Structural Insights Into 2’-O Ribosyl Methylation Of Mrna Cap By SARS-Cov-2

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SARS-CoV-2, the causative agent of COVID-19 illness, is responsible for more than 6 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 (m7GpppA) to Cap-1 (m7GpppAm). The 2'-O methylated RNA cap helps the virus evade immune surveillance in the host cell. Using X-ray crystallography and classical biochemistry methods, we captured the nsp16/10 complex in the act of transferring a methyl group to the mRNA cap. I will present several high-resolution crystal structures of nsp16/nsp10 representing different RNA cap modification states and discuss divalent metal ions' critical roles in this process. Our results inform the strategies for the structure-guided design of new antiviral drug candidates.

Representative publications:

1. Viswanathan T., Misra A., Chan S-H., Qi S., Dai N., Arya S., Martinez-Sobrido L., Gupta Y.K. A metal ion orients SARS-CoV-2 mRNA to ensure accurate 2'-O methylation of its first nucleotide. Nature Communications. 2021 Jun 29;12 (1):4020. PMID: 34078893.

2. Viswanathan T., Arya S., Chan S.H., Qi S., Dai N., Misra A., Park J.G., Oladunni F., Kovalskyy D., Hromas R.A., Martinez-Sobrido L., Gupta Y.K. Structural basis of RNA cap modification by SARS-CoV-2. Nature Communications. 2020 July 24: 3718.