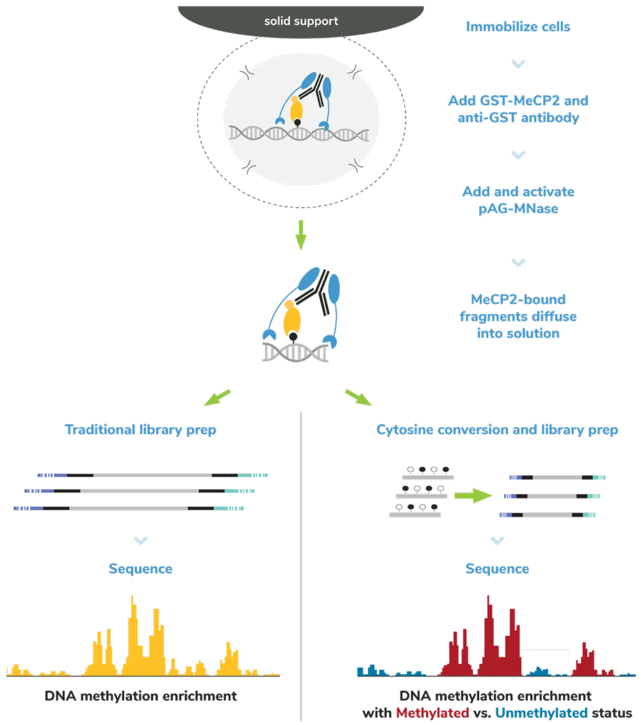
CUTANA™ meCUT&RUN

Genome-Wide DNA Methylation Sequencing



Immobilize cells

Add GST-MeCP2 and anti-GST antibody

Add and activate pAG-MNase

MeCP2-bound fragments diffuse into solution

Traditional library prep

Sequence

DNA methylation enrichment

Cytosine conversion and library prep

Sequence

DNA methylation enrichment with Methylated vs. Unmethylated status

Part 1: Enrich for methylated DNA

- A GST-tagged methylation-binding domain derived from human MeCP2 is used to capture methylated DNA fragments.

Part 2: Library prep and sequencing

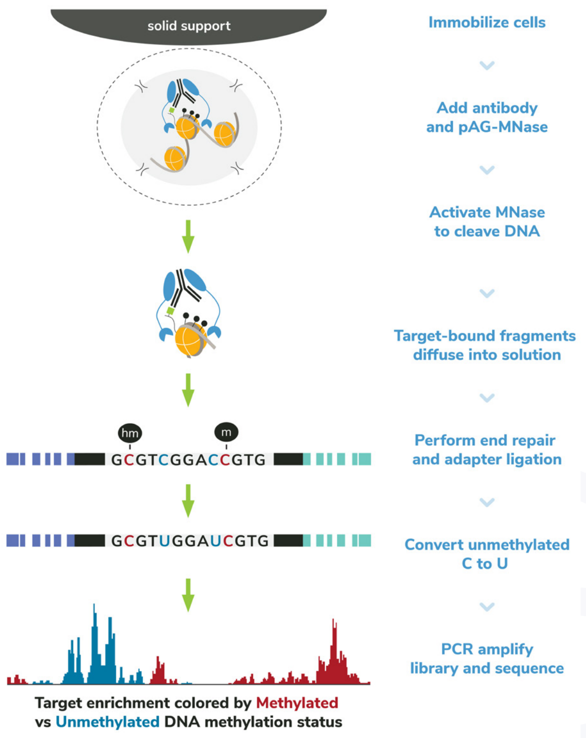
Users have two options, providing maximal flexibility:

- **Option 1 (meCUT&RUN):** Traditional library prep provides an overview of 5mC enrichment. Requires **15-20 M** total sequencing reads.
- **Option 2 (meCUT&RUN-EM):** Cytosine conversion and library prep provides base-pair resolution 5mC analysis.
  Requires **30-50 M** total reads.

Sep 2025 v1.0

CUTANA™ Multiomic CUT&RUN

Simultaneous analysis of DNA methylation and chromatin proteins



Immobilize cells

Add antibody and pAG-MNase

Activate MNase to cleave DNA

Target-bound fragments diffuse into solution

Perform end repair and adapter ligation

Convert unmethylated C to U

PCR amplify library and sequence

Target enrichment colored by Methylated vs Unmethylated DNA methylation status

Part 1: CUT&RUN to enrich target chromatin

- CUT&RUN technology is used to first enrich for antibody-bound chromatin.
- Robust for histone PTMs, transcription factors, and other chromatin protein targets.

Part 2: Cytosine conversion & library prep

- Methylated CpGs are detected at target proteins using either bisulfite conversion or Enzymatic Methyl-seq (NEB® EM-seq™).
- EM-seq is the preferred method for Multiomic CUT&RUN because it is less harsh than bisulfite, preserves DNA integrity, and is optimized for low-input samples — making it ideal for CUT&RUN applications.

