Infinium™ methylation microarrays: solutions for epigenetic researchers

Explore applications, insights, and research advantages

illumina®

M-GL-03307 v1.0

Introduction

DNA methylation analysis has emerged as a critical tool for uncovering novel insights into gene expression and cellular behavior.[1] These discoveries have driven progress in various fields, including cancer,[2–5] aging,[6,7] rare and neurological diseases,[8–11] and molecular epidemiology.[12]

Infinium methylation microarrays are powerful tools for exploring DNA methylation, offering cutting-edge content and streamlined, scalable workflows for generating high-quality data in epigenetic and epigenomic studies.[13] However, navigating today's research landscape requires increasingly strategic approaches that employ advanced methodologies and robust study designs. This guide presents information and resources on Infinium methylation microarrays and epigenetic research to support thoughtful study design, insight-driven data analysis, and effective scientific communication.

Strengthening research planning and communication

Effective research planning requires focus and clear communication on aligning scientific goals with evolving priorities. Illumina offers a range of resources to support researchers in this process, including guidance on study design and data analysis. For example, the Illumina eBook, *Understanding DNA methylation and its applications for human disease research*, provides comprehensive information on DNA methylation and epigenetic research, helping researchers to design robust studies and execute effective data analysis. Demonstrating the innovation, significance, and feasibility of a research effort—within a defined scope and timeframe—is essential when presenting ideas for review, collaboration, or investment. Key insights into how methylation microarrays deliver advanced solutions to support research goals include:

- **Cost-effective solution:** Microarrays provide a cost-effective option for research labs with limited budgets. They are less expensive per sample compared to sequencing methods like whole-genome bisulfite sequencing (WGBS), which can be costly and resource-intensive.[14] Microarrays also support high-throughput studies by analyzing multiple samples on a single chip, saving both time and money.[15] Their automated workflows reduce labor costs while providing accurate and reliable data, and analytical sensitivity equivalent to over 100× sequencing depth.[16]
- **A multiomic perspective:** Methylation microarrays excel at high-throughput epigenetic profiling, making them an ideal choice for multiomic studies.[13] The ability to integrate methylation data with other omics data sets, such as transcriptomics and proteomics, allows researchers to uncover complex interactions between genetic-, epigenetic-, and protein-level changes. This comprehensive approach reveals mechanisms underlying disease, identifies novel biomarkers, and provides a deeper understanding of biological pathways, strengthening the impact of research findings.
- **Enhanced translational potential:** Studies that integrate medical phenotypic information from sources like electronic health records (EHRs) are helping to advance translational research. For example, Thompson et al[17] combined methylation, genetic, and EHR data, including lab test results, from 831 patients in the UCLA Health biobank to predict clinical outcomes. The study used machine learning to develop methylation risk scores to help predict individual disease risk, severity, and treatment success. The addition of methylation risk scores improved predictions by nearly 50%. In a study by Wojewodzic and Lavender,[18] genome-wide DNA methylation data from the Genomic Data Commons was used to identify methylation biomarkers in cancer diagnostics. Similarly, EpiSign, a machine learning classifier, has demonstrated the potential to identify hundreds of rare diseases and neurodevelopmental disorders by detecting unique epigenetic signatures.[8] These findings demonstrate the value of methylation data in advancing precision medicine and expanding our understanding of complex disease biology.
- **Scalablity for diverse populations:** The scalability of methylation microarrays makes them an invaluable tool for analyzing methylation patterns across diverse populations. This capability ensures broader applicability of research findings and addresses health disparities, increasing the societal impact of research.
- **High-powered studies:** Sufficient statistical power is essential for generating meaningful, reproducible results from DNA methylation data. While the high-throughput capacity of microarrays enables large sample sizes in epigenome-wide association studies (EWAS), data complexity can complicate statistical power assessment. User-friendly tools like pwrEWAS

are designed to simplify sample size estimation, helping to improve study design and the reliability of downstream analyses.

