

Development of next-generation mRNA technology using chemical modifications and its application to vaccines for the prevention of infectious diseases

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mRNA vaccines have demonstrated efficacy against the COVID19 pandemic. However, serious adverse events such as myocarditis have been reported, making the development of safer and more reliable vaccines an important issue. Because mRNA is difficult to purify to high levels, the contaminants such as short RNA and dsRNA elicit innate immunity, leading to adverse events. We have succeeded in increasing the purity of mRNA to about 90% by modifying the 5' cap structure of mRNA (Nat Commun, 2023). Here, we will combine this technology with several chemical modifications to create next-generation mRNA molecules (NUmRNA).

By applying our novel mRNA molecule to vaccines, it will be possible to induce sufficient immunity with a smaller dose than conventional mRNA vaccines and reduce the occurrence of adverse events. In addition, the development and production of useful vaccines in Japan are largely dependent on foreign countries. Due to the unpredictable international situation, development of mRNA vaccines and its supply system domestically it an urgent social issue. The NU-mRNA, which we proposed in this research and development program, is a new modality for next generation mRNA vaccines that are able to be produced and supplied domestically. Therefore, our NU-mRNA technology can serve as a platform for building a safe and secure social infrastructure in Japan. We will develop an mRNA vaccine against cytomegalovirus (CMV) using the NU-mRNA technology and achieve nonclinical POC within this research period. CMV is a pathogen that are transmitted from mother to child efficiently. Infection of pregnant women with CMV can result in severe fetal disability or fetal death. Symptomatic congenitally infected babies are treated with antiviral drugs, but their efficacy is not sufficient. The vaccine to prevent maternal CMV infection has thus unmet medical needs. After achieving preclinical POC, we have a plan for achieving clinical POC through safety evaluations and Phase 1 trials.

Our next-generation multivalent mRNA vaccine using NU-mRNA technology can be applied to all infectious disease prevention vaccines as well as priority infectious diseases. We hope to contribute to the health of people living in Japan by developing NU-mRNA, a new modality that reduces adverse events and also ensures the highest level of safety and efficacy of its time.