Advances in Chromatin Remodeling Research

Chromatin remodeling complexes are crucial regulators of chromatin structure and gene expression. An estimated 20% of human cancers contain mutations in the SWI/SNF remodeling complex, making these proteins important drug targets. EpiCypher is at the forefront of epigenetics technology development, providing new tools to transform chromatin remodeling research.

SUBUNIT	CANCER
ARID1A	Ovarian, Hepatocellular, Bladder, Gastric, Endometrioid, Pancreatic, Colon, Lung, Neuroblastoma, Burkitt Lymphoma
ARID1B	Melanoma, Neuroblastoma, Hepatocellular, Pancreatic, Liver
PBRM1	Renal cell carcinoma, Breast, Gastric, Pancreatic
ARID2	Melanoma, Hepatocellular, Pancreatic
SMARCA2	Lung, Colon, Breast
SMARCA4	Lung, Medulloblastoma, Burkitt Lymphoma, SCCOHT
SMARCB1	Rhabdoid tumor, Familial Schwannomatosis
SMARCE1	Spinal meningioma
BRD7	Breast

TABLE 1

List of cancers associated with various SWI/SNF subunit mutations. *Adapted from Helming et al. Cancer Cell 26, 309-317 (2014).*

EpiDyne® Chromatin Remodeling Assays

Chromatin remodelers have been challenging to target for therapeutic development, as there were no assays to directly monitor remodeling activity. The EpiDyne® platform was created to address this problem in epigenetics research, leveraging recent advances in biochemistry to advance the study of remodeling complexes.

- Direct analysis of remodeling activity on a nucleosome substrate
- Many readouts available (radioactivity, FRET, etc.)
- Only commerical provider of enzymatically active SMARCA4/BRG1 and SMARCA2/BRM
- HTS-compatible for drug discovery

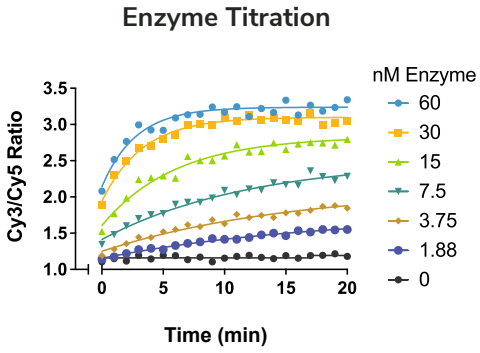

FIGURE 1

Ultra-sensitive readout of SWI/SNF remodeling activity using EpiDyne substrates and enzymes. *SMARCA4 enzyme was titrated against EpiDyne-FRET nucleosomes, and remodeling activity was determined by the ratio of Cy3/Cy5 at varying time points.*

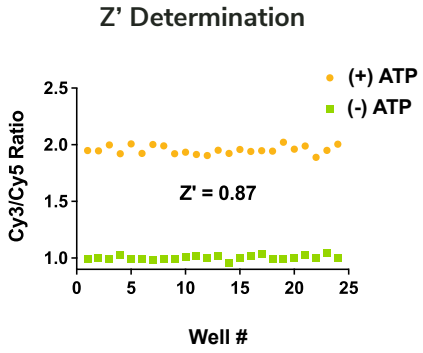

FIGURE 2

EpiDyne is suitable for high-throughput compound screening. *SMARCA4 was incubated in triplicate with EpiDyne-FRET substrates. Z' was calculated as an indicator of consistency and reliability for HTS. No ATP (-) is the negative control. All reactions contain DMSO vehicle control to mimic HTS conditions.*

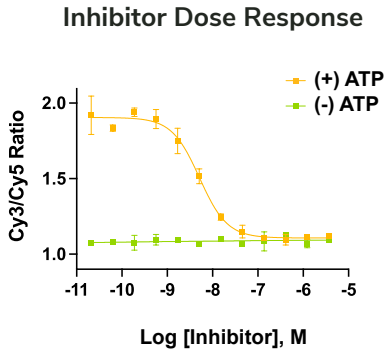

FIGURE 3

Characterization of a novel SWI/SNF inhibitor using EpiDyne assays. *The Novartis inhibitor BRM014/Compound 14 (Papillon et al. 2018; Jagani et al. 2019) displays dose-dependent inhibition of chromatin remodeling activity as indicated by a reduction in Cy3/Cy5 FRET.*

EpiCypher®

Stratech

CUT&RUN Assays for Chromatin Remodelers

The genome-wide localization of chromatin remodeler proteins is essential for understanding their function in disease but has been obscured by the stringent salt wash steps associated with ChIP-seq. CUTANA™ CUT&RUN provides a robust, low-cost approach to functionally characterize chromatin remodeling complexes *in vivo*. We have used our CUTANA™ CUT&RUN kits and antibodies to map major classes of chromatin remodeling enzymes, demonstrating high quality resolution (Figure 4).