- **Clear and robust bioinformatics:** A comprehensive analysis plan is essential for maximizing the value of DNA methylation data. Effective strategies include data preprocessing, normalization, and statistical analysis tailored to the study's objectives. Methylation array analysis benefits from both Illumina software and user-developed pipelines that streamline the analytical process and improve efficiency. DRAGEN™ Array and Partek™ Flow™ software provide end-to-end, point-and-click methylation analysis solutions. The most commonly used third-party packages include minfi, SeSAMe (Sensible Step-wise Analysis of DNA Methylation BeadChips), and ChAMP (Chip Analysis Methylation Pipeline). More information on these and other methylation data analysis tools can be found on the Illumina methylation microarray data analysis tips web page. These end-to-end solutions provide a clear path from data generation to interpretation and insights, supporting rigorous and well-structured research.

Infinium methylation microarrays

Over the past decade, Infinium methylation microarrays powered by BeadArray™ technology have facilitated groundbreaking discoveries on the role of epigenetic mechanisms in human health and disease.[19,20] These methylation arrays offer robust data affordability and scalability to meet diverse project size requirements, making them an ideal tool for a wide range of epigenetic research applications, including:

- Identifying methylation-based disease biomarkers
- Constructing epigenetic aging clocks
- Identifying cell type-specific methylation patterns
- Discovering disease biomarkers through EWAS
- Detecting environmental exposures
- Generating disease risk scores
- Developing disease classifiers

Illumina offers two powerful arrays for distinct research needs. The Infinium Methylation Screening Array is designed for targeted and cost-effective screening of known trait associations, while the Infinium MethylationEPIC v2.0 BeadChip provides broader, genome-wide analysis (Table 1).

Advantages of Infinium arrays

Infinium methylation microarrays offer several advantages, including:

- **Reliability:** Infinium chemistry employs several bead replicates for each CpG site queried, each with thousands of probes, providing highly precise measurements that have been equated to over 100× sequencing depth of even coverage[16]
- **Comprehensive content:** Infinium microarrays cover CpG islands, nonCpG and differentially methylated sites, enhancers, open chromatin, transcription factor binding sites, and miRNA promoter regions, ensuring broad genomic coverage
- **Scalability:** Infinium microarrays are adaptable to both small-scale pilot studies and large-scale population analyses, supporting diverse research needs
- **Sample compatibility:** Sample types include fresh, frozen, and formalin-fixed, paraffin-embedded (FFPE) tissues, enabling flexible sample processing
- **Accessible data analysis tools:** Researchers can analyze data using Illumina software or open-source R-based tools, facilitating both specific needs and full end-to-end analysis

Scalable, rapid workflow

The Infinium methylation microarray workflow enables scalable and reliable methylation analysis. The assays have been optimized for use with automated, rapid bisulfite conversion methods. From DNA extraction to intensity files, the entire workflow can be completed within just three days (Figure 1).

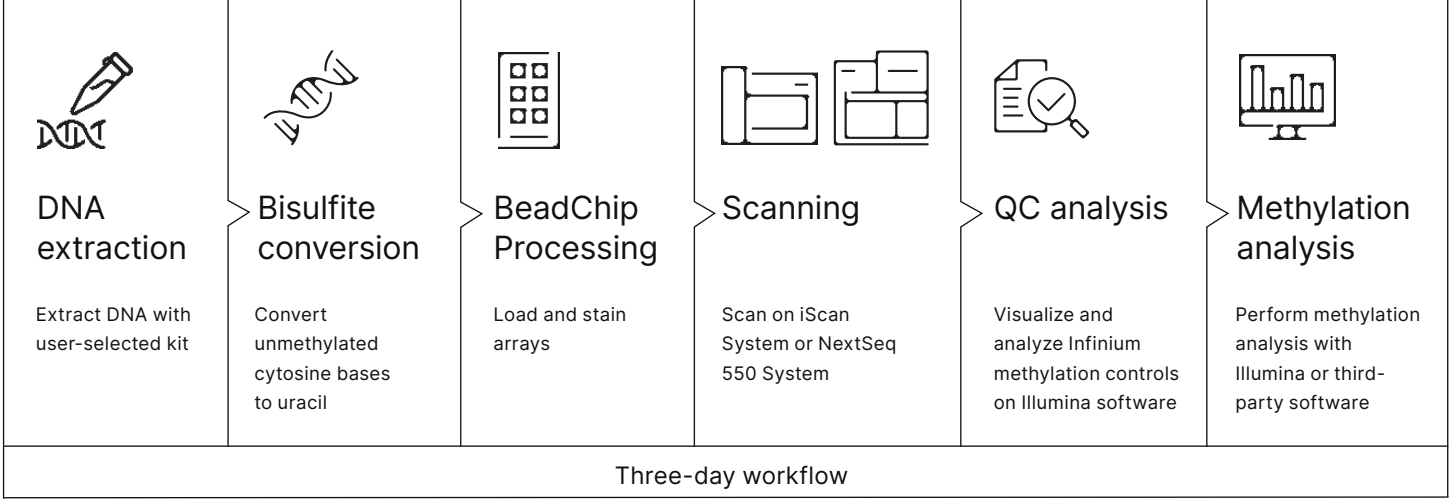
Table 1: Infinium methylation array specifications

