The RNA-RNA Interactome of SARS-CoV-2

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Abstract

The Coronaviridae is a family of RNA viruses that includes SARS-CoV-2, the causative agent of COVID-19. Bearing the largest single-stranded RNA genomes in nature, coronaviruses depend on short and long-distance RNA-RNA interactions to regulate their transcription, translation, and replication pathways inside the host cell. Using the COMRADES method [Ziv et al, Nat Methods, 2018], we elucidated the in vivo RNA-RNA interactome of the full-length SARS-CoV-2 genome and subgenomic mRNAs [Ziv et al, bioRxiv, 2020]. We uncovered a network of RNA-RNA interactions spanning tens of thousands of nucleotides. These interactions reveal that the viral genome and subgenomic mRNA adopt alternative co-existing topologies and engage in interactions with cellular RNA. We discovered a long-range RNA-RNA interaction - the FSE-arch - that encircles the programmed ribosomal frameshifting element of SARS-CoV-2, and demonstrated its conservation in other coronaviruses, including in the related MERS-CoV. Our findings illuminate RNA-based mechanisms governing discontinuous transcription and ribosomal frameshifting of coronaviruses and will aid future efforts to develop RNA-based antiviral strategies.

Biography

Dr. Omer Ziv holds a BSc degree in Biology from the Technion, Israel Institute of Technology, and MSc and PhD in biological chemistry from the Weizmann Institute of Science, Israel. He is passionate to explore pathways of interaction between the genomic material and the cellular environment, and he is keen to identify how pathogens exploit the base pairing capacity of RNA to interact with and manipulate their host.

Dr. Ziv joined the Gurdon Institute as a research fellow in 2014, funded by Human Frontier Science Program (HFSP), European Molecular Biology Organization (EMBO), and the Blavatnik Family Foundation. During the last 4 years he designed and developed the first high-throughput technology that monitors dynamic interactions between host and viral RNA molecules during pathogenic infections. He revealed the first-ever structure of a viral RNA genome inside its host, and identified multiple interactions between the Zika virus genomic RNA and human noncoding RNAs [Ziv et al, Nature Methods 2018].