REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Structural basis of mutagenic and translesion DNA synthesis by DNA Polymerase IV from Escherichia coli

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Abstract

The blueprint of life is resident in genomic DNA and the integrity of the genome has to be maintained for all cellular processes to function optimally. However, it has been seen that creation and retention of error in DNA - in the form of mutations- allows for the evolution of the genome in order to relieve selection pressure imposed on the organism by an adverse environment. These conflicting requirements have led to the presence of molecules that serve to either maintain genomic integrity or render plasticity to the genome. In my laboratory, we aim to elucidate the mechanisms utilized by these molecules to prevent or facilitate the appearance of mutations in the genome.

Prokaryotic error-prone DNA polymerases (dPols) are members of the group of molecules that are responsible for genomic plasticity. These enzymes exhibit low fidelity and low processivity and enhance the frequency at which mutations appear in the genome. The expression of these enzymes is up regulated when the organism encounters environmental and nutrient stress and their activity gives rise to multiple genomic templates for natural selection. In addition, these enzymes also function to rescue DNA replication stalled at unrepaired DNA lesions. DNA Polymerase IV (PolIV) from Escherichia coli is a representative member of this class of dPols and has been the subject of intense genetic and biochemical scrutiny in the past decade.

I will present the structural and biochemical analysis of PolIV. These studies highlight the unique attributes present in the structure and active site of PolIV that allows this enzyme to catalyze mutagenic and translesion DNA synthesis.