

# Correlated sequence signatures are present within the genomic 5'UTR RNA and NSP1 protein in coronaviruses

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The 5'UTR part of coronavirus genomes plays key roles in the viral replication cycle and the translation of the viral mRNAs. The first 75-80 nucleotides, also called the leader sequence, are identical for the genomic mRNA and for the subgenomic mRNAs. Recently, it was shown that cooperative actions of a 5'UTR segment and the non-structural protein NSP1 are essential for both the inhibition of host mRNAs and for specific translation of viral mRNAs<sup>1,2</sup>. Here, sequence analyses of both the 5'UTR RNA segment and the NSP1 protein have been done for several coronaviruses with special attention to the betacoronaviruses. The conclusions are (i) precise specific molecular signatures can be found in both the RNA and the NSP1 protein; (ii) both types of signatures strongly correlate between each other. Indeed, definite sequence motifs in the RNA correlate with sequence motifs in the protein indicating a co-evolution between the 5'UTR and NSP1 in betacoronaviruses. Experimental mutational data on 5'UTR and NSP1 from SARS-CoV-2 using cell-free translation extracts support those conclusions and show that some conserved key residues in the N-terminal half of the NSP1 protein are essential for evasion to the inhibitory effect of NSP1 on translation<sup>3</sup>.

<sup>1</sup>Miao, Z., Tidu, A., Eriani, G. and Martin, F. (2020) Secondary structure of the SARS-CoV-2 5'UTR. *RNA Biology*. 23, 1-10. DOI: 10.1080/15476286.2020.1814556.

<sup>2</sup>Tidu, A., Janvier, A., Schaeffer, L., Sosnowski, P., Kuhn, L., Hammann, P., Westhof, E., Eriani, G. and Martin, F. (2021) The viral protein NSP1 acts as a ribosome gatekeeper for shutting down host translation and fostering SARS-CoV-2 translation. *RNA*. 27, 253-264. DOI: 10.1261/rna.078121.120

<sup>3</sup>Sosnowski, P., Tidu, A., Eriani, G., Westhof, E. and Martin, F. (2022) Correlated sequence signatures are present within the genomic 5'UTR RNA and NSP1 protein in coronaviruses. *RNA*. PMID: 35236777 DOI: 10.1261/rna.078972.121