Synthetic hyper acetylation of histones with a chemical catalyst system and its application to *Xenopus laevis* sperm chromatin

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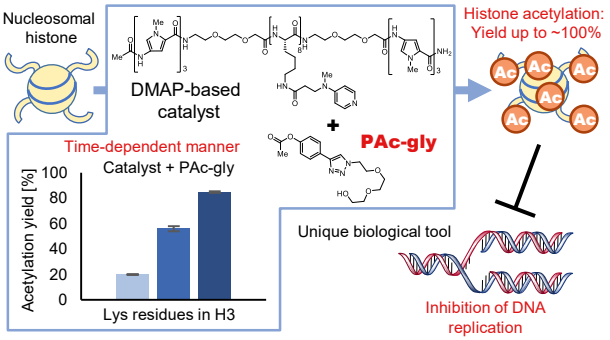
Keywords: Protein modification; Catalyst; Acetylation; Histone; *Xenopus laevis*

Post-translational modifications of histones are a critical chemical process in epigenetics. Chemical approaches to modulating post-translational modifications of histones under physiological conditions provide unique tools for elucidation of epigenetic mechanisms and for therapeutic purposes. Here, we report combinations of a DMAP-based catalyst[1] (PDP or 16DMAP) and a phenyl acetate with optimal electron density (PAc-gly) as a new chemical system for high-yield, selective synthetic acetylation of histone lysine residues. Although PAc-gly itself caused little background protein acetylation and underwent little unproductive hydrolysis, the DMAP-based catalysts promoted almost quantitative histone acetylation. This high reactivity is likely due to a stabilized transition state of the rate-determining acyl pyridinium-formation step through a ternary complex composed of the catalyst, the acetyl donor, and the reacting lysine.

We applied this chemical system to *Xenopus laevis* sperm chromatin (XSC). XSC is unreactive to histone acetyl transferase-mediated acetylation, but was approximately 90% acetylated under our reaction conditions. Acetylated XSC strongly inhibited DNA replication in the *Xenopus* egg extract system, suggesting the importance of a proper level of histone acetylation for cell cycle progression.[2]



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