RNA technologies offer a rapid approach to develop immunogenic vaccines against outbreak pathogens, such as COVID-19. RNA vaccines are designed using the genetic sequence of the viral antigen and rapidly manufactured using cell-free, rapidly scalable techniques. There are two main categories of RNA vaccines; 1) conventional messenger RNA (mRNA) vaccine, where the immunogen of interest is directly translated from the input vaccine transcript, and 2) newer self-replicating RNA (STARR) vaccines. Self-replicating vaccines encode replication machinery, usually alphavirus-based replication complex, that amplify sub-genomic RNA carrying the antigen of interest, resulting in the amplification of transcripts bearing the antigen by several orders of magnitude over the initial dose. In an effort to develop an immunogenic COVID-19 vaccine, our group conducted a head-to-head comparison of the immune responses elicited by SARS-CoV-2 Spike encoding mRNA and self-amplifying RNA vaccine platforms. The current preclinical work highlighted the differences in both antibody and cellular responses elicited by the two RNA vaccine platforms.

Following the approval/licensure of several COVID-19 vaccines using mRNA technology, phase III clinical trials observed protection as early as 2 weeks post-vaccination. Therefore, in an effort to decipher early correlates of immunogenicity, we have studied the human immune responses of currently approved mRNA vaccines against COVID-19. Current investigations highlight the importance of T cells and non-neutralizing antibodies very early after vaccination. This work provides an insight into the immunogenicity of different RNA vaccine platforms, which in the future can be used to design more efficacious RNA vaccines against both endemic and pandemic pathogens.