Establishing a production platform of high-purity mRNA in Japan based on PureCap technology for clinical development of safe mRNA vaccines without using delivery carriers

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Outline your research proposal, mentioning the anticipated results, in 400 words or less. To control coronavirus disease (COVID-19), Japan owes much on importing mRNA vaccines developed overseas. Based on the following two original technologies, in this proposed study, we will establish good manufacturing practice (GMP) production methods of mRNA and drastically improve mRNA vaccines' safety and storage stability by avoiding the use of lipid nanoparticles (LNPs) for mRNA delivery. (i) Our PureCap technology simultaneously simplifies the mRNA production process and increases mRNA purity. Notably, in vivo mRNA introduction efficiency increases by 10-fold only by improving mRNA purity, as byproducts in mRNA synthesis induce inflammatory responses and prevent mRNA translation. (ii) Intradermal administration of mRNA provides efficient vaccination effects even without using LNPs or other delivery carriers, as dermal tissues are rich in antigen-presenting cells. In contrast to LNP-based delivery, this strategy avoids systemic leakage of mRNA, drastically reducing systemic adverse effects in vaccination. Moreover, a final formulation of this vaccine comprises only mRNA, which enables lyophilization for storage without ultralow temperature and simplifies manufacturing processes. Further notably, our comprehensive patents allow us to produce mRNA without using patents from others. In the proposed study, we will establish systems for rapidly producing active pharmaceutical ingredients (APIs) and final formulations of mRNA vaccines upon pandemics and use the products for the clinical development of the new vaccine modality described above. Concurrently, we will undertake technological developments, including rational designing of mRNA sequences, plasmid DNA supply, next-generation in vitro transcription technology, and lyophilization methodology. Ultimately, we will prepare mRNA vaccines in compliance with GMP and evaluate their safety and vaccination efficiency in preclinical and phase I clinical trials by applying them with intradermal administration devices. After demonstrating its feasibility in a phase I clinical trial in this proposed study, our strategy provides a robust platform for rapidly controlling upcoming pandemics. Notably, various participating companies are specialized in biopharmaceuticals, nucleic acid therapeutics, and mRNA vaccines and are capable of producing APIs in Japan. Thus, our study will contribute to establishing reliable production systems of mRNA vaccines in Japan, which also apply to other formulations of mRNA vaccines and therapeutics.