第346回化学科コロキウムのご案内

“Structural basis for non-canonical pathway in DNA repair”

Dr Wen-Jin Winston Wu

Institute of Biological Chemistry, Academia Sinica, Taiwan

日時: 2024年2月9日（金）16:00－17:30

場所: 11号館201室

Abstract: The dogma in DNA repair by a DNA polymerase is that a DNA polymerase must bind the damaged DNA first, then followed by the binding of Mg-dNTP. This ensures fidelity control of DNA synthesis or repair based on Watson-Crick base pairing rule. In about a decade ago, we used solution NMR to discover that the DNA polymerase from Africa swine fever virus (Pol X) does not follow this conventional pathway. Instead, the highly error prone Pol X can pre-bind Mg-dGTP and stabilizes a syn dGTP conformation prior to DNA binding, therefore enabling it to escape from Watson-Crick base pairing rule, and catalyzes an anti:syn dG:dGTP (G:G) mismatch. We used NMR to refine the structure of apo-Pol X, determined the binary structure of Pol X:MgdGTP, and the ternary complex of Pol X:DNA:MgdGTP containing a G:G mismatch, identified active site His115 being responsible for the mismatch formation, and provided a structural view for the catalysis of a G:G mismatch [1]. Subsequently, we also discovered that mammalian DNA polymerase λ (Pol λ) also possess this productive Mg-dNTP pre-binding ability [2,3]. We then also reported another surprise for the ability of human DNA polymerase μ (Pol μ) to prebind MndTNP (but not MgdNTP) productively, solving the long-standing puzzle on the mutagenic property of this enzyme when replacing Mg^{2+} with Mn^{2+} [4]. In addition, I will also cover the recent collaborative research accomplishment in DNA repair by a photolyase making use of the SACLA facility in Spring 8 Japan and SWISSFEL in Switzerland.[5,6]

References: [1] W.-J. Wu et al., *J. Am. Chem. Soc.* **136**, 4927-4937 (2014); [2] M.-S. Liu et al., *J. Am. Chem. Soc.* **138**, 2389-2398 (2016); [3] W.-J. Wu, et al. *Nat. Rev. Chem.* **1**, 0068 (2017); [4] Y.-K. Chang et al., *J. Am. Chem. Soc.* **141**, 8489-8502 (2019); [5] M. Maestre-Reyna et al., *Nat. Chem.* **14**, 677-685 (2022); [6] M. Maestre-Reyna et al. *Science* **382**, eadd7795 (2023).

連絡先：理学研究科 化学専攻 伊藤　隆（内線:3538, e-mail: ito-yutaka@tmu.ac.jp）