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Infinium™ Global Screening Array-24 v3.0 BeadChip

A powerful, high-quality, cost-effective array for population-scale genetic studies.

Highlights

- **Optimized global content**
  Includes a multiethnic genome-wide backbone, clinical research variants, QC markers, and custom add-on content
- **Broad clinical research applications**
  Enables genotyping for complex disease studies, pharmacogenomics research, lifestyle and wellness characterization, and more
- **High-throughput workflow**
  Supports high-throughput processing of thousands of samples per week for population-scale studies
- **Robust, high-quality assay**
  Maintains the same data quality of Illumina genotyping arrays with call rates > 99% and reproducibility > 99.9%

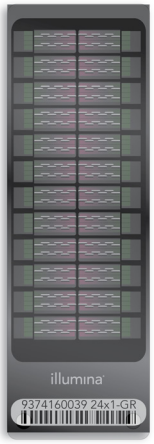

Figure 1: Infinium Global Screening Array-24 v3.0 BeadChip—Built on the trusted 24-sample Infinium HTS platform.

Introduction

The Infinium Global Screening Array-24 v3.0 BeadChip is an advanced genotyping array that provides a high-value, scalable, and cost-effective solution for population-scale genetic studies, variant screening, and precision medicine research (Table 1). Using the iScan™ System, integrated analysis software, and the Infinium high-throughput screening (HTS) assay, this high-density, 24-sample BeadChip (Figure 1) provides optimized content (Figure 2) for a broad range of applications, delivered with the same high-quality, reproducible data that Illumina genotyping arrays have provided for over a decade. The Global Screening Array Kit includes convenient packaging containing BeadChips and reagents for amplifying, fragmenting, hybridizing, labeling, and detecting genetic variants using the high-throughput, streamlined Infinium workflow.

Table 1: Product information[a]

Feature	Description
Species	Human
Total number of markers[b]	654,027
Capacity for custom bead types	100,000
Number of samples per BeadChip	24
DNA input requirement	200 ng genomic DNA
Assay chemistry	Infinium HTS
Instrument support	iScan System
Maximum iScan System sample throughput[a]	~5760 samples/week
Scan time per sample	1.3 minutes

a. Approximate values, scan times, and maximum throughput may vary depending on laboratory and system configurations.

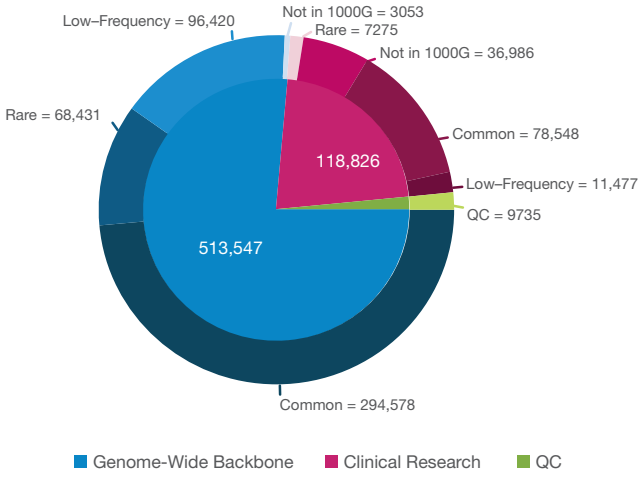

Figure 2: Summary of content— Genome-wide content enables a broad range of clinical research and genetic variant screening applications. Plotted in the inner pie is the proportion of the array selected for genome-wide coverage, clinical research, and quality control (QC). The outer ring summarizes the weighted reference global allele frequency for unique variants present in the 1000 Genomes Project (1000G).[1] Variants not in 1000G are labeled. Counts represent unique variants.

