CUTANA® platform assays use a proprietary immunotethering method to deliver ultrasensitive chromatin profiling. Based on the Chromatin Immuno-Cleavage (ChIC) method, this technology supports Cleavage Under Targets and Release Using Nuclease (CUT&RUN) and Cleavage Under Targets and Fragmentation (CUT&Tag) experiments. CUT&RUN reagents are available now, and CUT&Tag is launching in June 2020! See back cover for ordering information.

ADVANTAGES:
• Reduced cost
• Flexibility to customize experimental workflow

ORDERING INFO:
New to CUT&RUN? Lack the resources to perform assay internally? We can help! Inquire at info@epicypher.com to learn more about EpiCypher's 'end-to-end' assay services for ChIC/CUT&RUN

Enzyme Fusions
pAG-MNase for ChIC/CUT&RUN
Catalog No. 15-1
50 rxns
Catalog No. 15-1
116 250 rxns
pAG-Tn5 for ChIC/CUT&Tag
Catalog No. 15-1017 50 rxns
Catalog No. 15-1117 250 rxns

Do-It-Yourself CUTANA Compatible Antibodies
H3K4me3
Catalog No. 13-0041 100 µg
H3K27me3
Catalog No. 13-0030 100 µg
H3K36me3
Catalog No. 13-0031 100 µg
Rabbit IgG Negative Control
Catalog No. 13-0042 100 µg

Spike-in Controls
E. coli DNA
Catalog No. 18-1401 100 ng

Additional Tools & Reagents
ConA Conjugated Paramagnetic Beads
Catalog No. 21-1401 50 rxns
Catalog No. 21-1411 250 rxns
8-strip 0.2 mL PCR Tubes
Catalog No. 10-0009 120 strips
Magnetic Separation Racks
Catalog No. 10-0012 1.5 mL tubes
Catalog No. 10-0008 0.2 mL tubes
High Fidelity 2X PCR Master Mix for CUT&Tag
Catalog No. 15-1018 50 rxns
DNA Isolation Kit
Coming Soon

Validated Kits
ADVANTAGES:
• Optimized workflow (cells ➞ DNA)
• Validated reagents
• Streamlined sample handling for higher throughput
• Included controls for troubleshooting

ORDERING INFO:
Assay Kit for ChIC/CUT&RUN
Coming Soon
Assay Kit for ChIC/CUT&Tag
Coming Soon

Services
ADVANTAGES:
• End-to-end services
• Customized
• Optimized protocols designed to capture challenging targets
• High priority projects

CUTANA® ASSAYS
For ultrasensitive genomic mapping

EpiCypher.
Bringing Epigenetics to Life

CUTANA® ASSAYS
For ultrasensitive genomic mapping
**CUTANA® Products and Services**

**CUTANA® platform assays use a proprietary immunotethering method to deliver ultrasensitive chromatin profiling.**

Based on the Chromatin ImmunoCleavage (ChIC) method, this technology supports Cleavage Under Targets and Release Using Nuclease (CUT&RUN) and Cleavage Under Targets and Tagmentation (CUT&Tag) experiments. CUT&RUN reagents are available now, and CUT&Tag is launching in June 2020! See back cover for ordering information.

**Overview of the CUTANA CUT&RUN approach**

**FIGURE 1**

In CUTANA CUT&RUN, cells (or nuclei) are immobilized on lectin-coated magnetic beads, permeabilized, and incubated with an antibody to a chromatin target (e.g. histone PTM or chromatin/DNA interacting protein). Next, a fusion of Proteins A and G with micrococcal nuclease (pAG-MNase) is added and activated via Ca++. The clipped chromatin fragments diffuse out, followed by DNA purification and next-generation sequencing.

**CUTANA® CUT&RUN Assays offer distinct advantages over ChIP-seq**

- Low background: only 3-5 million sequencing reads required
- Lower cost: >10-fold less antibody and required sequencing depth
- High signal-to-noise (S/N), even down to low cell numbers
- Compatible with a variety of targets and sample types
- Robust, simple workflow, high throughput compatible

CUTANA is proprietary technology based on ChIC (US20070009937A1; Schmid et al, Mol Cell 2004) and CUT&RUN (patent pending; Skene and Henikoff, eLIFE 2017) methodology.
CUTANA® Products and Services

CUTANA CUT&RUN improves S/N and reduces sequencing depth

ChIP-seq requires deep sequencing (typically >30 million reads) to resolve signal from background. In CUT&RUN, targeted release of genomic fragments into solution results in inherently low background. Therefore, very low sequencing depth (only 3-5 million reads) is required, dramatically reducing experimental costs.

