

## Development of a Nipah measles vector vaccine

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Nipah virus (NiV) was first identified in Malaysia in 1998 in an outbreak of infection in pigs and humans, and incurred a high fatality rate in humans. Since the first emergence, it continued to re-emerge in South Asia almost every year causing severe acute respiratory disease and encephalitis with very high fatality rate as 70-90% in humans. Fruit bats, the natural host for the virus are found on five continents. However, there are no available therapeutic drugs or vaccines. Therefore, it is important to develop Nipah vaccine to prepare for future epidemics.

We have so far promoted the development of a Nipah vaccine using the measles virus (MV) vaccine strain as a vector. MV vaccine is an excellent live-attenuated vaccine that induces both humoral and cell-mediated immunity, provides lifelong protection, and is safe after many years of international use. Using the reverse genetics system of MV, we developed a vector vaccine candidate (MV-NiV) by inserting the G gene encoding the antigen protein of NiV (Malaysia strain) into the MV vaccine strain (Edmonston B strain). We have demonstrated a very high protective ability of MV-NiV using hamsters and monkeys. For practical use of MV-NiV, we established an international joint research consortium with the European Vaccine Development Initiative (EVI), Stanford University, Batavia Biosciences, and the Bangladesh International Diarrheal Disease Research Center (icddr,b) to promote practical development research, which have been supported by the Coalition for Epidemic Preparedness Innovations. We have already completed the development of the manufacturing process and prototype production of the vaccine, have obtained a proof-of-concept for efficacy testing using a hamster infection model, and are making various preparations for clinical trials. The purpose of this proposal is to clarify the safety and immunogenicity of MV-NiV in humans and lead to its practical application. To that end, we will conduct GMP manufacturing of MV-NiV, preclinical safety-tox study in non-human primates, and strategic consultations with regulatory authorities in the countries where clinical trials are being conducted, and then conduct clinical trials. In addition, we will establish a manufacturing system in Japan to enable prompt production in the event of an infectious disease. It is expected that the provision of a safe and highly effective Nipah vaccine will not only save lives in endemic areas, but also greatly contribute to preventing epidemics in Japan and around the world.