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Axiom Human Genotyping SARS-CoV-2 Research Array

Highly relevant research content covering cellular mechanisms in signaling pathways, underlying conditions, and immune response

This bulletin provides an overview of the content on the Applied Biosystems™ Axiom™ Human Genotyping (HG) SARS-CoV-2 Research Array. The array contains over 800,000 variants to conduct research into host genetics of SARS-CoV-2 infections and was designed in collaboration with several global organizations and biobank research communities.

There is currently an absence of a comprehensive solution that addresses the challenges in studying host genetics of SARS-CoV-2. Short-read sequencing and global generic screening arrays (GSAs) are unable to provide the resolution and comprehensive analysis for studies in genome-wide analysis (GWAS), cellular interactions in signaling pathways, pharmacogenetics, and immune response. The Axiom HG SARS-CoV-2 Research Array offers several advantages over GSAs by offering higher statistical power to help make scientific discoveries, and will help prevent false-positive identifications.

Key differentiators of the Axiom HG SARS-CoV-2 Research Array

- Array content contributions from key opinion leaders in the field, including relevant research content from pre-publications and peer-reviewed content

- Unique array design features that make it ideal for research into etiopathology of SARS-CoV-2 infections

- Dense coverage of various signaling pathways, such as the NF-kappa signaling pathway, involved in activating genes in immune response and inflammation; there are twice the number of markers on this array as on any other current GSA

- Rapid solution that converts samples to whole-genome data for multi-ethnic populations three times faster than whole-genome sequencing
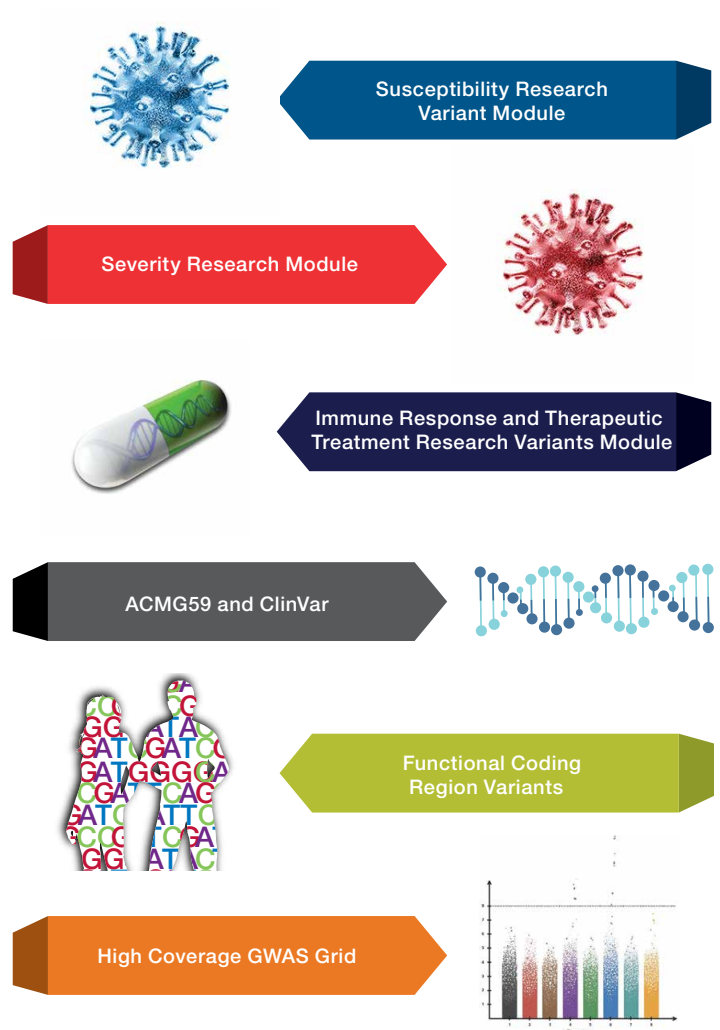

Figure 1. Key content modules on the Axiom HG SARS-CoV-2 Research Array.

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- Relevant modules for SARS-CoV-2 research are as follows:

  – SARS-CoV-2 Susceptibility Research Variant Module
    - Includes structural variants for viral entry points and pathways that are associated with immunity and inflammation
    - Coverage of various signaling pathways to help decipher differences in underlying host genetics and individual responses to SARS-CoV-2
    - Dense coverage of the X chromosome for research into innate immunity

  – SARS-CoV-2 Severity Research Module
    - Includes variants involved in chronic underlying conditions that are implicated in research on the severity of the disease
    - Blood group markers, including the *ABO* gene, and blood phenotypes that have been implicated in the severity of the disease

  – SARS-CoV-2 Immune Response and Therapeutic Treatment Research Variants Module
    - Includes variants that cover regions involved in immune response, also important in vaccine development and pharmacogenomics for drug discovery and development

Table 1. Number of markers in each of the SARS-CoV-2 modules.