FIGURE 2
A representative 350 kb region of an H3K4me1 profile in K-562 cells, generated using CUT&RUN (yellow panels), native ChIP-seq (blue panels), or crosslinked ChIP-seq (green panels). All data were generated by EpiCypher and are expressed as reads per million (RPM). Color-coded gradient (to left) represents S/N ratios determined by genome wide analysis (bamFingerprint data, not shown).

CUTANA CUT&RUN generates high quality data with low cell numbers

For initial optimization experiments, it is recommended to start with 500,000 cells. However, data quality is indistinguishable down to 5,000 cells with no changes to the optimized workflow (EpiCypher.com/protocols/).

FIGURE 3
In CUTANA CUT&RUN K-562 cell titration experiments, data quality is largely indistinguishable from 500,000 cells down to 5,000 cells. Genome tracks show representative regions from cell titration experiments for a variety of different targets, including a euchromatin-associated histone PTM (H3K4me3, left), heterochromatin-associated PTM (H3K27me3, middle) and a chromatin binding protein (BRD4, right).
CUTANA® Products and Services

CUT&RUN enables genomic mapping for diverse targets

- Histone PTMs, including euchromatin and heterochromatin associated marks
- Transient chromatin interacting proteins, such as transcription factors, epigenetic enzymes, and epigenetic readers
- Chromatin remodeling proteins, which are challenging to enrich using ChIP-seq

FIGURE 4
Representative CUT&RUN genome browser tracks (chr1:47,660,000-47,995,000) show high quality profiles generated for a variety of targets, including histone PTMs (methylation and acetylation: H3K4me3, H3K27me3, H3K27ac), transcription factors (CTCF), chromatin reader proteins (BRD4), chromatin writers (MLL histone methyltransferase), and chromatin remodeling enzymes (SMARCA4).

FIGURE 5
CUT&RUN data is indistinguishable regardless of whether fresh cells, cryopreserved cells, formaldehyde fixed cells, or nuclei are used as input. Data are visualized by heatmap where reads are aligned to the transcription start site (TSS, +/- 2kb) of 18,793 genes. High and low signal are ranked by intensity (top to bottom) and reflected by red and blue colors, respectively. Gene rows in each heatmap are aligned relative to fresh cells (far left), showing that all genes show similar enrichment patterns regardless of the sample preparation method.

CUT&RUN is compatible with diverse sample types
CUTANA® Products and Services

Streamlined workflow: From cells to data in < 4 days

EpiCypher has developed a robust protocol for CUT&RUN, available at EpiCypher.com/protocols/. Kits are also available to support the workflow, including step-by-step instructions with validated reagents to go from cells to DNA. Due to low sequencing requirements, benchtop sequencers (e.g. Illumina MiniSeq) can be used to quickly generate high resolution data.

Get started designing your experiment

Robust, easy to follow protocols

Follow these links to EpiCypher’s optimized CUTANA CUT&RUN and CUT&Tag protocols. Fully-validated CUT&RUN kits are coming soon, which will include reagents and a detailed protocol to support the workflow from cells or nuclei to isolated CUT&RUN DNA.

Control your experiment every step of the way using platform-validated reagents

- CUTANA Compatible Positive and Negative Control Antibodies: Tested for specificity using EpiCypher’s recombinant nucleosome panels, verified to yield robust results in CUT&RUN.
- E. coli DNA Spike-in Control: Directly verified in CUT&RUN; provides a standard for experimental normalization.

