DATA SHEET

Infinium™ Methylation Screening Array

High-throughput methylation analysis for population epigenomics research

- Focused coverage of 270K unique methylation sites associated with common human traits, disease phenotypes, exposures, aging, and more
- Scalable processing of up to 600K samples per year on a single iScan™ System using the 48-sample BeadChip
- Reliable methylation data with > 98% sample-to-sample reproducibility

illumina®

High-throughput array for methylation studies

Over the past decade, accurate and scalable Infinium methylation BeadChips have enabled epigenome-wide association studies (EWAS) and facilitated groundbreaking discoveries on the role of epigenetic mechanisms in human health and disease.[1] Recently, large-scale population genomics initiatives like Generation Scotland[2,3] and The Million Veterans Program[4,5] have generated extensive methylation data sets to gain insights into population health and its determinants. As the field of epigenetics evolves, scientists require more scalable tools to conduct larger methylation projects.

The Infinium Methylation Screening Array supports large-scale epigenetic analyses of population-size cohorts with expert content selection covering known and predicted epigenetic associations. The array is built on the 48-sample EX Methylation platform to create the most scalable and affordable Infinium methylation array to date, delivering reliable, accurate methylation data and simplified analysis (Table 1, Figure 1).

Expert content selection for population health EWAS

The Infinium Methylation Screening Array features 270K methylation sites focused on CpG regions associated with a range of common cell and organism traits, such as cell identity, nonmalignant disease phenotypes, and environmental exposures. BeadChip content was selected for having powerful published trait associations from a combination of Infinium methylation studies, functional genomics sequencing studies, and updated

Table 1: Infinium methylation array specifications

	Infinium Methylation Screening Array Targeted methylation screening for population health research	Infinium MethylationEPIC v2.0 Broad discovery backbone with genome-wide coverage
Recommended applications	• Common disease research (noncancer) • Environmental epidemiology • Population genomics • Consumer genomics	• Cancer research • Rare disease research
Content focus	• Known common disease trait associations • Known environmental exposure associations • Cell-type specific methylation • Intermediate methylation • Multiomic capabilities to measure high MAF SNPs	• Coverage of whole methylome (> 99% of RefSeq genes) • CNV detection • Comprehensive coverage of *MGMT* gene • Compatibility with published cancer classifiers • Compatibility with published rare disease classifiers • Cancer driver mutations
Total unique methylation sites	270K	930K
Number of samples per BeadChip	48	8
DNA input requirement	50 ng	250 ng
Assay chemistry	Infinium EX Methylation	Infinium HD Methylation
Instrument support	iScan System	iScan System NextSeq™ 550 System
iScan System maximum sample throughput[a]	16,128 samples/week	3024 samples/week
Liquid handling automation	Infinium Automated Pipetting System with ILASS (required)	Infinium Automated Pipetting System with IAC (recommended, not required)

a. Approximate values, scan times, and maximum throughput will vary depending on laboratory and system configurations. Sample throughput listed here is achieved with integration of AutoLoader 2.x automated array loading.

IAC, Illumina Automation Control, ILASS , Illumina Lab Automation Software Solution; MAF, minor-allele frequency; SNP, single-nucleotide polymorphism; CNV, copy-number variant

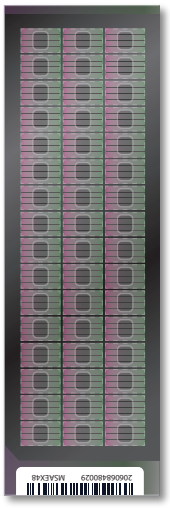


Figure 1: Infinium Methylation Screening Array—The BeadChip provides the capacity for efficient and accurate analysis of 270K expert-selected methylation sites for 48 samples per BeadChip.

