Regioselective histone acylation for DNA-damage repair mechanism study

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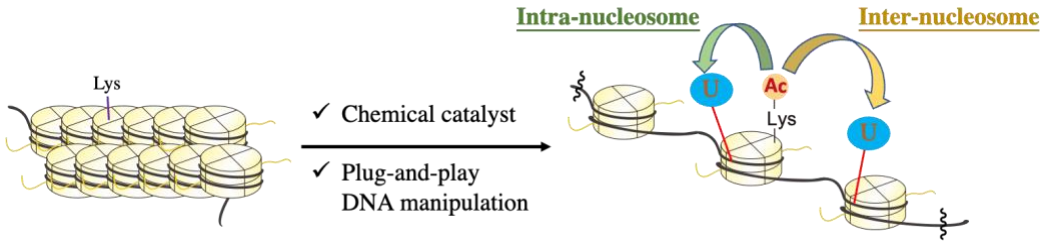
DNA damage repair is a fundamental biological mechanism to maintain homeostasis. There have been many reports on DNA damage repair in mono- or di-nucleosome but rare in poly-nucleosome levels, which are closer to the actual chromatin with higher-order structures. Additionally, relationships between histone post-translational modifications (PTMs) and DNA damage repair have increasingly attracted extensive attention. Thus, a chemical system to investigate the effects of histone PTMs on DNA damage repair in poly-nucleosome levels should be a useful tool.

In this presentation, we report regioselective histone lysine acetylation, an important histone PTM, in poly-nucleosome to investigate DNA damage repair mechanisms. The key methodologies are 1) a chemical catalyst system for regioselective lysine acetylation[1,2] and 2) the plug-and-play approach to regioselectively introduce DNA damage (uracil) into double strand DNA[3]. Combined with these two chemistries, we independently introduce histone lysine acetylation and DNA damage into desired positions in one poly-nucleosome with precision. We would like to discuss the catalyst design, the regioselectivity of histone lysine acetylation, and possibly its effect on base excision repair.



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