Development of infection-mimicking RNA vaccines

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Enterovirus A71 (EV-A71), along with other enteroviruses such as coxsackievirus A6 and A16, is a major causative agent of hand, foot, and mouth disease (HFMD), a highly contagious viral infection that primarily affects infants and young children. HFMD typically presents with fever, oral ulcers, and vesicular eruptions on the hands, feet, and buttocks. While most cases resolve without severe complications, in rare instances, patients infected with EV-A71 can develop life-threatening neurological conditions. These include brainstem encephalitis, which can cause autonomic dysfunction, and acute flaccid paralysis, which leads to severe muscle weakness or even permanent disability. In the most severe cases, these complications can result in death or long-term neurological sequelae, significantly impacting the affected individual's quality of life.

The ultimate goal is to develop a vaccine modality that can be widely applied to picornavirus infections. As a first step, we aim to develop an infection-mimicking RNA vaccine against EV-A71 to mitigate the damage caused by this virus. This infection-mimicking RNA vaccine is highly versatile and a promising modality that can be rapidly adapted for use against emerging or previously unknown enteroviruses.

Currently, most mRNA vaccines in clinical use or under development induce immunity by expressing a single viral protein, typically a surface protein that triggers an immune response. However, RNA vaccines that provide strong protection against enteroviruses need to express virus-like particles (VLPs) composed of several viral proteins as vaccine antigens. VLPs are efficiently formed by expressing the polyprotein P1 along with the viral protease 3CD. This co-expression mimics the natural viral infection process, leading to proper protein cleavage and assembly of the structural components required for induction of protective immunity. In other words, for a highly effective RNA vaccine against enteroviruses, two different viral proteins (P1 and 3CD) must be co-expressed within a single cell to facilitate VLP formation. This strategy enhances antigen presentation and strengthens the protection, making it a promising approach for developing next-generation vaccines against enteroviruses.