ABSTRACT: Our research aims to understand the evolved strategies of viruses such as genome protection, genome delivery, and self-replication, and to use this knowledge to develop self-replicating mRNA therapeutics that can be delivered to cells in virus-like particles assembled in a test tube (in vitro). mRNA therapeutics involve delivering messenger RNA (mRNA) molecules encoding a therapeutic gene of interest to a cell and relying on host cell machinery to translate the mRNA into protein. Self-replicating mRNAs not only contain the therapeutic gene of interest, but also encode an RNA replicase molecule that will amplify the mRNA. Much like a viral genome, this mRNA will be replicated up to a million-fold, resulting in increased expression of the therapeutic gene of interest. Because a single molecule of this genome will result in millions of copies, very few molecules need to be delivered to cells. Therefore, we aim to deliver these self-replicating mRNAs in virus-like particles (VLPs) that can be assembled in vitro from purified components – namely, RNA and protein. We exploit two unique plant viruses that have been shown to assemble in vitro – cowpea chlorotic mottle virus and tobacco mosaic virus – to produce spherical and rod-like VLPs containing our self-replicating mRNAs.