"Recent Advances in the Development of Human Enterovirus 71 Vaccines"

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Abstract

Human enterovirus 71 (HEV71) is a highly neurotropic enterovirus that has increased in prevalence in the Asia-Pacific region during the past fourteen years. HEV71, together with the closely related Coxsackievirus A16 (CVA16), is associated with large epidemics of the common childhood exanthem known as hand, foot and mouth disease (HFMD) and occurs mainly in children below the age of five-years-old. In contrast to CVA16 infection, infection with HEV71 infection is frequently complicated by acute neurological disease, including aseptic meningitis, poliomyelitis-like paralysis and brainstem encephalitis. HEV71-associated brainstem encephalitis is a characteristically severe disease of rapid onset and is associated with a high mortality (40-50%) and high rates of neurological sequelae (50-60%) in survivors.

Intensive clinical and laboratory surveillance and public health interventions have failed to prevent HEV71 epidemics, indicating that a vaccine will be necessary to control this disease. Experience with the related poliovirus indicates that both inactivated and live attenuated vaccines are likely to protect children from HEV71 encephalitis but that a live attenuated vaccine will be most effective in large-scale disease control and possible eradication. Knowledge gained from decades of enterovirus research can now be applied to the development of HEV71 vaccines. The mechanism of replication of enteroviruses has progressively been elucidated and has provided a clear picture on the role of RNA secondary structures located in untranslated regions of the genome in the control of viral replication. Mutagenesis of enterovirus RNA secondary structures not only alters viral replication functions but also attenuates virulence in animal and cell culture models. Furthermore, attenuation achieved by mutation of replication control elements does not lead to alteration of the amino acid composition of the viral structural proteins, avoiding interference with protective immune responses. I will discuss these concepts in relation to the development of live attenuated HEV71 vaccines and also review progress in the development and efficacy testing of inactivated vaccines.

Selected Publications