	Infinium Methylation Screening Array Targeted methylation screening for population health research	**Infinium MethylationEPIC v2.0 Kit** 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 diesease trait associations • Known environmental exposure associations • Cell-type specific 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 classifers • Compatibility with published rare disease classifers • 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; MGMT, O^6-methylguanine-DNA methyltransferase; SNP, single nucleotide polymorphism; CNV, copy number variant.

Figure 1: Workflow for Infinium methylation arrays



Array kits provide all the required reagents for performing methylation analysis, except for the bisulfite conversion kits, which are purchased separately. Converted DNA is hybridized to the array and scanned using the Illumina iScan™ System or the NextSeq™ 550 System.* The information is compiled into an IDAT file, which contains the raw intensity values for each probe and is used for downstream analysis.

Data analysis

Infinium methylation microarrays offer flexible and efficient options for data management and analysis. DRAGEN Array provides cloud-based high-throughput quality control analysis and quantitative reporting, while GenomeStudio Software facilitates quality control analysis. Partek methylation provides an end-to-end solution for comprehensive genomic studies, from QC to differential methylation analysis. Data output is compatible with advanced tools like disease classifiers and epigenetic clocks, providing insights into disease mechanisms and aging. The minimal storage and computing requirements offer a cost-effective solution for analysis while remaining scalable for larger studies. These features enable researchers to build effective strategies for preprocessing, quality control, and analysis, strengthening their overall approach to data generation and bioinformatics.

* NextSeq 550 Systems support the Infinium MethylationEPIC v2.0 BeadChip only.

Summary

Infinium methylation microarrays, together with the resources described in this guide, can support researchers in the design and execution of studies to deepen our understanding of epigenetic mechanisms in human health and disease. These solutions can aid in research planning, methodological innovation, data interpretation, and communciation to strengthen study design and impact.

