Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Comprehensive Seminar

Investigating the interplay between NER factors & chromatin dynamics in response to UV-damage

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DNA in our cells is subject to damage, both from exogenous & endogenous sources. Of particular interest is UV-induced DNA damage (from sunlight) which is known to cause bulky helix-distorting lesions, majorly cyclobutane pyrimidine dimers (CPDs) and 6-4 pyrimidine-pyrimidone photoproducts (6-4 PPs), repaired by the nucleotide-excision repair (NER) pathway in cells. This process requires local chromatin unfolding to facilitate the access of repair factors to the lesions, failure of which can result in unfaithful repair, causing chromosomal mutations, ultimately leading to cancers of the skin. However, the role of chromatin factors & their crosstalk with the repair machinery in regulating UV-DNA damage responses currently remains enigmatic. While the main molecular players have been identified, questions have emerged about their temporal dynamics and order of recruitment to sites of UV damage. Rather than a linear-sequence of recruitment, multiple feedback-loops among the components can possibly fine tune the responses & orchestrate the regulation of NER.

To directly assess the importance of each component for resolving UV lesions, we have standardized the technique of causing local UV-C damage in nuclei. We have also developed an ergonomic, novel technique of causing localized UV-A damage on a widefield-epifluorescence microscope, potentially allowing us access to the early dynamics of repair factors like DDB2, PARP1 and XPC. Together with chromatin-retention assays for fractionation of chromatin-bound components, our results indicate a close interplay between repair & chromatin-remodelling factors at the lesion-recognition step of NER.

In this seminar, I will cover the relevant extant literature and pose questions that I aim to address in my thesis.

Friday, May 12th 2023

09:30 AM (Tea / Coffee 09.15 AM)

Auditorium, TIFR-H