Development of enteroviral vaccines

Intravacc has extensive experience and knowledge on the production of poliovirus vaccines. This production process can also be used as a platform process to develop non-polio enteroviral vaccines. For that, Intravacc has the capacity to design and generate its own unique enteroviral vaccine strains. Several enterovirus strains are available.

A prototype inactivated EV-A71_C4 vaccine to prevent Hand, Foot and Mouth Disease (HFMD) was developed, which generated a high neutralizing antibody response in a preclinical model. Currently, Intravacc is developing a bivalent vaccine consisting of both inactivated EV-A71 and CV-A16 virus to prevent HFMD.

Benefits

- Regulatory approved and cGMP qualified Vero cell line production platform
- Construction of (proprietary) enterovirus seeds
- Fast track process development
- High immunogenicity in animal models
- Several strains available for combination vaccines

Fast track enteroviral vaccine development

Intravacc has extensive experience with the production of poliovirus vaccines. In short, Vero cells are expanded prior to poliovirus infection. The downstream process consists of clarification, concentration, purification and inactivation using formaldehyde (see Figure 1). Because the majority of enteroviruses have similar characteristics, the polio vaccine production process was chosen as a platform for non-polio enteroviruses. All viruses capable of replicating on Vero cells could successfully be concentrated, purified and inactivated using the platform poliovirus vaccine production process as a basic protocol. Enteroviruses capable of replicating in Vero cells can thus follow fast-track development into inactivated vaccines using the poliovirus vaccine production process as a platform.

Hand, Foot and Mouth Disease

HFMD is a viral illness which commonly causes lesions involving the mouth, hands and feet. HFMD is causing large problems in South-East Asia, but also smaller outbreaks have occurred in Europe recently. HFMD is normally a mild, self-limiting illness but occasionally has serious neurological complications, and fatalities have occurred in epidemics around the world. There is a clear need for HFMD combination vaccines. HFMD can be caused by several enteroviruses but the most common viruses causing HFMD are Enterovirus A71 (EV-A71) and Coxsackievirus A16 (CV-A16).
Development of an EV-A71_C4 vaccine

EV-A71 is one of the viruses causing HFMD. A synthetic EV-A71_C4 strain was designed by Intravacc and this EV-A71_C4 strain was rescued by transfection of RNA into Vero cells and working virus banks were generated at R&D level (see Figure 2). A prototype vaccine for EV-A71_C4 was produced in a 10L bioreactor. Specific EV-A71 assays were designed and implemented in the process, as outlined in figure 1.

The preclinical study in mice showed that the inactivated EV-A71_C4 vaccine has the capacity to generate a high neutralizing antibody response that can also protect against infection with other EV-A71 serotypes (cross-neutralization).

Development with respect to EV-A71_C4 focuses on further optimization of the production process, the production of GMP virus seedlots and the construction of attenuated EV-A71_C4 strains is ongoing.

Combination vaccines

Because HFMD can be caused by several enteroviruses, currently a similar process is being developed for CV-A16 in order to develop a bivalent vaccine to prevent HFMD more broadly. Because the technology to rescue enteroviruses can be used for every enterovirus, any combination vaccine consisting of several inactivated enteroviruses can be developed quickly by Intravacc.