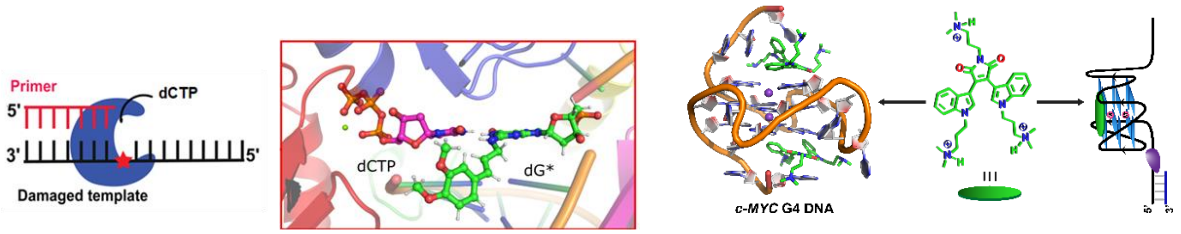
**Chemical Biology of DNA Damaging Agents and G4-DNA Targeting Molecules**

Pradeepkumar P.I.
Department of Chemistry, IIT Bombay, Powai, Mumbai-400076, India

DNA is in continuous contact with various exogenous and endogenous damaging agents, and many of them make covalent adducts with nucleobases. If these damages are not repaired, they can lead to mutation, which can be carcinogenic. In the replication fork, they can halt the function of high fidelity polymerases. One natural way to rescue the replication is to bypass the damages with the help of low fidelity translesion polymerases belonging to the Y-family. This process is called translesion synthesis (TLS), which can be error-free or error-prone. Our lab is interested in the chemical synthesis of DNA damages and study the structural and functional properties of bacterial, viral, and human TLS polymerases. The first half of the presentation will discuss the synthesis of food-borne $N^2$-dG and $N^6$-dA DNA adducts (methyleugenol, safrole, etc.) and TLS by human Y family polymerases κ and η. The second half of the presentation will discuss the selective targeting of G-quadruplex (G4) structures using designer molecules. Potential G4 forming sequences are present across the genome and transcriptome. To harness their therapeutic potential, G4 structures are to be stabilized. Using a chemical biology approach, we have shown that the parallel topology of promoter G4 structures linked to oncogenes (*c-MYC*, *c-KIT* etc.) can be selectively stabilized with the help of small-molecule ligands having diverse chemical nature. This leads to gene downregulation and apoptosis.




References

1. Sale, J. E.; Lehmann, A. R.; Woodgate, R. *Nat. Rev. Mol. Cell Bio.* **2012**, *13*, 141.
2. Ghodke, P. P.; Bhommisetti, P.; Nair, D.T.; Pradeepkumar, P. I. *J. Org. Chem.* **2019**, 84, 1734.
3. Ghodke, P. P.; Pradeepkumar, P. I. *Eu. J. Org. Chem* **2020,** *44*, 6831.
4. Neidle, S. J. *Med.Chem.* **2016**, *59,* 5987.
5. Dhamodharan, V.; Pradeepkumar, P. I. *ACS Chem. Biol.* **2019***, 14*, 2102.