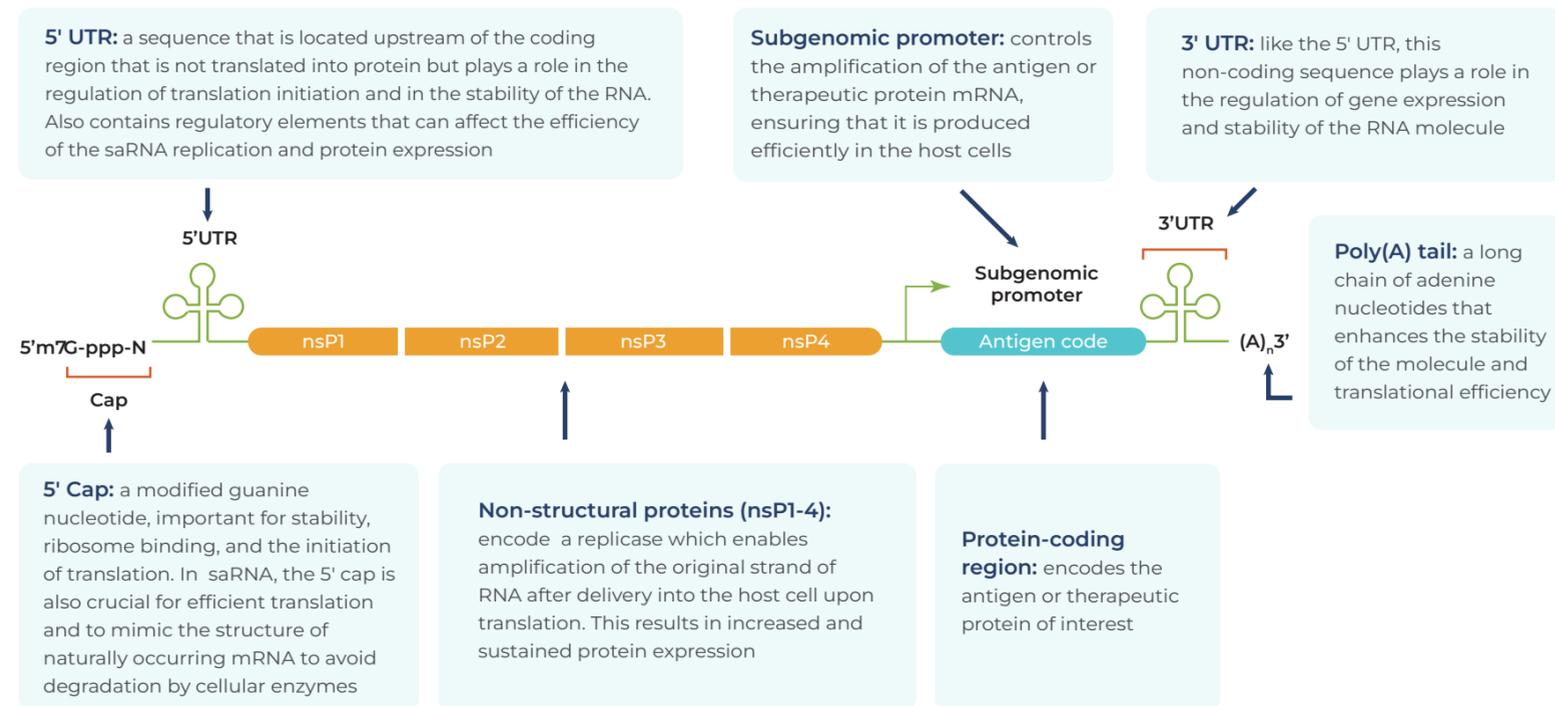


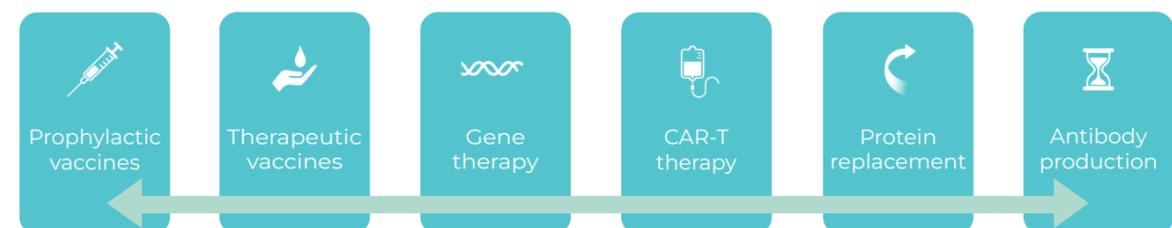
A beginner's guide to self-amplifying RNA

Self-amplifying RNA, or saRNA, is a special type of mRNA that contains a viral gene that allows it to self-replicate in the cell cytoplasm, in addition to a gene encoding a therapeutic protein. Due to this unique self-amplifying nature, saRNA-based vaccines and therapies have the potential to achieve the desired effects with significantly lower injection dosages and sustained and high-level expression of protein without the need for repeated doses.