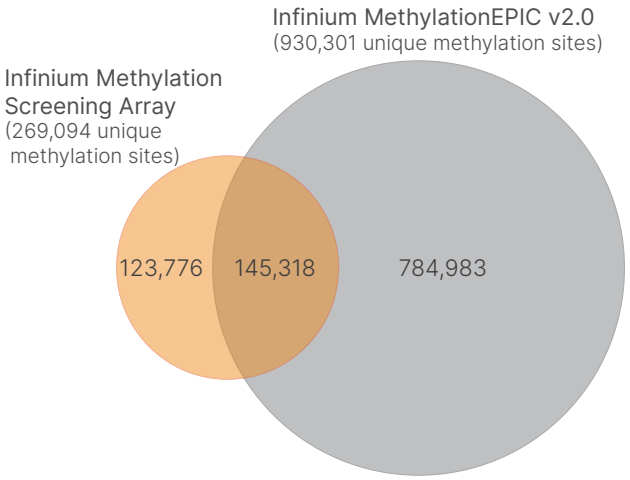


Figure 2: Methylation Screening Array and MethylationEPIC v2.0 BeadChip overlap of unique methylation sites.

genomic databases. The focused design and higher sample throughput of the Infinium Methylation Screening Array enables researchers to apply DNA methylation screening to large population health projects to discover disease targets.

Known associations from Infinium Methylation Arrays

Approximately 50% of the loci on the Infinium Methylation Screening Array were identified from analysis of published data, scientific literature, and Infinium methylation arrays to find associations of CpG methylation with diverse traits or diseases (Figure 2 and Table 2). Over 1000 EWAS studies were curated and filtered based on sample size, statistical robustness, and scientific impact. Probes with the highest statistical significance and effect size were prioritized and selections were balanced to maximize representation across traits and diseases. The selected content is associated with a broad spectrum of biological categories, encompassing cardiovascular, metabolic, neurodegenerative/psychiatric, autoimmune, respiratory, reproductive, renal, aging, genetic, environmental exposure, and infection-related traits and diseases. Epigenetic clock and cell deconvolution panels from previous and existing Infinium BeadChip platforms were also included to provide backward compatibility with established predictors of cell type estimates and phenotype predictions in EWAS studies (Table 3 and Figure 3).

Table 2: High-level comparison of Infinium Methylation Screening Array and Infinium MethylationEPICv2.0 BeadChip content

	Infinium Methylation Screening Array	Infinium MethylationEPIC v2.0
Total unique sites	269,094	930,301
CpG	262,470	926,849
From Infinium methylation arrays	161,598	-
From sequencing studies and databases	100,872	-
CpH	2776	2914
From Infinium methylation arrays	308	-
From sequencing studies and databases	2468	-
SNP rsID	3848	538
From Infinium methylation arrays	64	-
From sequencing studies and databases	3784	-

Table 3: Previously validated trait-associated content on Infinium Methylation Screening Array

Trait category	No. of probes targeting trait association
Development/aging	102,533
Environmental exposures	44,043
Inflammation/autoimmune diseases	41,894
Ancestry	31,843
Sex	23,806
Infectious diseases	14,844
Metabolic diseases	13,739
Rare genetic disorders	13,429
Neurological/neurodevelopmental diseases	8874
Body features (body morphology)	8109
Psychiatric disorders	7280
Cardiovascular disease	7007
Reproductive biology/health	6999
Neurodegenerative diseases	4733
Lung/respiratory diseases	1748
Renal disease	982

Novel content from WGBS

The Infinium Methylation Screening Array backbone also includes content selected from a comprehensive analysis of publicly available bulk and single-cell whole-genome bisulfite sequencing (WGBS) data sets,[6] including a brain single-cell methylome atlas comprised of over 15,000 cells[7,8] and a pan-tissue methylome atlas of sorted human cell types.[9] These expertly designed probes target loci where DNA methylation has been associated with cell type, gene expression, chromatin accessibility, monoallelic methylation, and interindividual methylation variation. Genomic features from ENCODE[10] candidate cis regulatory element annotations and partially methylated domains were also targeted. Altogether, ~100K novel probes were created to profile the methylation of new CpGs relatively enriched in regulatory and cell-specific chromatin states.

