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Title: Harnessing the power of RNA-based therapeutics to combat viral diseases

Abstract:
RNA biologics are now emerging as realistic and achievable clinically translatable treatment modalities for a range of human diseases. Importantly, respiratory viruses and viral cancers are amenable to gene therapy-based targeting. Despite the deployment of several vaccines, SARS-CoV-2 variants are emerging, and a direct acting therapeutic is of dire need. Similarly direct acting antivirals against other emerging respiratory viruses, respiratory syncytia virus (RSV) and human metapneumovirus (hMPV) is needed. There is an urgent need to bring new antivirals for SARS-CoV-2 and RSV to the market. We have been exploring the use of RNAi (RNAi) to directly target respiratory viruses and show that RNAi is an effective approach to reducing, or even eliminating viral replication in animals. Notably, we have developed lipid nanoparticles (LNPs) that effectively deliver short interfering RNAs (siRNAs) via intravenous and intranasal routes to target SARS-CoV-2 and RSV infection in lungs and the nasal cavity. Our approach will not only result in the ushering in of an entirely new cost-effective and rapidly deployable RNA platform technology, but also could deliver the first in class RNA drugs suitable for any new RNA respiratory viruses of concern. We are also developing CRISPR-based therapeutics against several human papilloma virus (HPV) driven cancers, including cervical and oropharyngeal cancers. We hypothesize that HPV cancers are 'oncogenically addicted' to the major HPV oncogene, E7. Using a CRISPR-based approach, genetic deletion of this single oncogene was sufficient to effectively eliminate HPV+ cervical and oropharyngeal tumors in vivo. Our preclinical data strongly supports the notion that targeting a single major oncogene is efficient at killing HPV driven tumors.