Category	Number of markers*
SARS-CoV-2 Susceptibility Research Variant Module	**>180,000**
SARS-CoV-2 putative receptor variants	>1,200
Signaling pathway variants	>122,000
Variants on the X chromosome	>60,000
SARS-CoV-2 Severity Research Module—underlying conditions implicated in severity of SARS-CoV-2 infections	**>16,000**
Blood phenotypes and blood groups	>1,200
Diabetes	>800
Cardiovascular disease	>1,300
Stroke	>50
Lung function and COPD	>9,000
BMI	>1,000
CKD/RAAS	>450
Asthma	>500
SARS-CoV-2 Immune Response and Therapeutic Treatment Research Variants Module	**>24,000**
ADME and protein markers for druggable targets	>6,000
Immunoglobulin and miRNA markers for vaccine research	>5,800
HLA/KIR markers for immune response research after vaccination	>13,500
Multi-ethnic GWAS grid	**>725,000**
ACMG 59 variants	**>6,000**
Functional coding-region variants including eQTL and loss-of-function variants	**>24,000**

* A marker may appear in more than one category.

Table 2. Full list of signaling pathways covered on the array.

Signaling pathways, regulatory pathways, and cellular mechanisms*	Number of genes	Variants
NF-kappa signaling	103	>2,500
AMPK signaling	128	>4,600
B cell receptor signaling	80	>2,500
TNF signaling	112	>2,300
MAPK signaling	289	>10,500
IFN signaling	473	>14,400
TGF-beta signaling	92	>2,600
FoxO signaling	128	>3,600
Endoplasmic reticulum stress	930	>28,000
Renin angiotensinogen	23	>1,763
Notch signaling and ligands	53	>1,800
NOD-like receptor pathway	175	>3,400
Toll-like receptor signaling	103	>1,600
Apoptosis	4,038	>100,000

* An explanation of various pathways can be found in **genome.jp/kegg/pathway.html**.

Table 3. Markers classified into selected disease research categories.

Details on sub-categories of markers	Variants
Mental, behavioral, neurological, and neurodevelopmental risk variants	
Alzheimer's disease including ApOE markers	>170
Parkinson's disease	>70
Schizophrenia	>400
Autoimmune and inflammatory disease risk variants	
Inflammatory bowel disease	>170
Celiac disease	>60
Crohn's disease	>300
Graves' disease	>30
Inherited eye disease	
Macular degeneration	>100
Glaucoma	>70
Blood phenotypes and blood groups	>1,200
Asthma	>500
Body mass index	>1,100
Lung function phenotypes	>8,000
Copy number variation	>3,000
Markers from Applied Biosystems™ UK Biobank Axiom™ Array	>21,700
Diabetes	>800
Cardiovascular disease	>1,300
Stroke	>50
Lung function and COPD	>9,000
Chronic kidney disease/RAAS	>450

Table 4. Number and accuracy of markers with $r^2 > 0.8$ covering the ancestral populations in phase 3 of the 1000 Genomes Project.

Ancestral population covered on array	Imputation accuracy*		Number of imputed markers with $r^2 > 0.8$
	MAF > 1%	MAF > 5%	MAF > 1%
African (AFR)	90%	92%	14.9M
Admixed American (AMR)	92%	94%	10.2M
East Asian (EAS)	87%	92%	7.3M
European (EUR)	91%	94%	8.8M
South Asian (SAS)	88%	93%	8.7M

* Accuracy is the mean r^2 calculated across autosomal SNPs from the highest-ranked markers.

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In summary, the various research modules create a powerful, scalable, and economical array for studies of host genetics involved in SARS-CoV-2 infections, population genomics, and vaccine and drug development research.

Acknowledgments

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Ordering information

Product	Description	Cat. No.
Axiom Human Genotyping SARS-CoV-2 Research Array	Includes one 96-array plate	952401
Axiom Human Genotyping SARS-CoV-2 Research Array Assay Kit	Includes one 96-array plate (Cat. No. 952401); Axiom 2.0 reagent kit (Cat. No. 901758); and GeneTitan MC consumables kit	952402
Axiom Human Genotyping SARS-CoV-2 Research Array Plus Assay Kit	Includes one 96-array plate (Cat. No. 952401); Axiom 2.0 Plus reagent kit (Cat. No. 951960); and GeneTitan MC consumables kit	952403

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