Check out these papers for validated approaches to get ideas for your next experiment

CUT&RUN workflows
- Skene and Henikoff, eLIFE 2017 (PMID : 28079019)
- Thakur and Henikoff, G&D 2018 (PMID : 29386331)
- Liu et. al, Cell 2018 (PMID : 29606353)
- Skene et. al, Nat. Protoc. 2018 (PMID : 29651053)
- Janssens et. al, Epi. Chromatin 2018 (PMID : 30577869)
- Brahma and Henikoff, Mol. Cell 2019 (PMID : 30554944)
- Oomen et. al, Genome Res. 2019 (PMID : 30655336)
- Zheng and Gehring, Plant Reprod. 2019 (PMID : 30719569)
- Ernst et. al, Nat. Commun. 2019 (PMID : 30890697)
- Hainer et. al, Cell, 2019 (PMID : 30955888) **Single Cell**
- Meers et. al, eLIFE 2019 (PMID : 31232687)*  
* Paper describes optimized protocol using pAG-MNase
- Li et. al, Cell Rep. 2020 (PMID : 31940490)

ChIC workflows
- Ku et. al, Nat. Methods 2019 (PMID : 30923384) **Single Cell**

Upcoming technology: CUT&Tag workflows
Go from cells to NGS sequencing libraries by direct tagmentation of sequence adapters to target genomic loci! Learn about this new & upcoming technology and stay tuned for new product releases and validated protocols!
- Kaya-Okur et. al, Nat. Comm. 2019 (PMID : 31036827) **Single Cell**
- Schmunk et. al, bioRxiv. 2020 (2020.03.24.006874v1)
- Henikoff and Henikoff, bioRxiv. 2020 (2020.04.15.043083)*  
* Uses EpiCypher’s pAG-Tn5 and CUTANA compatible antibodies
CUTANA® platform assays use a proprietary immunotethering method to deliver ultrasensitive chromatin profiling. Based on the Chromatin Immuno Cleavage (ChIC) method, this technology supports Cleavage Under Targets and Release Using Nuclease (CUT&RUN) and Cleavage Under Targets and Fragmentation (CUT&Tag) experiments. CUT&RUN reagents are available now, and CUT&Tag is launching in June 2020! See back cover for ordering information.

**ADVANTAGES:**
- Reduced cost
- Flexibility to customize experimental workflow

**ORDERING INFO:**

**Enzyme Fusions**
- pAG-MNase for ChIC/CUT&RUN
  - Catalog No. 15-1016 50 rxns
  - Catalog No. 15-1116 250 rxns
- pAG-Tn5 for ChIC/CUT&Tag
  - Catalog No. 15-1017 50 rxns
  - Catalog No. 15-1117 250 rxns

**CUTANA Compatible Antibodies**
- H3K4me3
  - Catalog No. 13-0041 100 µg
- H3K27me3
  - Catalog No. 13-0030 100 µg
- H3K36me3
  - Catalog No. 13-0031 100 µg
- Rabbit IgG Negative Control
  - Catalog No. 13-0042 100 µg

**Additional Tools & Reagents**
- ConA Conjugated Paramagnetic Beads
  - Catalog No. 21-1401 50 rxns
  - Catalog No. 21-1411 250 rxns
- 8-strip 0.2 mL PCR Tubes
  - Catalog No. 10-0009 120 strips
- Magnetic Separation Racks
  - Catalog No. 10-0012 1.5 mL tubes
  - Catalog No. 10-0008 0.2 mL tubes
- High Fidelity 2X PCR Master Mix for CUT&Tag
  - Catalog No. 15-1018 50 rxns
- DNA Isolation Kit
  - Coming Soon

**Spike-in Controls**
- E. coli DNA
  - Catalog No. 18-1401 100 ng

**ADVANTAGES:**
- Optimized workflow (cells ➞ DNA)
- Validated reagents
- Streamlined sample handling for higher throughput
- Included controls for troubleshooting

**ORDERING INFO:**

**Validated Kits**
- Assay Kit for ChIC/CUT&RUN
  - Coming Soon
- Assay Kit for ChIC/CUT&Tag
  - Coming Soon

**ADVANTAGES:**
- End-to-end services
- Customized
- Optimized protocols designed to capture challenging targets
- High priority projects

**Services**

New to CUT&RUN? Lack the resources to perform assay internally?

**We can help!**
Inquire at info@epicypher.com to learn more about EpiCypher’s ‘end-to-end’ assay services for ChIC/CUT&RUN

EpiCypher.com
855.374.2461
info@epicypher.com