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A New Paradigm for DNA Repair Revealed through Structural Biology of Bacterial DNA Glycosylases

DNA glycosylases safeguard genomic integrity by initiating base excision repair (BER) of a broad spectrum of chemically altered nucleobases. It is generally accepted that base flipping, in which the modified nucleotide is extruded from the DNA helix and pulled into an active site pocket, is required for identification and excision of the modified nucleobase. I will describe our work on a recently discovered superfamily of bacterial DNA glycosylases specific for alkylated DNA. A series of time-resolved crystal structures of the *Bacillus cereus* AlkD glycosylase caught in the act of excising an alkylated nucleobase revealed that the enzyme catalyzes base excision without base flipping. This unique mechanism enables AlkD to repair large DNA adducts of yatakemycin, a potent antimicrobial natural product. Bulky adducts of this or any type are not excised by DNA glycosylases that utilize a traditional base-flipping mechanism.

For further details, contact Mr. Steven Watkins at 5-9749

QCB

Seminar Series

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Program in Biochemistry**

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CHEMISTRY

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