GS02-5 **Artificial Catalyst System for In-Cell Histone Acylation**

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Posttranslational modifications of histones play an important role in gene transcription. We are developing chemical catalysts that can introduce posttranslational modifications to histones at will. Previously we reported a synthetic catalyst DMAP-SH (DSH), which activates an endogenous acyl donor acyl-CoA, and selectively acylates the neighboring lysine residues. We also reported that the construct LANA-DSH, in which DSH is conjugated with the histone-binding peptide, LANA, promotes selective acylation at the lysine-120 residue of histone H2B (H2BK120) close to the DSH moiety in vitro. In the living cells, however, LANA is facilely decomposed and LANA-DSH does not function.

Herein, we succeeded in developing PEG-LANA-DSH, a stable analog of LANA-DSH for in-cell histone acylation. It is known that introduction of polyethylene glycol (PEG) chains to peptides stabilizes the peptides from peptidases digestion in living cells. Thus, we synthesized LANA-DSH analogs containing PEG chains. Optimizing the number of residues in LANA peptide, the length of the PEG chains, and the linker part between them, PEG-LANA-DSH exhibited sufficient stability in living cells and with a binding affinity to chromosome. PEG-LANA-DSH was shown to promote residue-selective H2BK120 acylation, even in living cells. This result is an important first step towards artificial epigenetics.