Next-generation subunit vaccine utilizing AAV

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The recent COVID-19 pandemic has realized the need for technology to produce novel vaccines in emergency situations. Live-attenuated vaccines are highly effective; however, they take time to develop and cannot meet urgent needs. In contrast, viral vector vaccines can respond rapidly to novel mutations, and co-infection with both pathogen's antigen and endogenous adjuvant (vector itself) can induce vaccine effects similar to pathogen's infection. Currently, mRNA vaccines are mainly utilized; however, they are sometimes contraindicated due to allergy to lipid nanoparticles and require cryopreservation at ultra-low temperatures. Adeno-associated virus (AAV) has relatively low immunogenicity, is expected to provide lifelong immunity through longterm antigen expression, and can be stored in refrigeration (4° C). Several gene therapy trials with AAV vectors have been approved, its market is rapidly expanding internationally, and it is safe for intramuscular administration. Therefore, this project aims to develop a safe and effective next-generation COVID-19 vaccine by using AAV-related technology. We have experience in gene therapeutic product technology development, GMP manufacturing, and clinical trials. Here, we confirm the specifications of the AAV vector vaccine and expand the small-scale GMP facility for the manufacturing of investigational drugs. It is also applicable for the development of gene therapy products, and the effective usage via dual use as well as bidirectional development of fundamental technologies are expected. In preclinical safety tests, preclinical PoC acquisition, and physician-led clinical trials, we evaluate the safety and possibility of long-term immunogenicity. In parallel, for the development of basic technology to further enhance the efficacy, we aim to apply the oral administration method by lyophilization, as well as the technology to encapsulate nucleic acids in AAV empty particles (capsid). The AAV empty particles with PCR product or mRNA encapsulation are superior in low risk of insertion, antigen delivery, and high immunogenicity. There are no reports of similar technologies, making it highly competitive internationally. Furthermore, we possess technology for exosomal delivery of AAV particles (vexosomes) and aim to establish a method for their production and purification,escape from the immunoreaction, effective gene expression, and development of intranasal mucosal administration methods. AAV vector vaccines are also important as countermeasures against outbreaks of emerging and reemerging infectious diseases or bioterrorism and can be applied to various diseases including Alzheimer's disease, lifestyle-related diseases, and malignant tumors. As multidisciplinary research, the project aims to establish an efficient production supply and value chain in collaboration with various departments in the university and CDMOs.