Structural Basis of RNA Cap Modification by SARS-CoV-2

SARS-CoV-2, the causative agent of COVID-19 illness is responsible for nearly four million deaths worldwide. The nsp16/nsp10 enzyme complex of SARS-CoV-2 modifies the 2'-OH of the first transcribed nucleotide of the viral mRNA thereby converting the status of RNA cap from Cap-0 (^{m7}GpppA) to Cap-1 (^{m7}GpppAm). The 2'-O methylated RNA cap helps the virus evade immune surveillance in the host cell. By using X-ray crystallography and classical biochemistry methods we captured the nsp16/10 complex in the act of attaching a methyl group to the RNA cap. I will present several high-resolution crystal structures of nsp16/nsp10 heterodimer representing different states of RNA cap modification and discuss important roles of divalent metal ions in this process. I will also present strategies for structure-based development of antiviral drug candidates.

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