

# H2A Ubiquitylated Mononucleosomes

## Next-Generation Substrates for Deubiquitylation Enzyme (DUB) Assays

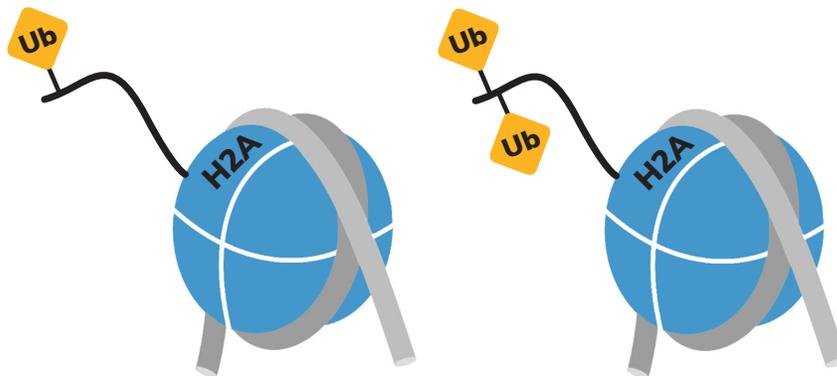


**Next-Generation DUB Assay Substrates are here. Get results that matter.**

- Enabling access to DUB targets that require nucleosome substrates *in vitro*
- Proper substrates for DUB inhibitor development
- Unmatched quality control for results you can trust

Histone monoubiquitylation (ub1) acts as a critical signaling center that regulates cascades of downstream epigenetic enzymes to modify gene transcription. The physiological substrate for chromatin-targeting DUBs is the nucleosome (Nuc), the basic repeating unit of chromatin (comprised of histone proteins wrapped by DNA).

Current high-throughput screening (HTS) DUB assays use unnatural modified or diubiquitin conjugates as substrates, which poorly mimic endogenous targets *in vivo*. **In collaboration with Boston Biochem, EpiCypher is delivering ubiquitylated nucleosome substrates for drug screening and chromatin biology research.**



**FIGURE 1**

Schematic representation of mononucleosomes assembled from recombinant human histones expressed in *E. coli* (two each of histones H2A, H2B, H3 and H4).

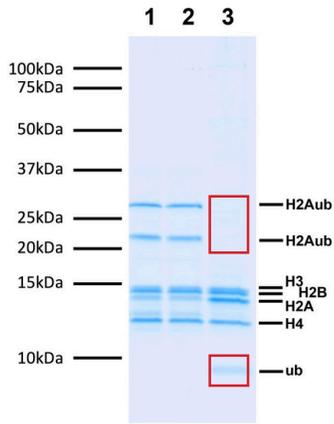
Approximately 50% of the nucleosomes are monoubiquitylated on histone H2A lysine 118, while the other 50% are monoubiquitylated on both histone H2A lysine 118 and histone H2A lysine 119 (multi-monoubiquitylated).

## Next Generation Deubiquitylation Enzyme (DUB) Assay Substrates

EpiCypher has developed recombinant mononucleosomes carrying monoubiquitylation on H2A. These ubiquitylated nucleosomes are generated enzymatically using the RING1B/BMI1 ubiquitin ligase complex. The resulting product is highly pure (>95% of nucleosomes are ubiquitylated) and consists of nucleosomes monoubiquitylated at H2A lysine 118/119 (**Figure 1**; the physiological target of RING1B/BMI1 *in vivo*).

**FIGURE 2**

Deubiquitylation Assay Data: Mononucleosomes H2A Ubiquityl, Recombinant Human, Biotinylated (1 µg) were employed in a deubiquitylation (DUB) assay using no enzyme (Lane 1), USP5 (Lane 2) or USP16 (Lane 3) and run on an SDS PAGE gel. Only the USP16-treated sample shows the elimination of H2Aub bands, the appearance of monoubiquitin (ub) and the reappearance of unmodified H2A. (**Red** boxes)



**Chromatin-targeting deubiquitylation enzymes (DUBs) are extremely valuable therapeutic targets, highly druggable and associated with many diseases**

DUBs	Target	Disease
2A-DUB	H2A	Prostate cancer
<b>USP16</b>	<b>H2A</b>	<b>Stem cell defects in Down syndrome</b>
USP21	H2A	Upregulated in many cancers
BAP1	H2A	Mesothelioma, uveal melanoma
USP51	H2AK13/15ub1	Breast cancer cell proliferation
USP8	H2B	Lung cancer
USP10	H2B	Gastric carcinoma
USP3	H2A/H2B	Gastric cancer
<b>USP12</b>	<b>H2A/H2B</b>	<b>Prostate cancer</b>
USP22	H2A/H2B	Poor cancer prognosis biomarker
<b>USP46</b>	<b>H2A/H2B</b>	<b>Colon Cancer</b>

**TABLE 1**

DUBs that target chromatin. **Red** = nucleosome-dependent activity *in vitro*.

### ORDERING INFO

#### H2A Ubiquitylated Mononucleosomes

Catalog No. 16-0020

Price: \$449 / 50 micrograms

Website: [EpiCypher.com/H2Aub](http://EpiCypher.com/H2Aub)

#### Related Products (Coming Soon)

Mononucleosomes H2B Ubiquityl

#### Related Nucleosome Products

Modified recombinant nucleosomes (dNucs)



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