



Study on the development of non-replicating attenuated vaccinia virus against orthopoxvirus infections, including monkeypox

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Mpox, which was traditionally endemic in central and western Africa, has spread worldwide since May 2022, resulting in more than 93,000 cases and more than 130 deaths. In Japan, the number of patients has been increasing since 2023, and approximately 240 patients have been reported so far. There are concerns that the monkeypox endemic will spread further in the future.

The vaccinia virus vaccines, smallpox vaccines, has been reported to be effective against mpox as well as smallpox. In Europe and North America, the non-replicating highly attenuated vaccinia virus MVA strain has been approved as a mpox vaccine, and the low replicating attenuated vaccine LC16m8 strain was additionally approved as a mpox vaccine in Japan in 2022. Since both vaccine strains are produced using primary cell cultures, rapid mass production is a future challenge.

The DIs strain is a highly attenuated mutant strain isolated from the vaccinia virus Dairen-1 by Tagaya, et al. in 1961 using the hen egg culture method and does not replicate in almost all of eukaryotic cells. The safety of the DIs strain was confirmed in approximately 50 children in the 1970s. Recently, we have also established a production system that enables the rapid and mass production of DIs strain using the cell line suspension culture method.

In this study, we will establish a non-clinical test method for DIs formulations against mpox and orthopoxvirus infections in mice and non-human primates. Based on the GMP formulation manufacturing system at overseas CMOs and various test implementation systems at domestic and overseas CROs that we have been established, we will manufacture GMP-grade vaccines for DIs using the suspension cell culture system and use the formulations to conduct preclinical tests and Phase I trials. In addition, we will investigate serum HA antibody, HBc antibody, Through this research and strategic discussion with PMDA, we aim to commercialize the original Japanese strain DIs which exhibits high safety as a vaccine against mpox and other orthopoxvirus diseases.