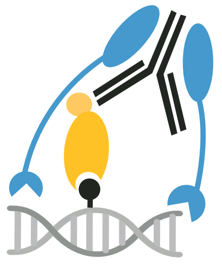
EpiCypher
Bringing Epigenetics to Life

epicypher.com | info@epicypher.com
855.374.2461

EpiCypher
Bringing Epigenetics to Life

CUTANA™
DNA Methylation Sequencing Assays

meCUT&RUN



Low-cost, Genome-Wide DNA Methylation Mapping

Multiomic CUT&RUN

Simultaneously map DNA methylation and chromatin proteins

CUTANA™ meCUT&RUN

An Affordable Solution for Genome-Wide DNA Methylation Sequencing

CUTANA™ **meCUT&RUN** is a novel enrichment-based method for DNA methylation (DNAme) sequencing that delivers **high-quality, genome-wide profiles** at a **fraction of the cost and input required** for whole-genome bisulfite sequencing (WGBS).

WGBS require deep sequencing, while targeted methods sacrifice coverage and resolution. DNAme researchers thus face a tough choice between expensive whole-genome bisulfite sequencing (WGBS) or limited insights from reduced representation bisulfite sequencing (RRBS) and other assays.

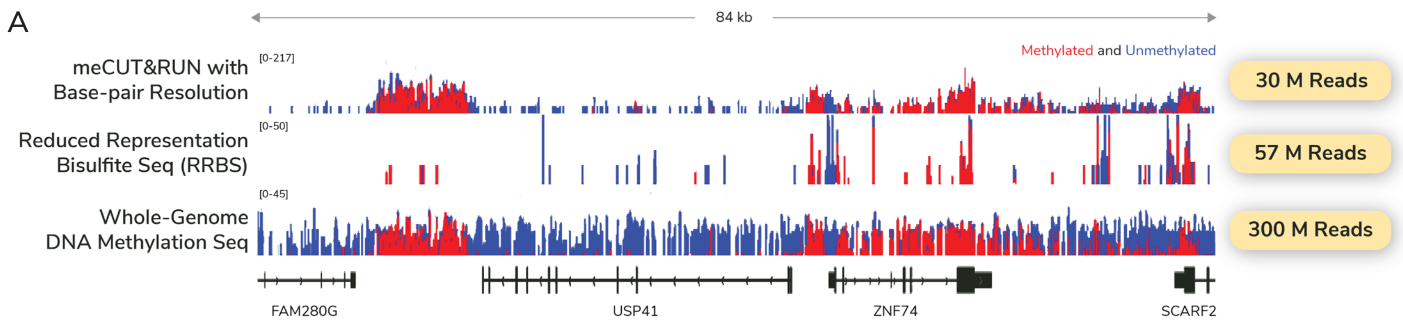
meCUT&RUN is a low-cost DNAme mapping solution that doesn't sacrifice coverage

Why Choose meCUT&RUN:

- **High coverage**
  Captures 80% of methylated CpGs.
- **Low cost**
  20-fold reduced sequencing costs vs. WGBS.
- **Compatible with precious samples**
  Robust down to 10,000 cells.
- **Minimal bias**
  Avoids destructive bisulfite conversion.

Technology	meCUT&RUN	RRBS	Microarrays	Hybridization Panels	WGBS
Input	**10k - 500k cells**	10 - 500 ng DNA	250 ng DNA	200 ng DNA	50 ng - 5 µg DNA
Coverage	**80% Methylated CpGs**	Limited (5-15% CpGs)	Limited (~3% CpGs)	Limited (~15% CpGs)	Whole genome
Recommended Sequencing Depth	**>15 M reads**	50-100 M reads	N/A	>100 M reads	>800 M reads
Turnaround Time	**Days**	Weeks	Days	Weeks	Weeks
Base-Pair Conversion	**Optional**	Required	Required	Required	Required
Overall Cost	**$**	$$	$$	$$	$$$

meCUT&RUN delivers genome-wide signal with low sequencing requirements



meCUT&RUN provides comprehensive coverage across functional elements, far exceeding RRBS

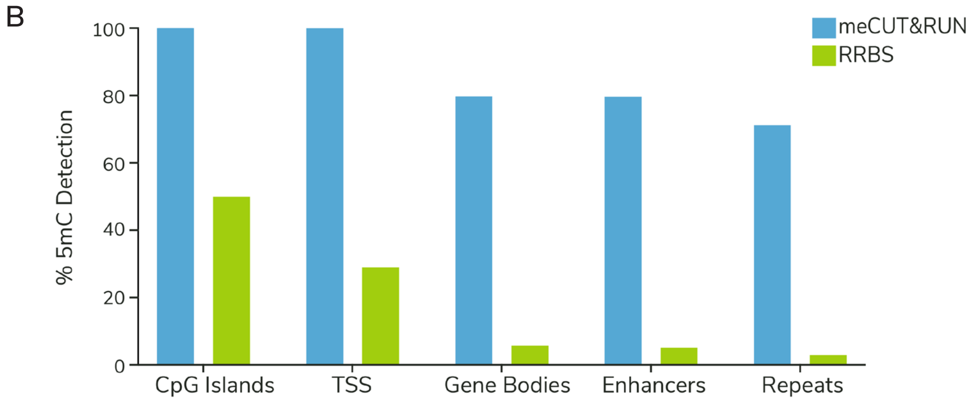


FIGURE 1

CUTANA™ meCUT&RUN was paired with enzymatic conversion to thoroughly evaluate its performance against targeted bisulfite-conversion assays (RRBS) and whole-genome, enzymatic-based approaches (EM-seq; 300 M reads) in K562 cells.