→

Resources

Introduction to Methylation Array Analysis

Infinium MethylationEPIC v2.0 Kit

Infinium Methylation Screening Array-48 Kit

References

1. Barnes KC. Chapter 1 - Epigenetics and methylation risk scores. In: Kelly L, Stanford WP, eds. *Implementation of Personalized Precision Medicine*. Academic Press; 2025:1-22. doi:10.1016/B978-0-323-98808-7.00006-0
2. Sharma S, Kelly TK, Jones PA. Epigenetics in cancer. *Carcinogenesis*. 2010;31(1):27-36. doi:10.1093/carcin/bgp220
3. Papanicolau-Sengos A, Aldape K. DNA methylation profiling: an emerging paradigm for cancer diagnosis. *Annu Rev Pathol*. 2022;17:295-321. doi:10.1146/annurev-pathol-042220-022304
4. Kulis M, Queirós AC, Beekman R, Martín-Subero JI. Intragenic DNA methylation in transcriptional regulation, normal differentiation and cancer. *Biochim Biophys Acta*. 2013;1829(11):1161-1174. doi:10.1016/j.bbagrm.2013.08.001
5. Singh J, Sahu S, Mohan T, et al. Current status of DNA methylation profiling in neuro-oncology as a diagnostic support tool: a review. *Neurooncol Pract*. 2023;10(6):518-526. doi:10.1093/nop/npad040
6. Horvath S, Raj K. DNA methylation-based biomarkers and the epigenetic clock theory of ageing. *Nat Rev Genet*. 2018;19(6):371-384. doi:10.1038/s41576-018-0004-3
7. Hao Y, Han K, Wang T, Yu J, Ding H, Dao F. Exploring the potential of epigenetic clocks in aging research. *Methods*. 2024;231:37-44. doi:10.1016/j.ymeth.2024.09.001
8. Reilly J, Kerkhof J, Sadikovic B. EpiSigns: DNA methylation signatures in mendelian neurodevelopmental disorders as a diagnostic link between a genotype and phenotype. *Adv Mol Pathol*. 2020;3:29-39. doi:10.1016/j.yamp.2020.07.018
9. Parenti I, Rabaneda LG, Schoen H, Novarino G. Neurodevelopmental disorders: from genetics to functional pathways. *Trends Neurosci*. 2020;43(8):608-621. doi:10.1016/j.tins.2020.05.004
10. Sadikovic B, Levy MA, Kerkhof J, et al. Clinical epigenomics: genome-wide DNA methylation analysis for the diagnosis of Mendelian disorders. *Genet Med*. 2021;23(6):1065-1074. doi:10.1038/s41436-020-01096-4
11. Giuili E, Grolaux R, Macedo CZNM, et al. Comprehensive evaluation of the implementation of episignatures for diagnosis of neurodevelopmental disorders (NDDs). *Hum Genet*. 2023;142(12):1721-1735. doi:10.1007/s00439-023-02609-2
12. Nwanaji-Enwerem JC, Colicino E. DNA methylation-based biomarkers of environmental exposures for human population studies. *Curr Environ Health Rep*. 2020;7(2):121-128. doi:10.1007/s40572-020-00269-2
13. Illumina. Infinium Methylation Screening Array. illumina.com/content/dam/illumina/gcs/assembled-assets/marketing-literature/infinium-methylation-screening-array-data-sheet-m-gl-01893/infinium-methylation-screening-array-data-sheet-m-gl-01893.pdf. Published 2024. Accessed January 22, 2025.
14. Marabita F, Almgren M, Lindholm ME, et al. An evaluation of analysis pipelines for DNA methylation profiling using the Illumina HumanMethylation450 BeadChip platform. *Epigenetics*. 2013;8(3):333-346. doi:10.4161/epi.24008
15. Bibikova M, Le J, Barnes B, et al. Genome-wide DNA methylation profiling using Infinium assay. *Epigenomics*. 2009;1(1):177-200. doi:10.2217/epi.09.14
16. Zhou L, Ng HK, Drautz-Moses DI, et al. Systematic evaluation of library preparation methods and sequencing platforms for high-throughput whole genome bisulfite sequencing. *Sci Rep*. 2019;9(1):10383. doi:10.1038/s41598-019-46875-5
17. Thompson M, Hill BL, Rakocz N, et al. Methylation risk scores are associated with a collection of phenotypes within electronic health record systems. *npj Genom Med*. 2022;7(1):1-11. doi:10.1038/s41525-022-00320-1
18. Wojewodzic MW, Lavender JP. Diagnostic classification based on DNA methylation profiles using sequential machine learning approaches. *PLoS One*. 2024;19(9):e0307912. doi:10.1371/journal.pone.0307912
19. Wei S, Tao J, Xu J, et al. Ten years of EWAS. *Adv Sci (Weinh)*. 2021;8(20):2100727. doi:10.1002/advs.202100727
20. Moran S, Arribas C, Esteller M. Validation of a DNA methylation microarray for 850,000 CpG sites of the human genome enriched in enhancer sequences. *Epigenomics*. 2016;8(3):389-399. doi:10.2217/epi.15.114

illumina®

1.800.809.4566 toll-free (US) | +1.858.202.4566 tel
techsupport@illumina.com | www.illumina.com

M-GL-03307 v1.0