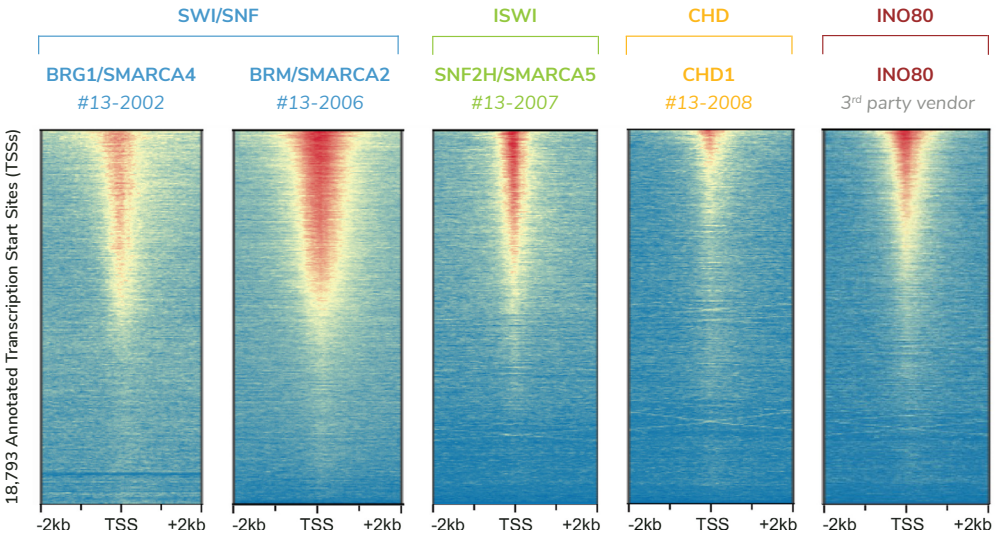

FIGURE 4

CUT&RUN generates reliable profiles with high signal-to-noise for diverse chromatin remodeling enzymes. *Reactions were performed using K562 cells (500,000) and the CUTANA™ CUT&RUN Kit. Heatmaps are aligned to transcription start sites (TSS) and ranked by peak signal intensity.*

CUTANA™ CUT&RUN Antibodies

EpiCypher offers extensively validated CUTANA™ CUT&RUN antibodies to key chromatin remodeling enzymes, including the high-value drug target SMARCA4/BRG1. Each antibody is rigorously lot-tested in CUT&RUN, and genome-wide distribution is compared with known overlapping signaling pathways for unprecedented biological validation. Our final antibodies generate reliable profiles with high signal-to-noise, providing a powerful approach to study chromatin remodelers *in vivo*.

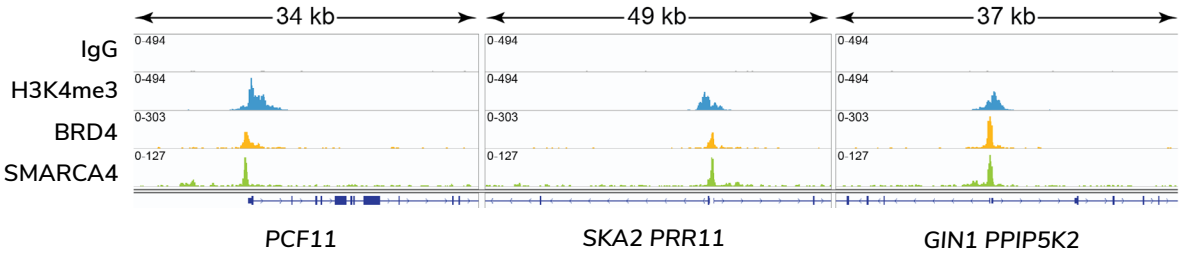

FIGURE 5 ***SMARCA4/BRG1 was mapped in K562 cells using our CUTANA™ CUT&RUN antibody and CUT&RUN kit.*** *To validate this antibody, we compared SMARCA4/BRG1 maps with CUT&RUN profiles for related targets, including H3K4me3 (denotes TSS) and BRD4 (interacts with SMARCA4/BRG1). IgG included as negative control.*