CONFÉRENCE

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Promiscuity of deazaguanine insertion in DNA

Mardi 4 Aout à 11 h 00
Pavillon Charles-Eugène Marchand, salle Hydro-Québec (1210)

Résumé:

In the evolutionary arms race between bacteriophages and bacteria, both sides continuously evolve sophisticated molecular strategies for survival. A primary bacterial defense mechanism relies on restriction endonucleases that cleave exogenous, non-methylated double-stranded DNA. As a countermeasure, phages utilize elaborate DNA epigenetic marks to evade detection by restriction enzymes and other host defenses. Our group identified eight unique 7-deazaguanine modifications in phage DNA, alongside two novel putative modifications currently undergoing confirmation. These modifications are inserted post-replicatively, with guanine replacement efficiencies ranging from 0.1% to 100%. These modifications are introduced via a complex, branching metabolic pathway that we are actively elucidating. The cornerstone protein family of this pathway, DpdA, comprises four subfamilies with distinct properties that substitute the guanine base in DNA with a modified deazaguanine base. Notably, the DpdA2 subfamiliy exhibit substrate promiscuity regarding the free base, albeit yielding lower insertion efficiencies, whereas DpdA3 preferentially utilize deoxynucleoside substrates to achieve complete genomic replacement. Once inserted into the DNA, the 7-deazaguanine residue may undergo hypermodification through the addition of a methyl, formyl, or amide group. The structural and catalytic diversity of the DpdA pathway underscores a sophisticated mechanism of viral evasion, demonstrating how phages modulate both the identity and density of their DNA modifications to circumvent highly specific bacterial immune responses.

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