Lectures

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Reverse transcriptases – a family of versatile and diverse DNA polymerases

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Reverse transcriptases (RTs) are unique enzymes capable of converting single-stranded RNA into double-stranded DNA. They thus reverse the flow of information in life. Their activity is required for the replication of retroviruses such as the human immunodeficiency virus and retractions such as the LINE-1 element, which are abundant in the human genome. I will discuss our studies of the structure and mechanism of reverse transcriptases. In particular, orthoretroviral monomeric enzymes such as XMR RT (1) and spumaretroviral RT (2). I will also talk about ancestral retroelement RTs such as the enzymes from the Ty3 element (3). The main focus of my talk will be on the structure and mechanism of bacterial RTs, in particular those belonging to the Abik and Abi-P2 families (4). These enzymes are involved in an antiphage mechanism called abortive infection. In this mechanism, an infected bacterial cell commits an altruistic suicide to prevent the spread of the infection. AbiK and Abi-P2 are very unusual. They possess DNA polymerase activity but do not require a template or primer. DNA synthesis begins with the attachment of the first nucleotide to the protein itself. We reported the crystal and cryo-EM structure of Abik and Abi-P2 and showed that both enzymes function as trimers, which is the first instance of such architecture of an RT. We also showed that a unique helical domain stabilizes nascent DNA. We identified the tyrosine residues to which the DNA is attached and showed that they are localized in flexible loops that can undergo large conformational changes to position the tyrosine residue for priming. In summary, this talk will provide an overview of the highly diverse and versatile DNA polymerase of the reverse transcriptase family.

References

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