Captify™ Platform for interrogating the histone code

Chromatin-associated proteins regulate diverse cell processes and represent attractive therapeutic targets. Identifying the binding specificity of these proteins is crucial for drug development, but is challenged by the abundance of potential epigenomic targets and the complexity of nucleosome assembly, leading to widespread use of inaccurate modified histone peptide arrays [1-4]. The Captify™ platform was created to enable rapid characterization of chromatin-associated proteins against biologically relevant nucleosome substrates. This versatile technology can be applied to binding assays, inhibitor screening and more.

Advantages of Captify™ assays vs. histone peptide arrays

- Screen against >100 modified nucleosomes
- Improved sensitivity & accuracy
- Lower protein input (nM)
- Use full-length proteins and domains
- Expert assay services available

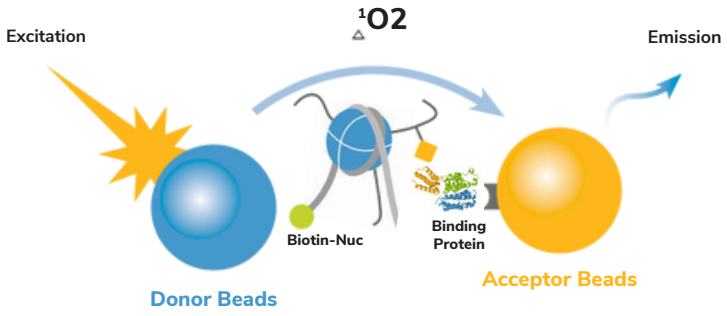


FIGURE 1 The Captify platform uses a luminescent bead-based assay to quantify protein-nucleosome interactions.

Validate novel chemical probes for drug development studies

The Structural Genomics Consortium used Captify assays to assess a chemical probe to NSD2[5], a H3K36 methyltransferase and cancer drug target that requires nucleosome substrates. Blocking the NSD2-PWWP1 domain was sufficient to disrupt NSD2 binding (Figure 2), providing new strategies for drug research.

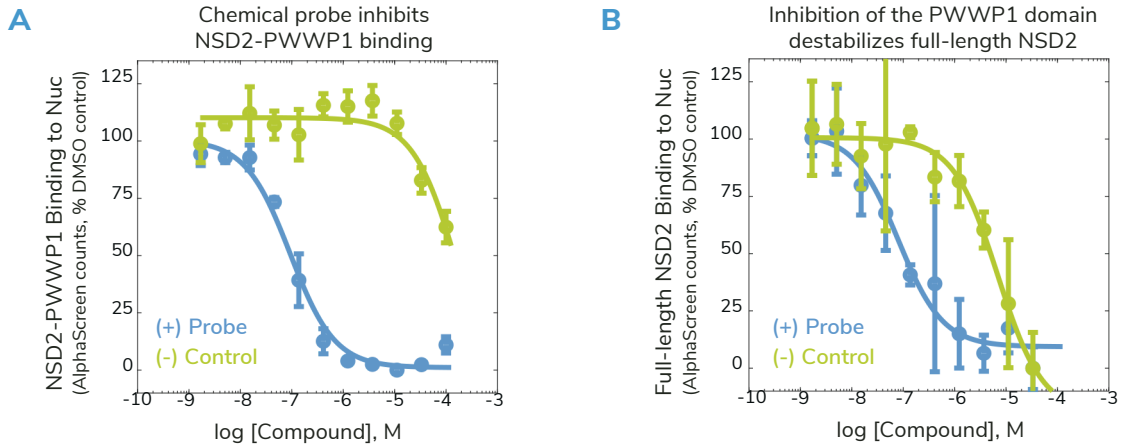


FIGURE 2 **Optimized Captify assays validate a new NSD2 chemical probe and identify new approaches for NSD2 drug development. The NSD2-PWWP1** probe (UNC6934; blue) or negative control (UNC7145; green) was titrated in Captify assays that quantified protein binding to H3K36me2 nucleosomes. The probe inhibits the NSD2-PWWP1 domain (A) and full-length NSD2 (B), suggesting an important role for the PWWP1 domain in NSD2-chromatin interactions[5].

EpiCypher®

A powerful approach to study epigenetic crosstalk signaling

Captify™ assays define complex mechanisms linking histone PTMs and DNA methylation. Here, Captify assays were used to characterize the DNA methyltransferase DNMT3A. The isolated PWWP domain showed distinct PTM binding specificity compared to full-length protein, revealing two competing methods of DNMT3A recruitment[6-7].

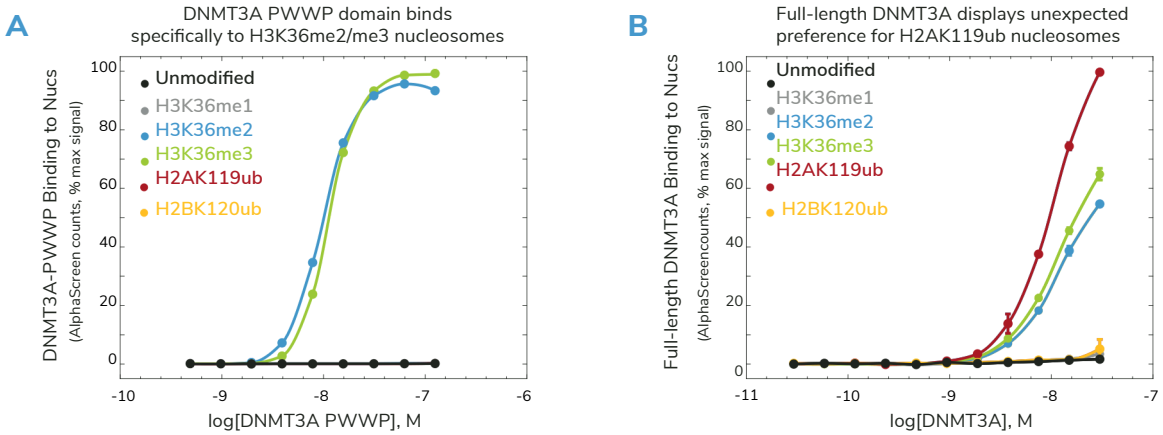


FIGURE 3 **Captify assays reveal two pathways modulating DNMT3A binding. (A) DNMT3A PWWP was titrated against** multiple nucleosomes in a single Captify experiment[6]. (B) Titration of DNMT3A against modified nucleosomes identified a new ubiquitin binding region in DNMT3A[7].

Captify™ assay services

Take the guesswork out of your chromatin binding assays. EpiCypher scientists meticulously optimize every aspect of your assay and screen protein-nucleosome interactions using our collection of over 100 modified nucleosome substrates.

Sample applications

- Examine chromatin regulatory pathways
- Drug discovery pipelines
- Enzymatic assays
- Protein interaction studies
- Structural studies
- Assess antibody performance

vNucs

Assembled with histone variants

Acidic Patch Nucs

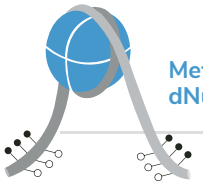
Mutations in the H2A/H2B acidic patch

oncoNucs

Oncogenic amino acid substitutions in histones

dNucs

Defined histone modifications



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Citations

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(3) Jain et al. eLife, (2023)
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