Study for development on practical application of oral vaccine using acid-resistant microalgae

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Current available vaccines are mainly administered by injection, which poses challenges in terms of materials, labor, adverse reactions, and the need for a cold chain. We aim to commercialize oral vaccines that uses the acid-resistant microalgae as an antigen delivery platform as a new modality for vaccines, and in this study a nonclinical POC is aimed to be obtained.

Research on development of oral vaccines using many kinds of crops or lactic acid bacteria have been conducted, but none have been on the market at present, except for live vaccines, due to issues such as digestive denaturation by gastric acid, limited number of amino acids that can be expressed, manufacturing time and cost. We succeeded in establishing monoploid strains of the microalgae from a domestic acidic hot spring using an original induction method. The genetic recombination technology for this strain has already been established, and it is easy to produce vaccine antigen-expressing strains when the genetic information of the target pathogen is available. And the inserted gene has been stable more than 9 years in culture. In an oral administration of GFP-expressing strain to mice, it was confirmed that it avoided digestive degeneration by gastric acid and reached the small intestine, where exposure to a neutralizing hypotonic environment caused the cells to break up and release GFP into the intestinal tract. In addition, an oral administration of intestinal M cell recognition epitope attached rabies virus G protein-expressing strain to mice was also confirmed the induction of G protein-specific antibodies in the blood. Culture can be performed using only inorganic media, light, and air, and we established a technique for aseptic culture in an open system.

In this study, as a preclinical POC for aiming at social implementation of oral vaccines using this acid-tolerant microalgal monoploid strain as a platform, we will 1) develop vaccine antigen-expressing strains of non-enveloped and enveloped viruses to verify their usefulness as a vaccine platform for a variety of viruses, and 2) confirm their immunogenicity in mice. To establish an antigen expression system, enterovirus A71 (EV-A71) is selected as a non-enveloped virus and Japanese encephalitis virus as an enveloped virus. This will lead to develop new effective vaccines against EV-A71 infection, Dengue fever, and Zika fever, for which no effective vaccine exists, and Japanese encephalitis for which new genotypes have been recognized as prevalent. Additionally, this study leads to vaccines against various other infectious diseases.