Solution - Biomolecular

P-1231

NMR Screening of SARS-CoV-2 Pseudoknot

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The programmed -1 ribosomal frameshifting (-1 PRF) is a mechanism of gene expression used by all coronaviruses to ensure the synthesis of essential viral proteins, such as the RNA-dependent RNA polymerase (RdRp). One of the essential components of the frameshifting system in SARS-CoV-2 is a three stemmed pseudoknot structure that stimulates high -1 PRF rates. Altering the frameshift efficiency has drastic consequences on viral replication, suggesting that this activity should be an excellent target for the development of antiviral agents. Recent experiments showed that small molecules bind and reduce its stimulation of -1 PRF. Using NMR-based fragment screening (FBS), we screened more than 760 low-molecular-weight fragments for several substructures of the SARS-CoV-2 RNA genome, including the -1 PRF pseudoknot.

Solution - Biomolecular

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Monitoring The Interaction of α-Synuclein with Calcium Ions Through Exclusively Heteronuclear NMR Experiments

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Thanks to their dynamic properties, intrinsically disordered proteins (IDPs) can perform their biological function despite lacking a stable tridimensional structure. Their features are susceptible to the cellular environment and they are expected to be modulated by side-chains' interactions as well as local solvent exposure. Here we propose a set of exclusively heteronuclear NMR experiments providing a unique tool to investigate IDPs' behavior in different experimental conditions relevant for their physiological function. The set of NMR experiments was exploited to monitor the interaction of the intrinsically disordered protein α-synuclein with Ca^{2+} ions. The approach allowed us to obtain a fingerprint of this IDP and to zoom into the metal ion coordination sphere, revealing the motifs involved in the interaction.