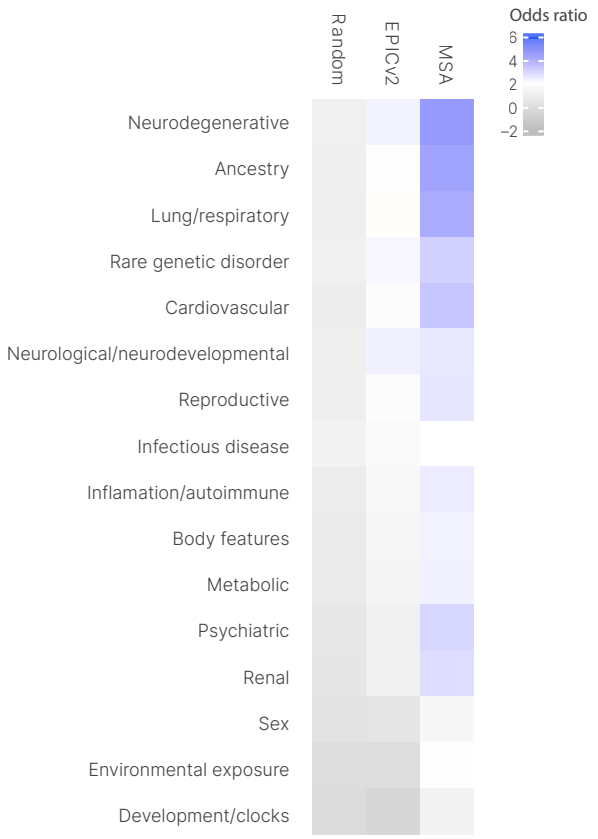


Figure 3: Markers on the Infinium Methylation Screening Array are highly enriched in known trait-associated CpGs across diverse trait types—Markers on the Methylation Screening Array (MSA) are selected based on evidence for trait association, shown in comparison with trait enrichment on Infinium MethylationEPIC v2.0 (EPICV2).

Beyond CpG: multiomic capabilities

The Infinium Methylation Screening Array supports multiomic studies beyond CpG methylation, including coverage of 2776 non-CpG methylation sites (methylated CpH sites, where H indicates A, T, or C) (Table 2). CpH methylation probes are highly enriched in gene bodies where CpH methylation has been implicated in transcriptional regulation and development.[11]

The Infinium Methylation Screening Array also Ingerrogates 3848 single nucleotide polymorphisms (SNPs) with high minor allele frequencies selected from genomic databases, providing unique multiomic insights into disease mechanisms across diverse populations. In addition, an innovative use of Type I CpG probes indirectly targets over 10,000 high minor allele frequency SNPs. These dual methylation–SNP probes can be used to query both

methylation levels and genetic variations, facilitating the discovery and the genetic determination of methylation levels, such as potential methylation quantitative trait loci (meQTL).* More information about probes that target SNPs directly or indirectly can be accessed on the product support page.

Reliable methylation data

Infinium array chemistry employs many bead replicates for each CpG site queried, each with thousands of probes attached. As a result, the Infinium methylation assay provides highly precise methylation measurements that have been equated to over 100× sequencing depth of even coverage.[13] This is evidenced by internal tests of the Infinium Methylation Screening Array on Coriell and blood samples demonstrating > 98% reproducibility between technical replicates (Table 4 and Figure 4).

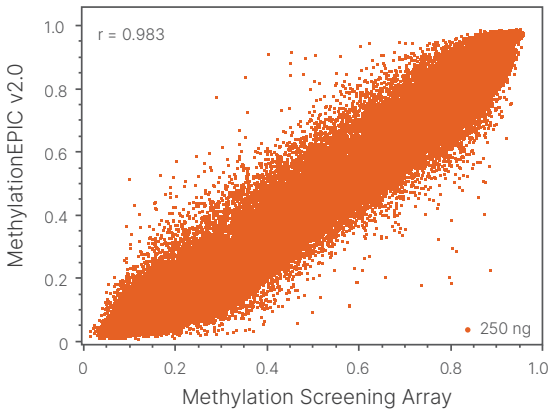
Furthermore, overlapping probes between the Infinium Methylation Screening Array and the Infinium MethylationEPICv2.0 BeadChip show > 96% sample-to-sample reproducibility, demonstrating robust performance of the EX Methylation assay.

