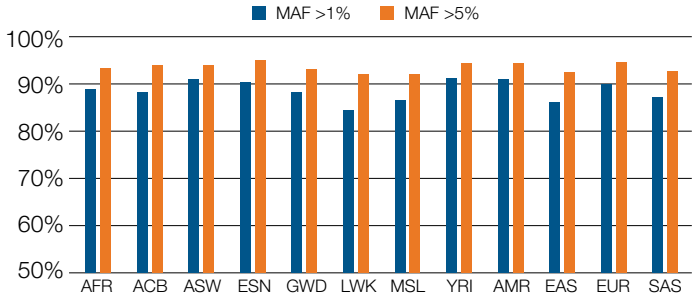

Figure 1. Imputation accuracy of common (MAF >5%) and rare (MAF >1%) variants for the Axiom Pan-African Cancer Research array 1, for 1000 Genomes phase 3 super populations and African subpopulations. Accuracy is the mean r^2 calculated across autosomal SNPs from the highest-ranked 801K array 1 markers.

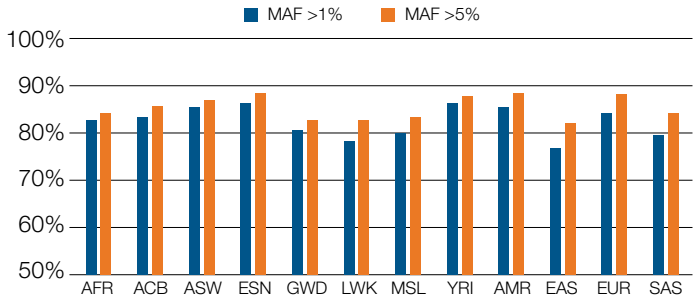

Figure 2. Imputation accuracy of common (MAF >5%) and rare (MAF >1%) variants for the Axiom Pan-African Cancer Research array 2, for 1000 Genomes phase 3 super populations and African subpopulations. Accuracy is the mean r^2 calculated across autosomal SNPs from the highest-ranked 790K array 2 markers.

NHGRI-EBI GWAS catalog variants

The Axiom Pan-African Cancer Research Array contains over 38,000 variants from the NHGRI-EBI GWAS catalog relevant to research on a variety of disease conditions and traits. Overall, 5,337 cancer and cancer-related associations were derived using population-based statistics for NHGRI variants [1].

Specifications

The genotyping performance of the Axiom Pan-African Cancer Research Array has been evaluated using over 800 samples (399 CaP, 403 controls) from African individuals, sourced from several study sites as shown in Table 3. Samples were restricted to individuals with sub-Saharan African ancestry. Stringent quality control metrics that include average sample call rate, sample concordance, and reproducibility are used with performance as shown in Table 4 [7]. Performance metrics for both array 1 and array 2 all exceeded 99.5%.

Table 3. Study sites and numbers of cases and controls used to evaluate performance of the Axiom Pan-African Cancer Research Array [1].

Study site	Number of cases	Number of controls
Hospital General de Grand Yoff	56	59
37 Military Hospital (37 Military)	59	59
Korie-Bu Teaching Hospital	53	58
University College Hospital	56	56
University of Abuja Teaching Hospital	56	57
WITS Health Consortium	61	61
Stellenbosch University	58	53

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Table 4. Genotyping metrics for array 1 and array 2 of the Axiom Pan-African Cancer Research Array [1].

QC metric	Specification	Performance	
		Array 1	Array 2
Number of samples		802	802
Average call rate	≥98.0%	99.55%	99.63%
Reproducibility	≥99.8%	99.85%	99.90%
Average concordance*	≥98.0%	99.53%	99.56%

* Evaluated as the same call across 28 technical replicates.

References

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Ordering information

Product	Description	Cat. No.
Axiom Pan-African Cancer Research Array Plate, array 1	96-array plate	952404
Axiom Pan-African Cancer Research Array Plate, array 2	96-array plate	952405
Axiom Pan-African Cancer Research Assay Kit, array 1	Includes one 96-array plate (array 1), Axiom reagents, and GeneTitan Multi-Channel Instrument consumables for running 96 samples	952406
Axiom Pan-African Cancer Research Assay Kit, array 2	Includes one 96-array plate (array 2), Axiom reagents, and GeneTitan Multi-Channel Instrument consumables for running 96 samples	952407

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