Table 2: High-value content

Content	No. of markers[a]	Research application/note	Content	No. of markers	Research application/note
ACMG[2] 59 2016 gene coverage	21,730	Variants with known clinical significance identified from clinical WGS and WES samples	GO[9] CVS genes	105,219	Cardiovascular conditions
ACMG 59 all annotations	15,208		Database of Genomic Variants[10]	507,399	Genomic structural variation
ACMG 59 pathogenic	7023		eQTLs[11]	2704	Genomic loci regulating mRNA expression levels
ACMG 59 likely pathogenic	3039		Fingerprint SNPs[12]	566	Human identification
ACMG 59 benign	567		gnomAD[13] exome	64,575	WES and WGS results from unrelated individuals from various studies
ACMG 59 likely benign	932		HLA genes[14]	455	Disease defense, transplant rejection, and autoimmune disorders
ACMG 59 VUS	2205		Extended MHC[14c]	8367	Disease defense, transplant rejection, and autoimmune disorders
ADME[3] core and extended + CPIC genes	14,608	Drug absorption, distribution, metabolism, and excretion	KIR genes[4]	27	Autoimmune disorders and disease defense
ADME core and extended + CPIC genes +/- 10 kb	17,551	Includes regulatory regions	Neanderthal SNPs[15]	1528	Neanderthal ancestry and human population migration
AIMs[b]	2923	Ancestry-informative markers	Newborn/carrier screening gene coverage	25,827	Genes associated childhood diseases included in the TruSight™ Inherited Disease Sequencing Panel[19]
APOE[4]	18	Cardiovascular disease, Alzheimer's disease, and cognition	NHGRI-EBI GWAS catalog[16]	16,160	Markers from published GWAS
Blood phenotype genes[5]	1931	Blood phenotypes	PharmGKB[17,18] all	4125	Human genetic variation associated with drug responses
ClinVar[6] variants	45,998	Relationships among variation, phenotypes, and human health	PharmGKB level 1A	30	
ClinVar pathogenic	15,213		PharmGKB level 1B	2	
ClinVar likely pathogenic	6584		PharmGKB level 2A	17	
ClinVar benign	7820		PharmGKB level 2B	60	
ClinVar likely benign	4668		PharmGKB level 3	1300	
ClinVar VUS	5548		PharmGKB level 4	154	
COSMIC[7] genes	301,888	Somatic mutations in cancer	RefSeq[20] 3' UTRs	14,313	3' untranslated regions[d]
CPIC[8] all	231	Variants with potential guidelines to optimize drug therapy	RefSeq 5' UTRs	6519	5' untranslated regions[d]
CPIC-A	114		RefSeq All UTRs	20,214	Untranslated regions[d]
CPIC-A/B	1		RefSeq	336,086	All known genes
CPIC-B	17		RefSeq +/- 10 kb	392,003	Regulatory regions[d]
CPIC-C	14		RefSeq Promoters	14,976	2 kb upstream to include promoter regions[d]
CPIC-C/D	15		RefSeq Splice Regions	3536	Variants at splice sites[d]
CPIC-D	70				

a. The number of markers for each category may be subject to change
b. Based on internal calculations
c. Extended MHC is a 8 Mb region
d. Of all known genes

Abbreviations: ACMG: American College of Medical Genetics; ADME: absorption, distribution, metabolism, and excretion; AIM: ancestry-informative marker; APOE: apolipoprotein E; COSMIC: catalog of somatic mutations in cancer; CPIC: Clinical Pharmacogenetics Implementation Consortium; EBI: European Bioinformatics Institute; eQTL: expression quantitative trait loci; gnomAD: Genome Aggregation Database; GO CVS: gene ontology annotation of the cardiovascular system; GWAS: genome-wide association study; HLA: human leukocyte antigen; KIR: killer cell immunoglobulin-like receptor; MHC: major histocompatibility complex; NHGRI: national human genome research institute; PharmGKB: Pharmacogenomics Knowledgebase; RefSeq: NCBI Reference Sequence Database; UTR: untranslated region; VUS, variant of unknown significance; WES, whole-exome sequencing; WGS, whole-genome sequencing

Table 3: Marker information

Marker categories			No. of markers
Exonic markers[a]			85,342
Intronic markers[a]			262,173
Nonsense markers[b]			5904
Missense markers[b]			51,188
Synonymous markers[b]			9273
MItochondrial markers[b]			1138
Indels[c]			10,118
Sex chromosomes[c]	X	Y	PAR/homologous
	27,176	4138	879

a. RefSeq - NCBI Reference Sequence Database.[20] Accessed May 2020.
b. Compared against the UCSC Genome Broswer.[4] Accessed May 2020.
c. NCBI Genome Reference Consortium, Version GRCh37.[21] Accessed May 2020.
Abbreviations: indel, insertion/deletion; PAR, pseudoautosomal region.