Table 4: Performance and reproducibility specifications[a]

	Specifications	
DNA input amount	50 ng	250 ng
Sample-to-sample reproducibility	r ≥ 0.98	r ≥ 0.98
No. of sites detected	> 96%	> 96%

a. Using the GenomeStudio Methylation Module.

A. MethylationEPICv2.0 vs. Methylation Screening Array



B. Methylation Screening Array replicates

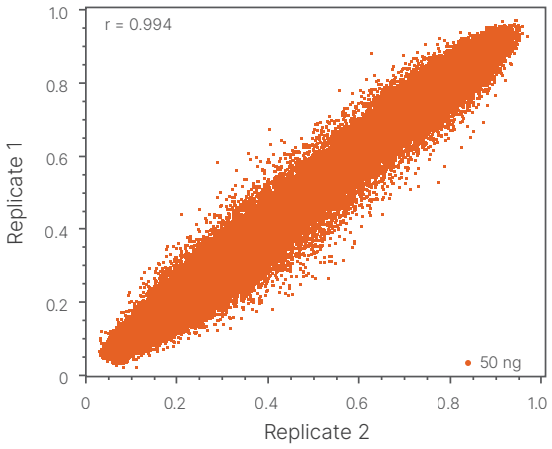


Figure 4: Highly reproducible methylation results—(A) Methylation results are highly correlated between Infinium Methylation Screening Array and Infinium MethylationEPIC v2.0 BeadChips. (B) Methylation results demonstrate excellent reproducibility between replicate samples analyzed on the Infinium Methylation Screening Array.

Improved scalability with EX Methylation workflow

The Infinium Methylation Screening Array, powered by EX Methylation, is the highest-throughput methylation assay to date. The 48-sample BeadChip format and automated liquid handling reduce per sample processing costs and deliver exceptional scalability for population-level methylation projects compared with other platforms. The three-day Infinium EX Methylation workflow features rapid

* The Bioconductor SeSAMe tool can be used to analyze Infinium Methylation Arrays, including dual methylation–SNP probes.

bisulfite conversion, automated BeadChip processing steps, and high throughput scanning (Figure 5). The advanced workflow also makes the Infinium Methylation Screening Array an excellent choice for high-volume methylation studies in comparison to other array formats and technologies (Figure 6).

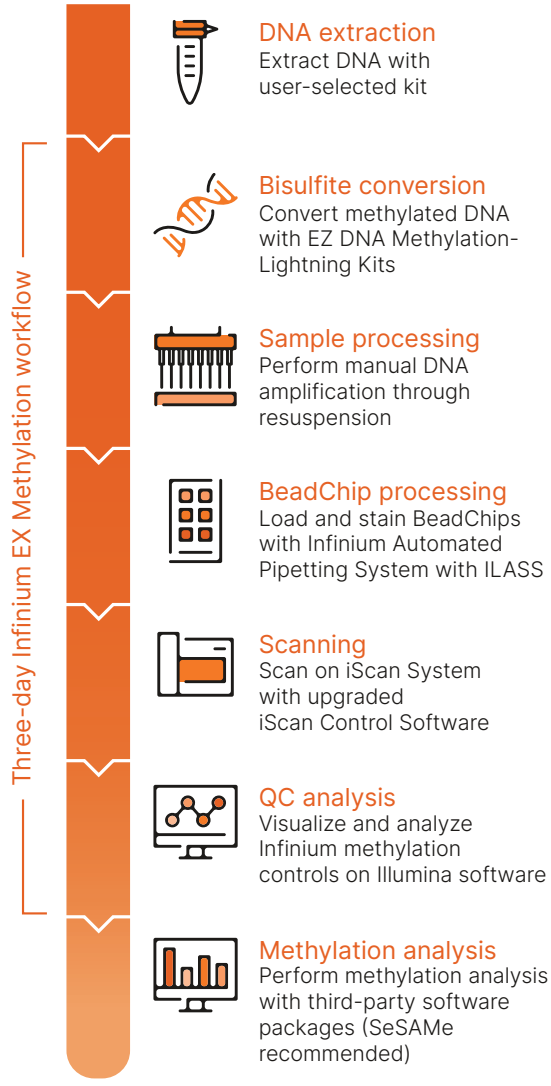


Figure 5: The Infinium Methylation Screening Array workflow—The workflow provides a three-day turnaround time from sample prep through QC analysis.

