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Analyzing the dynamics of the Nsp13 helicase in the SARS-CoV-2 replication-transcription complex

At around 30 kb, the SARS-CoV-2 genome is one of the largest viral genomes among RNA viruses. As such, the replication machinery must be prepared to quickly and efficiently replicate this genome in order for the viral infection to effectively persist. The SARS-CoV-2 replication-transcription complex (RTC) involves several non-structural proteins encoded by the viral genome that accomplish this goal. The complex includes the RNA-dependent RNA polymerase (RdRP) Nsp12, the helicase Nsp13, and the cofactors Nsp7 and Nsp8, which assemble with RNA to form the RTC. While there are some structures of the replication-transcription complex (RTC) that show the stoichiometry of the proteins and their location within the complex, there still remain some questions about the dynamics of these proteins in complex. One of the remaining questions regards the dynamics of Nsp12 and Nsp13 with RNA, as the placement of these in complex and the directionality of the polymerase and helicase activities seem to be at odds. One explanation for this could be that the helicase allows for backtracking of the RNA in case of a polymerase mistake. By performing SEC-SAXS on different components of the RTC complex, we hope to elucidate the dynamics of these different proteins with each other and with RNA.

Topical Area

Biology and life sciences

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