Widespread adoption

The Infinium Global Screening Array-24 v3.0 BeadChip builds on the success of the consortium version of the product that has been widely adopted by a community of human disease researchers, health care networks, consumer genomics companies, andgenomic service providers. Over 15 million samples of the Global Screening Array have been ordered by a global community of users powering discovery through collaboration and data sharing.

Optimized global and high-value content

The Infinium Global Screening Array-24 v3.0 BeadChip combines highly optimized multiethnic genome-wide content, curated clinical research variants, and QC markers for a broad range of clinical research and variant screening applications (Table 2 and Table 3). These applications include disease association and risk profiling studies, pharmacogenomics research, disease characterization, lifestyle and wellness characterization, and marker discovery in complex disease research.

Expertly selected content empowering clinical research applications

The clinical research content of the Infinium Global Screening Array-24 v3.0 BeadChip was designed through collaboration with medical genomics experts using multiple annotation databases[6-21] to create an informative, cost-effective panel for clinical research applications (Table 2 and Figure 3).

Variants included on the array consist of markers with known disease association based on ClinVar,[6] the Pharmacogenomics Knowledgebase (PharmGKB),[17] and the National Human Genome Research Institute (NHGRI)-EBI database. In addition to disease-associated markers, the Infinium Global Screening Array-24 v3.0 BeadChip contains imputation-based tagSNPs for HLA alleles, extended MHC region, the KIR gene, and exonic content from the gnomAD database.[13]

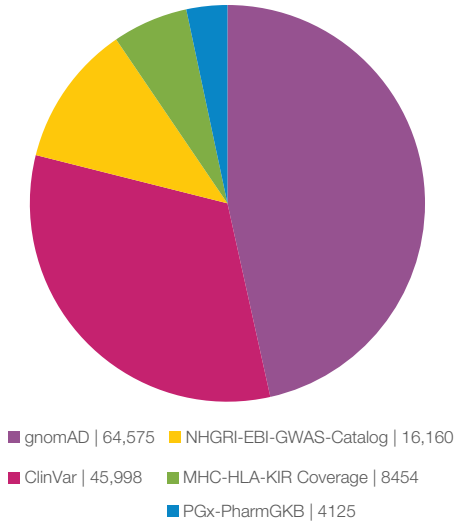

Figure 3: Clinical research content—Content was expertly selected from scientifically recognized databases to create a highly informative array for clinical research applications. Variant counts may be subject to change.

Broad spectrum of pharmacogenomics markers and exonic content

The Infinium Global Screening Array-24 v3.0 BeadChip provides coverage of pharmacogenomics variants associated with absorption, distribution, metabolism, and excretion (ADME) phenotypes based on PharmGKB[17] and Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines[8] (Figure 4). It also features diverse exonic content from the ExAC database,[13] including both cross population and population specific markers (Table 4) with either functionality or strong evidence for association.

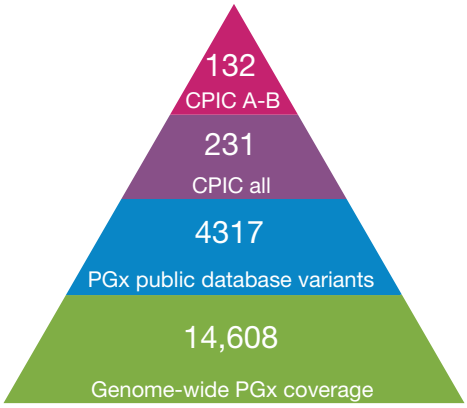

Figure 5: Broad spectrum of pharmacogenomics markers—Clinical research content features an extensive list of pharmacogenomics markers selected based on CPIC guidelines and the PharmGKB database.[16] **PGx public database variants**, variants annotated in PharmGKB, PharmVar, CPIC; **Genome-wide PGx coverage**, includes markers located in an extended ADME genes or CPIC level A genes including targeted imputation tag SNPs and CPIC level A copy number variation (CNV) tags.