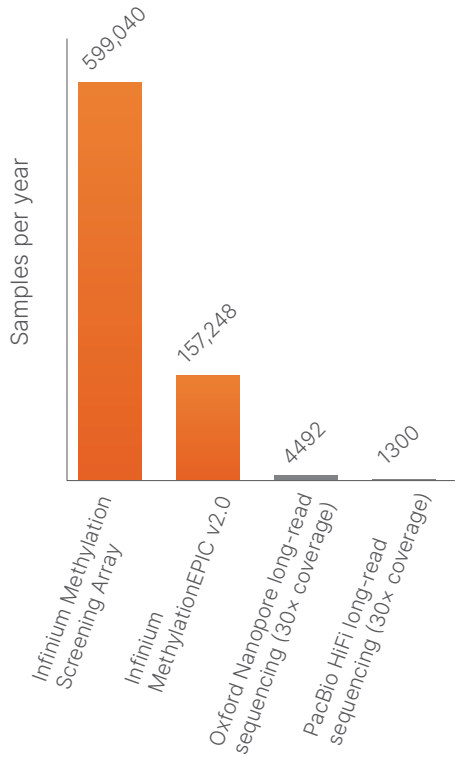


Figure 6: Annual sample throughput comparison for methylation analysis by common methods—The Infinium Methylation Screening Array provides the potential for exceptional sample throughput compared to other Infinium BeadChip formats and methylation sequencing methods.[14]

Simple QC and data analysis

Illumina offers software tools for quality control analysis of Infinium methylation BeadChips. The software provides visualization and simplified determination of pass or fail status using built-in controls as part of the Infinium methylation assay. For more information, visit the methylation array data analysis page.

Illumina recommends third-party user-friendly Bioconductor packages for downstream methylation data analysis. For example, SeSAMe offers signal preprocessing, detection calling, quality control, differential methylation modeling, visualization, inference, functional enrichment analysis, low-input data analysis, and population-specific analysis. SeSAMe also enables the interpretation of novel dual methylation-SNP probes on the Infinium Methylation Screening Array.

Flexible custom content

The Infinium Methylation Screening Array is also available in a semi-custom format that provides enhanced flexibility for unique projects. The semi-custom Infinium Methylation Screening Array combines the 270K backbone of the Methylation Screening Array with add-on content between 3,000 and 100,000 user-defined methylation sites. For additional information on adding custom content to the Infinium Methylation Screening Array, contact your local sales representative.

Summary

The Infinium Methylation Screening Array offers focused content for highly scalable analysis of methylation associations for common disease, exposures, aging, cell types, SNPs, and more. Expert content selection coupled with sample processing improvements enabled by the EX Methylation platform makes the Infinium Methylation Screening Array a cost-effective tool to power the new wave of population epigenomics research.

Learn more

Infinium Methylation Screening Array

Infinium Methylation Screening Array support

Methylation array data analysis

Ordering information

Product	Catalog no.
Infinium Methylation Screening Array-48 Kit (48 samples)	20112611
Infinium Methylation Screening Array-48 Kit (96 samples)	20112612
Infinium Methylation Screening Array-48 Kit (1152 samples)	20112613
Infinium Methylation Screening Array-48+ Kit (48 samples)[a]	20119540
Infinium Methylation Screening Array-48+ Kit (96 samples)[a]	20119541
Infinium Methylation Screening Array-48+ Kit (1152 samples)[a]	20119542

a. Kits with "+" designation indicate the capacity for custom marker content.

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