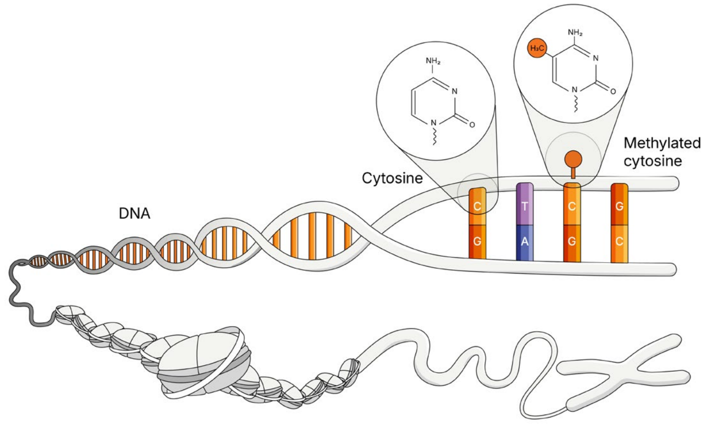
Illumina 5-base solution

One assay. Dual insights.

Integrated genomics and epigenomics to accelerate rare and undiagnosed disease research

Unlock genomic variants and disease-specific DNA methylation signatures simultaneously— using a single, streamlined Illumina 5-base assay.



Why it matters

Advancing the understanding of rare diseases
Some rare diseases are caused by gene dysregulation and exhibit disease-specific episignatures. In other cases, rare-disease variants can be difficult to interpret. An integrated epigenomic and genomic analysis can help elucidate rare disease mechanisms, improve variant interpretation, and advance research.

Integrated discovery in a single workflow
Detect genomic variants (SNVs,* indels,* CNVs/SVs)* and DNA methylation (5mC)* together—reducing time, cost, and sample requirements compared to multi-assay approaches.

Multiomic insight in rare disease research
Multiomic readouts enable classifiers, computational tools, for the identification of epigenetic fingerprints (eg, imprinting and chromatin disorders), supporting deeper, more confident insights.

Key features of the Illumina 5-base solution

Dual-omic output in one run
Variant calling and methylation profiling from the same library and sequencing workflow, enabling simplified preparation and analysis.

Integrated analysis
DRAGEN™ pipelines for combined methylation including differentially methylated regions (DMR) detection and variant calling, plus Illumina Connected Multiomics for visualization and interpretation—no advanced bioinformatics required.

Works with precious, limited DNA
Supports low-input samples typical of rare disease cohorts, including genomic DNA (gDNA) from blood or saliva. A single assay conserves sample, requiring only 50–100 ng gDNA.

Scalable throughput
Compatible with NovaSeq™ X Series for cohort studies, enabling streamlined turnaround from DNA to results. Up to 15,000 genome/methylomes estimated per system per year whole-genome sequencing, automation-enabled.

Flexible study designs
Run whole-genome sequencing (WGS) for broad discovery or targeted enrichment for deeper coverage across disease-relevant loci and panels.

* SNVs, single nucleotide variants; indels, insertions-deletions; CNVs, copy number variants; SVs, structural variants; 5mC, 5-methylcytosine

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How Illumina 5-base advances rare disease research

- **Improve variant interpretation**
  Strengthen variant resolution, such as variant of unknown significance (VUS) or *de novo* variants, by understanding gene regulation, function or specific episignatures of rare disease.

- **Imprinting and chromatin disorders**
  Comprehensive coverage across imprinting regions, with the potential to assess low-level mosaicism.

- **Pattern recognition in cohort studies**
  Strengthen interpretation by identifying disease-specific episignatures, stratify research cohorts, classify beyond genetic heterogeneity, or improve confidence in variant classification.

- **Classifier integration**
  Compatible with established computational tools used in rare disease research (eg, EpiSign), alongside secondary and tertiary analysis workflows (eg, Emedgene™ software).

Example applications

- **Shortening the path to disease research insight**
  Multiomic profiles provide integrated genomic and epigenomic insights that help stratify undiagnosed subjects and prioritize follow-up research.

- **Gene panel and enrichment studies**
  Deepen coverage across known disease genes and regulatory regions to capture sequence and methylation signals together.

- **Population and registry studies**
  Scalable WGS plus methylome profiling enables epigenome-wide association studies (EWAS) for discovery of novel disease markers and epigenetic signatures.

- **Epigenotyping**
  Comprehensive profiling of DNA methylation patterns (episignatures) to classify rare diseases, resolve VUS, and uncover novel epigenetic biomarkers.

Integrated workflow for rare disease research

1. Library prep
Illumina 5-Base DNA Prep and Illumina 5-Base DNA Prep with Enrichment

2. Sequencing
NovaSeq systems, NextSeq™ 2000 for flexible throughput

3. Analysis
Integrated DRAGEN methylation + variant calling; Connected Multiomics for interpretation/visualization

Ready to advance rare disease research?

Learn more about the Illumina 5-base solution

Workflow advantages

- **Minimal incremental sequencing** required for methylation insights
- **Seamless integration** with existing Illumina systems and software

Illumina 5-base solution workflow

Prepare libraries

Sequence

Analyze data

Interpret results (genomic & epigenomic)

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