(A) Representative sequencing tracks.
(B) Percent 5mC coverage calculated relative to EM-seq.

CUTANA™ Multiomic CUT&RUN

Next-Gen Multiomic Profiling of DNA Methylation and Chromatin Proteins

CUTANA™ **Multiomic CUT&RUN** is a next-generation epigenomic mapping strategy that **profiles chromatin proteins and DNA methylation together** in a **single reaction**, capturing novel insights to drive biological discovery.

Traditional multiomic DNA methylation approaches integrate ChIP-seq with whole genome bisulfite sequencing (WGBS) datasets. However, these assays are cost-prohibitive for many labs, require large numbers of cells, take weeks (or longer!) to complete, and generate data that are indirect, restricting biological interpretations.

Multiomic CUT&RUN provides insights of chromatin regulation in a single workflow

Why Choose Multiomic CUT&RUN:

- **Reveal the full regulatory landscape**
  Map DNA methylation at protein binding sites with base-pair resolution.
- **Streamline discovery with a single workflow**
  Multiple -omic insights from one sample.
- **Low cost, maximal sensitivity**
  Low cell inputs and sequencing requirements provide flexibility.

Technology	Multiomic CUT&RUN	ChIP-seq + Whole Genome Bisulfite Sequencing	
	1 Simple Workflow	Workflow 1: ChIP-seq	Workflow 2: WGBS
Input	**5k-500k cells**	>1 million cells	50 ng - 5 µg DNA
Turnaround Time	**4-5 Days**	Weeks	Weeks
Multiomic Data?	**Yes**	No	No
Recommended Sequencing Depth	**>30 M reads**	>30 M reads	>800 M reads
Computational Complexity	**Low**	Requires complex integration of two distinct datasets	
Overall Cost	**$**	$$$	

Multiomic CUT&RUN maps DNA methylation at diverse chromatin targets

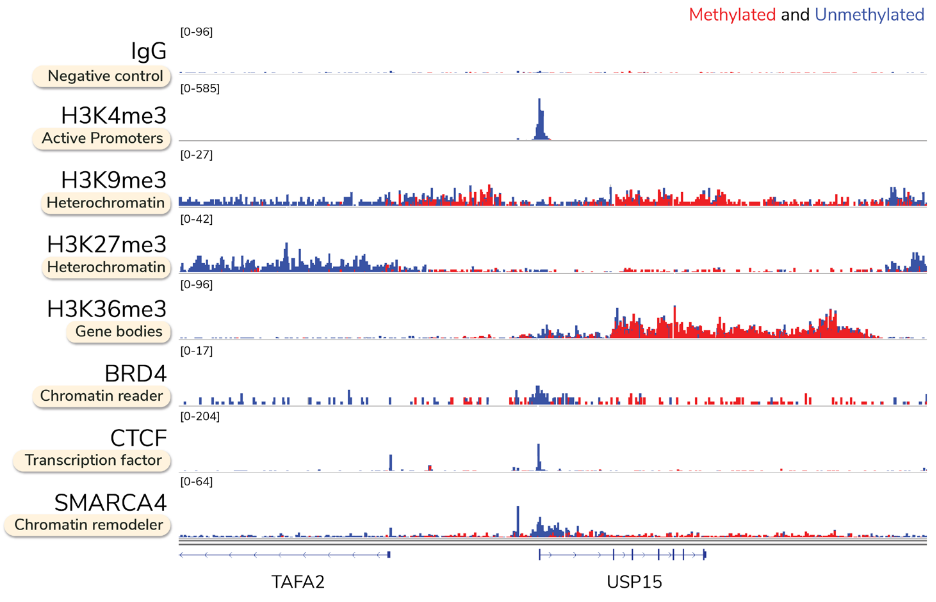


FIGURE 2

CUTANA™ Multiomic CUT&RUN provides base-pair resolution of CpG methylation at transcription factor binding sites, histone PTMs, and chromatin-modifying enzymes.

Each reaction used 500,000 K562 cells. Target chromatin was enriched with the CUTANA Multiomic CUT&RUN Workflow, followed by Enzymatic Methyl-seq (NEB® EM-seq™) conversion and library prep.

Key Applications:

- Gauge the impact of DNA methylation on transcription factor binding
- Resolve crosstalk between histone modifications and DNA methylation
- Understand the epigenetic mechanisms of gene regulation