Table 4: Global exonic content

Population(s)[a]	No. of markers
EUR	52,980
EAS	31,375
AMR	45,977
AFR	43,122
SAS	40,298

a. www.internationalgenome.org/category/population

Extensive range of disease categories covered

Clinical research content on the Infinium Global Screening Array-24 v3.0 BeadChip enables validation of disease associations, risk profiling, preemptive screening research, and pharmacogenomics studies. Variant selection includes a range of pathology classifications based on ClinVar and American College of Medical Genetics (ACMG) annotations (Figure 5A).[2] The BeadChip contains extensive coverage of phenotypes and disease classifications based on ClinVar (Figure 5B) and the NHGRI-EBI GWAS catalog (Figure 6).

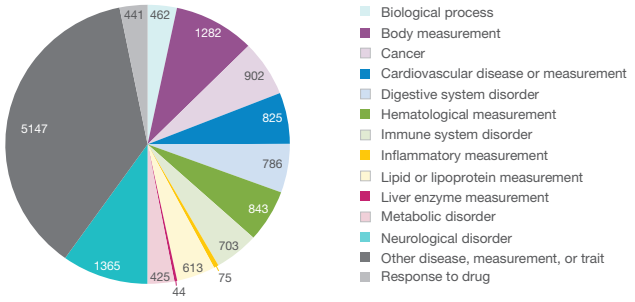

Figure 4: NHGRI disease categories—Global Diversity Array clinical research content features markers across a broad range of disease coategories based on the NHGRI database.

QC markers for sample identification, tracking, and stratification

The Infinium Global Screening Array-24 v3.0 BeadChip includes quality control (QC) markers for large-scale studies, enabling sample identification, tracking, ancestry determination, and stratification (Figure 7).

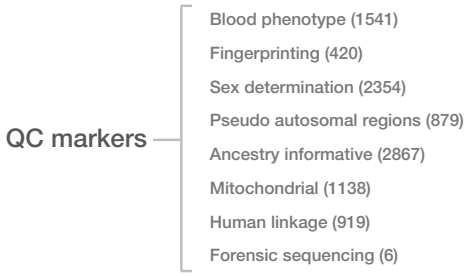

Figure 7: QC markers—QC variants on the array enable various capabilities for sample tracking such as sex determination, continental ancestry, and human identifcation and more.

Flexible content options

The Infinium Global Screening Array-24 v3.0 BeadChip can be customized to incorporate up to 100,000 custom bead types or a predesigned content panel (Table 5). The DesignStudio™ Microarray Assay Designer can be used to design targets such as SNPs, copy number variants (CNVs), and indels.

Table 5: Flexible content options

Compatible content	No. of markers	Description
Custom content	~100,000	Custom design virtually any target (eg, SNP, CNV, indel) using the DesignStudio Microarray Assay Designer[a]
Multi-disease drop-in panel	~50,000	Fine-mapping content derived from exome sequencing and meta analysis of phenotypespecific consortia focused on the following traits: psychiatric, neurological, cancer, cardiometabolic, autoimmune, anthropometric
Infinium PsychArray-24 focused content panel	~30,000	Markers from the Infinium PsychArray-24 BeadChip[b] associated with common psychiatric disorders including, schizophrenia, bipolar disorder, autism spectrum disorders, attention deficit hyperactivity disorder, major depressive disorders, obsessive compulsive disorder, anorexia, Tourette's syndrome

a. www.illumina.com/informatics/sample-experiment-management/custom-assay-design.html
b. www.illumina.com/products/by-type/microarray-kits/infinium-psycharray.html

