

Development of Viral Vaccines: Zika, Adenovirus type 55 and Hepatitis A virus

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Infectious diseases pose continual threats to public health, necessitating ongoing efforts in vaccine development. This study presents advancements in the development of vaccines targeting Zika virus, human adenovirus type 55 (hAd55), and hepatitis A virus (HAV).

Zika virus, primarily transmitted through the bite of *Aedes aegypti* mosquitoes in tropical and subtropical regions, has been associated with severe neurological complications such as microcephaly in infants and Guillain-Barre syndrome in adults. Despite a World Health Organization (WHO) emergency declaration in February 2016, no approved vaccine exists to date. For the Zika vaccine development, we used vesicular stomatitis virus (VSV) as a vaccine platform because VSV showed 100% protective efficacy in Ebola vaccine study. Preclinical studies demonstrated induction of Zika-antigen-specific neutralizing antibodies and cellular immune responses, along with protective efficacy in mice against Zika virus infection.

hAd55 infection can lead to acute respiratory disease with relatively severe symptoms. While initially reported predominantly in Korean military camps, community infection cases have emerged, particularly in China. Similar to hAd55 infection cases in Korea military camp, hAd4 and hAd7 infection cases have been prevalent in US military camp, leading to development of the vaccine. Since the introduction of hAd4 and hAd7 vaccine dramatically decreased the virus-induced respiratory disease, we started to develop hAd55 vaccine in 2019 in collaboration with Armed Forces Medical Research Institute. Isolation of hAd55 from infected patients yielded vaccine candidates, with inactivated hAd55 isolates inducing neutralizing antibodies in murine model.

HAV vaccines are commercially available, but the prices are relatively high because low production efficiency and long time to production. To address these, we produced HAV vaccine strain in Vero cells using reverse genetics (RG-HAV). After generation of RG-HAV in Vero cells, further adaptation was conducted, which improved production efficiency. Immunization with the inactivated RG-HAV elicited HAV-specific antibody responses in mice.

These findings underscore the progress in vaccine development against Zika virus, hAd55, and HAV, demonstrating promising strategies for combating infectious diseases and mitigating their public health impact.