What parts make up saRNA and what does each do?



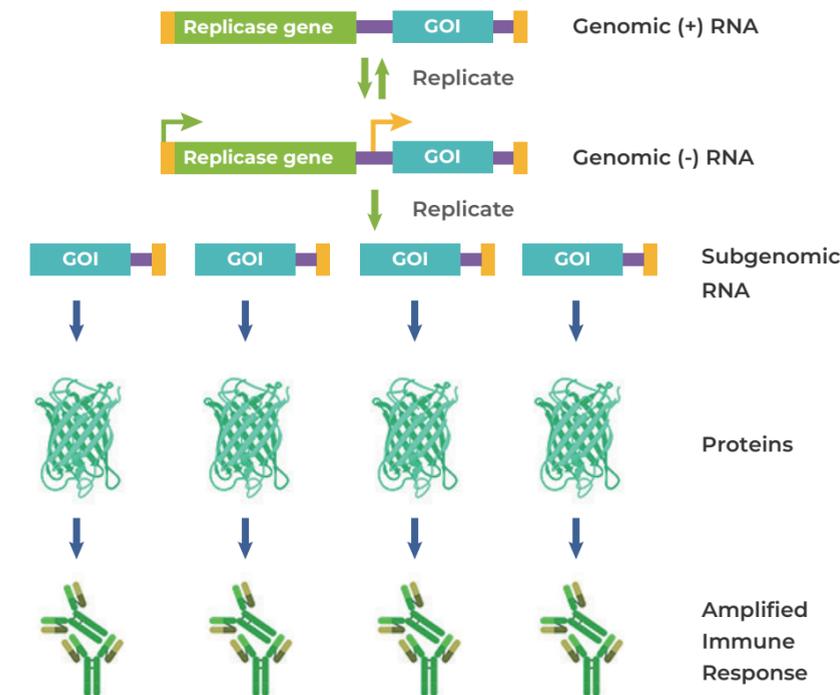
What are the potential applications for saRNA?



saRNA's potential to prolong protein expression and reduce dosage requirements makes it an attractive tool for a variety of therapeutic applications

How does saRNA replicate and translate into protein?

Self-Amplifying RNA



saRNA replicates by harnessing the machinery of RNA viruses, which have evolved to self-replicate within a host cell:

1. The saRNA is delivered into the host cell, often through a delivery system such as a lipid nanoparticle. Once inside the cell, the saRNA is released into the cytoplasm.
2. The saRNA contains a region that encodes non-structural proteins, which are immediately translated by the host cell's ribosomes. These non-structural proteins include the RNA-dependent RNA polymerase (RdRp), which is essential for the replication process.
3. The translated RdRp and other non-structural proteins form a replication complex on the saRNA template. This complex is responsible for the synthesis of new RNA molecules.
4. The RdRp begins by using the positive-sense saRNA as a template to synthesize a complementary negative-sense RNA strand.
5. The RdRp uses the negative-sense RNA as a template to produce multiple copies of the original positive-sense saRNA. The RdRp also cooperates with the subgenomic promoter to amplify the subgenomic RNA.
6. The amplified positive-sense saRNA continue translating RdRp and maintain the amplification process. The subgenomic RNA serve as a template to translate the protein of interest.

Current clinical progress for saRNA

On November 27, 2023, the Japanese Ministry of Health, Labour and Welfare approved ARCT-154, a self-amplifying RNA (saRNA) COVID-19 vaccine developed jointly by CSL and Arcturus Therapeutics, for use in initial and booster vaccinations in adults aged 18 and above. ARCT-154 became the world's first saRNA vaccine to be approved for marketing. This vaccine triggers a highly efficient immune response at extremely low doses, making it a pioneering breakthrough in the next generation of RNA vaccines.

Interested in GenScript's custom IVT saRNA synthesis services? Learn more at www.genscript.com/self-amplifying-rna.html