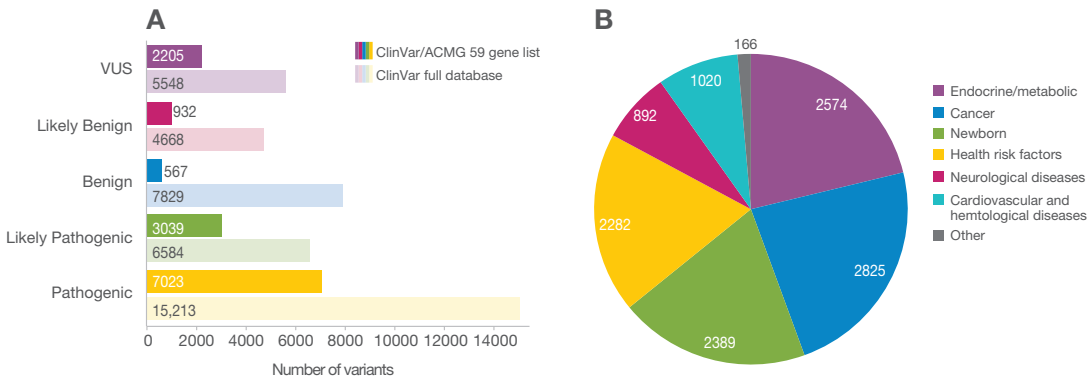

Figure 6: Broad coverage of disease catogories—(A) Variants sorted by range of pathology classifications according to ClinVar American College of Medical Genetics (ACMG) annotations. (B) Global Diversity Array clinical research content by category within the ClinVar database. Variant counts may be subject to change.

High-throughput workflow

The Infinium Global Screening Array-24 v3.0 BeadChip uses the highly scalable Infinium 24-sample Infinium HTS format, which enables laboratories to efficiently scale as needed. For flexible throughput processing, the Infinium HTS assay provides the capability to run hundreds to thousands of samples per week. The Infinium HTS assay provides a rapid, three-day workflow that allows users to gather and report data quickly (Figure 8). For labs interested in quickly scaling or increasing efficiency and operational excellence, the Illumina ArrayLab Consulting Service offers customized solutions.

Robust and trusted, high-quality assay

The Infinium Global Screening Array-24 v3.0 BeadChip uses trusted Infinium assay chemistry to deliver the same high-quality, reproducible data (Table 6) that Illumina genotyping arrays have provided for over a decade. The Infinium product line provides high call rates and high reproducibility for numerous sample types including, saliva, blood, solid tumors, fresh frozen, and buccal swabs. It is compatible with the Infinium FFPE QC and DNA Restoration Kits, enabling genotyping of formalin-fixed, paraffinembedded (FFPE) samples. In addition, the high signal-to-noise ratio of the individual genotyping calls from the Infinium assay provides access to genome-wide copy CNV calling.

Table 6: Data performance and spacing

Data performance	Value[a]	Product specification[b]	
Call rate	99.5%	> 99.0% avg	
Reproducibility	99.99%	> 99.90%	
Log R deviation	0.15[c]	< 0.30 avg[d]	
Spacing			
Spacing (kb)	Mean	Median	90th%[c]
	4.4	2.3	10.7

a. Values are derived from genotyping 1725 HapMap reference samples.
b. Excudes Y chromosome markers for female samples.
c. Based on results from GenTrain sample set.
d. Value expected for typical projects using standard Illumina protocols. Tumor samples and samples prepared by methods other than standard Illumina protocols are excluded.

High imputation accuracy for global populations

High imputation accuracy provides increased power to support population-scale disease research and population-specific causal variant detection. Leveraging available whole-genome reference data from over 26 global populations in 1000G Phase 3,1 the genome-wide content on the Infinium Global Screening Array-24 v3.0 BeadChip has been selected to generate high imputation accuracy for low-frequency and common variants—minor allele frequencies (MAF) of > 1% (Table 7, Table 8).

Imputation calculation methodology

Imputation performance is measured by simulating Global Screening Array-24 v3.0 genotyped variants on 1000G samples (Table 7, Table 8). A random sample from all 26 1000G global populations were selected, stratified by super population, and tested against variants on the array. The remaining 1000G samples were treated as the reference (1000G data is already phased using BEAGLE). Minimac3 was used to perform imputation and imputation quality was measured using the correlation r^2 from the info file produced by minimac3.

