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Hemorrhagic Fever with Renal Syndrome Vaccine in Korea

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Hemorrhagic fever with renal syndrome(HFRS), an acute interstitial nephropathy characterized by high fever and varying degrees of renal insufficiency and haemorrhage, is caused by viruses belonging to the *Hantavirus* genus of the family Bunyaviridae. Approximately 200,000 cases of HFRS occur annually in Eurasia, with a case fatality rate ranging from less than 1% to more than 10%. Because there is no specific treatment so far, the management of patients with HFRS mainly depends on supportive care. We have developed a formalin-inactivated vaccine for HFRS and evaluated in preclinical and clinical trials. The vaccine was prepared from the brains after purification according to a modification of the method used to prepare Japanese encephalitis virus mouse brain vaccine followed by inactivation with formalin. The content of myelin basic protein causing experimental allergic encephalomyelitis is less than 0.1ng/ml calculated by ELISA. In the preclinical studies, the antigenic potency of HFRS vaccine had been studied in mice. Immunized mice developed detectable antibody which in measurable by IFA. These animals were challenged with live Hantaan virus. No vaccinated animals showed any indication of infection. In contrast, all the unvaccinated control animals showed multiplication of Hantaan virus in the lung. In the clinical studies, antibody response to HFRS vaccine given was excellent. During 1996-1997, an epidemiological study of protective effect of this vaccine against HFRS was carried out in adult people living in several endemic areas of HFRS in Yugoslavia and the number of vaccinees was 2,000. The clinical responses were observed and the antibodies against Hantaan virus were examined at different intervals after 3 doses of vaccination. There was no remarkable side effect in the vaccinees either locally or in general after inoculation of the vaccine. The results showed that no confirmed cases of HFRS were observed among 2,000 HFRS vaccinees but 3 cases of HFRS were reported among 2,000 control populations.

SI-2-1

Poliovirus Sabin 1 as a Live Vector : Expression of HIV-1 p24

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Poliovirus Sabin 1 strain has features that make it a particularly attractive live recombinant mucosal vaccine vehicle. Sabin 1 cDNA was manipulated to have multiple cloning site and viral specific 3C-protease cutting site at the N-terminal end of the polyprotein. The gene for the N-terminal 169 amino acids of the HIV-1 p24 was cloned into the multiple cloning site of the manipulated Sabin 1 cDNA. Recombinant progeny virus was produced from the HeLa cells when transfected with the RNA synthesized from the p24-Sabin 1 chimeric cDNA. The recombinant progeny virus expresses substantial amounts of HIV-1 p24 protein, which was clearly detected in the infected cell lysates and culture supernatants in western blot experiments with mAb and antisera. The recombinant Sabin 1 poliovirus maintained the foreign gene stably during the subsequent passages. Replication capacity was about 1 log lower than that of wild type Sabin. These results suggests that the chimeric Sabin 1 poliovirus can be used for the development of mucosal vaccines as a live viral vaccine vector.