**Chemistry and Biology of DNA-Protein Cross-Links**

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Understanding how DNA is damaged and how the damage is repaired is critical. This is because DNA damage contributes to genome instability, aging, and diseases, and DNA-damaging agents are used in chemotherapy. Covalent DNA-protein cross-links (DPCs) are ubiquitous and bulky DNA lesions. Despite that it has been well accepted that DPCs are highly toxic, compared to other types of DNA damage, DPCs are much less well studied mainly due to the lack of approaches to detect, quantify, and synthesize DPCs. My research group currently focuses on DPCs derived from abasic DNA lesions, which form endogenously and are induced by many exogenous genotoxins including some anti-cancer drugs. In this seminar, I will discuss our recent work including (1) developing qualitative and quantitative mass spectrometry approaches to detect and quantify DPCs, (2) chemical synthesis of site-specific, structure-defined, and biologically relevant DPCs, and (3) investigating DPC repair mechanisms using *in vitro* reconstitution and plasmid-based reporter assays. Our work advances the fundamental understanding of DNA damage and repair, and such new knowledge may inform the development of novel therapeutic interventions.