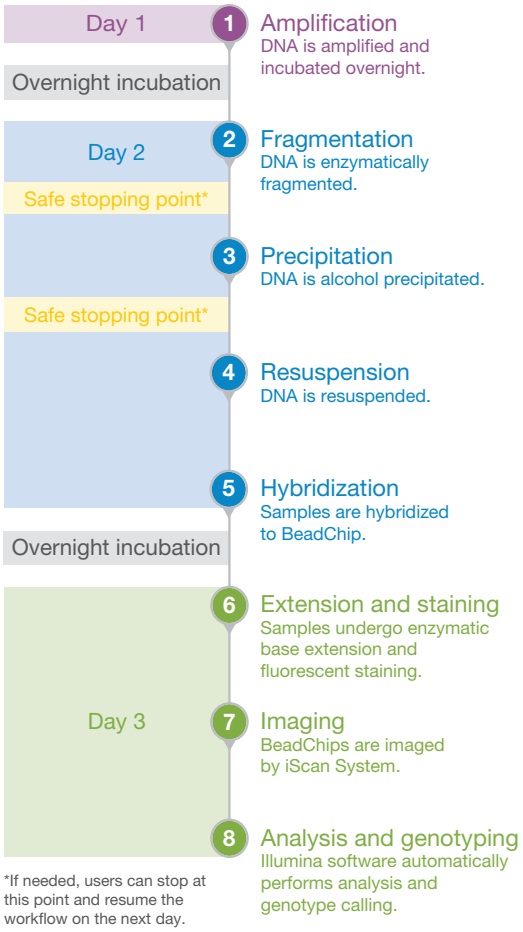

Figure 8: The Infinium 24-sample format workflow—The Infinium HTS format provides a rapid three-day workflow with minimal hands-on time.

Table 7: Imputation accuracy from 1000G at various MAF thresholds

Population	Imputation accuracy		
	MAF ≥ 5%	MAF ≥ 1%	MAF 1–5%
AFR	0.86	0.84	0.80
AMR	0.90	0.83	0.70
EAS	0.84	0.81	0.72
EUR	0.88	0.86	0.79
SAS	0.91	0.87	0.77

a. Compared against Phase 3, version 5 of the 1000G. www. www.internationalgenome.org. Accessed May 20. 2020. Imputed using minimac3.
b. www.internationalgenome.org/category/population

Table 8: Number of markers imputed at $r^2 \geq 0.80$ from 1000G[a]

Population[b]	No. of imputed markers		
	MAF ≥ 5%	MAF ≥ 1%	MAF 1–5%
AFR	7,186,582	12,181,676	4,995,094
AMR	5,911,729	8,411,902	2,500,173
EAS	4,464,253	5,768,496	1,304,243
EUR	5,512,064	7,542,581	2,030,517
SAS	6,005,008	8,179,336	2,174,328

a. Compared against Phase 3, version 5 of the 1000G. www. www.internationalgenome.org. Accessed May 20. 2020. Imputed using minimac3.
b. www.internationalgenome.org/category/population

Summary

The Infinium Global Screening Array-24 v3.0 BeadChip provides a cost-effective solution for population-scale genetic studies, variant screening, and precision medicine research. It builds on the success of the consortium version of the product and has been widely adopted with over 15 million samples ordered worldwide. Using the proven iScan System, Infinium HTS Assay, and integrated analysis software, the high-density, 24-sample Infinium Global Screening Array-24 v3.0 BeadChip provides optimized content for a broad range of clinical research applications.

Ordering Information

Order Illumina Infinium products online at www.illumina.com

Infinium Global Screening Array-24 v3.0 BeadChip Kit	Catalog no.
48 samples	20030770
288 samples	20030771
1152 samples	20030772
Infinium Global Screening Array-24+ v3.0 BeadChip Kit[a]	**Catalog no.**
48 samples	20030773
288 samples	20030774
1152 samples	20030775

a. Enabled for custom content

Learn more

Learn more about the Infinium Global Screening Array-24 v3.0 BeadChip and other Illumina genotyping products and services at www.illumina.com/techniques/microarrays.html.

For labs interested in higher throughput processing with the Infinium Global Screening Array-24 v3.0, contact your local account manager for more information about Infinium HTS Extra high-throughput kit configurations.

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