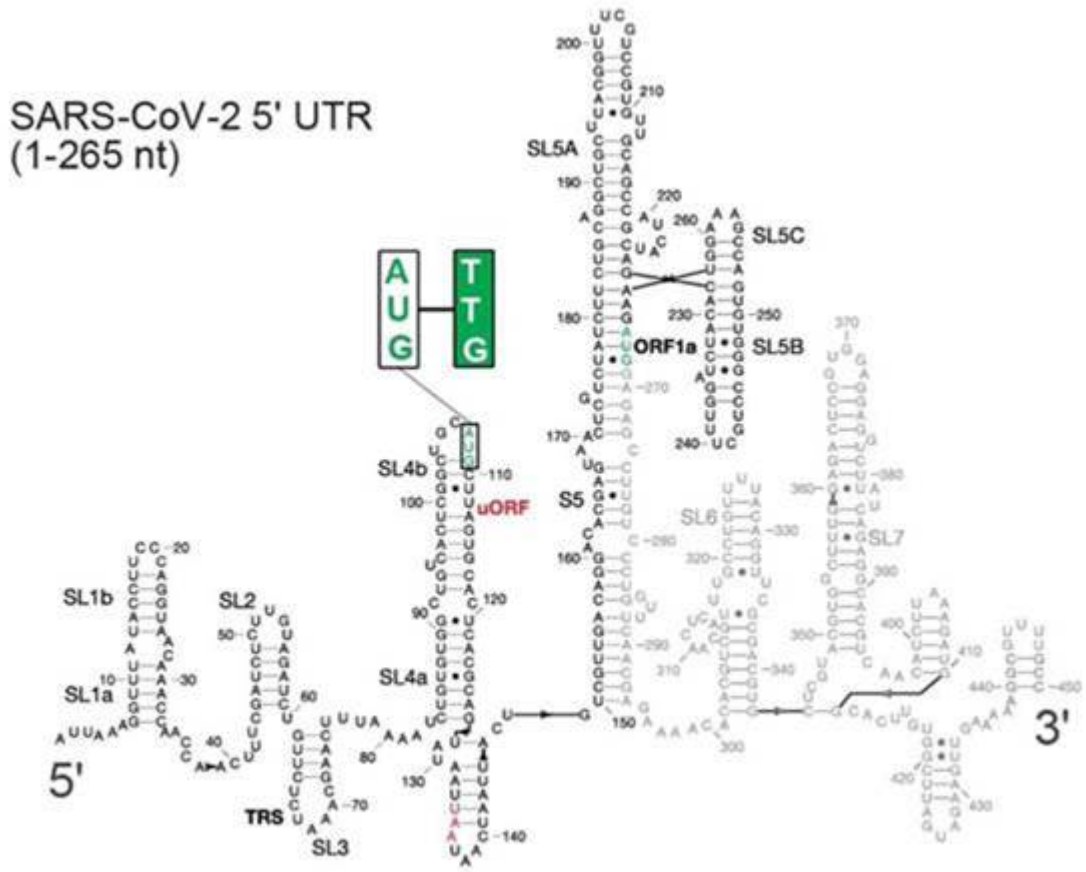
Docket #: S20-205

Repurposing the SARS-CoV2 5'-UTR for RNA Based Therapeutics

Stanford researchers have found a solution to enhance mRNA translation and stability by harnessing SARS-CoV2 genomic sequences themselves. They discovered that the SARS-CoV2 5' untranslated region (5' UTR) can be repurposed for increased translation and stability of any mRNA. In particular, they found that a modified 5' UTR with a mutation of the AUG codon of an upstream open reading frame (uORF) has the ability to promote translation initiation at an extremely high level, outcompeting known constitutively highly expressed 5' UTRs from housekeeping genes. As it is highly structured, it has also been shown to be more stable when expressed in cells. Efficient, robust, high fidelity production of mRNAs is essential in the development of mRNA vaccines and other RNA-based therapeutics. These production qualities are critical for obtaining pharmaceutical quality vaccines, viruses and expression constructs, and for eliminating noise in experimental assays due to batch-to-batch variation. The efficient expression mediated by the SARS-CoV2 5' UTR and its derivatives described here allow for less overall mRNA delivered per patient and thus increases the distribution of mRNA vaccines to a larger number of people at lower doses.

This technology is part of a portfolio of innovations aimed at fighting the COVID-19 pandemic.



A structure of a SARS-CoV2 5' untranslated region (5'-UTR) is illustrated attached to an open reading frame (credit: Barna Lab)

Related technologies for optimizing RNA-based therapeutics and vaccine design:

Stanford docket S20-176: Software for Rapid Mapping of RNA Structure
Stanford docket S20-135: Translation Enhancer for Gene Regulation
Stanford docket S19-310: Rational Design of Ultratight RNA Aptamers against Protein Targets
Stanford docket S19-143: Primerize: Software for Designing Primers for Rapid RNA Synthesis
Stanford docket S20-174: Optimized Synthesis and Translation of RNA Therapeutics

Applications

- Development of RNA based therapeutics such as mRNA vaccines that require highly efficient, high fidelity, and robust production of mRNAs

- The efficient expression mediated by the SARS-CoV2 5' UTR and its derivatives allow for less amount of mRNA delivered per patient and increases mRNA vaccine distribution
- COVID-19 mRNA vaccines

Advantages

- SARS-CoV2 5' UTR and its derivatives enables optimal expression of any ORF and protein
- SARS-CoV2 5' UTR and its derivatives enhances mRNA translation and stability

Publications

- Leppek et al. bioRxiv (2021) Combinatorial optimization of mRNA structure, stability, and translation for RNA-based therapeutics

Patents

- Published Application: WO2021231503
- Published Application: 20240043835

Innovators

- Maria Barna
- Kathrin Leppek

Licensing Contact

Sam Rubin

Licensing Associate, Life Science

Email