Single Dose of an Adenovirus Vectored Mouse Interferon-α Protects Mice from Lethal EV71 Challenge and Enhance the Production of Specific Anti-EV71 Neutralizing Antibodies

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Background/Objective

Enterovirus 71 (EV71) causes hand, foot and mouth diseases as well as neurological complications in young children and immuno-compromised adults. Currently, there is no approved drugs or vaccines for EV71. Interferon (IFN) can inhibit the replication of many viruses with low cytotoxic effects. However, due to the short half-life of IFN, its application in the clinics is restricted. To prolong the half-life and enhance the antiviral effects of IFN, an adenovirus vectored mouse interferon-α (DEF201) was generated previously. In this study, the antiviral effects of DEF201 against EV71 was evaluated in a murine model

Method

6-day-old BALB/c mice were pre- or post-treated with single dose of DEF201 and infected with lethal dose of EV71. The survival rate, clinical symptoms, tissue viral load and histology pathogenesis were evaluated

Result

IFN driven by single dose of DEF201 was maintained at high concentrations for more than 7 days in mice serum. Pre-treatment of mice with single dose of 10^6 PFU of DEF201 offered full protection of the mice against EV71 infection while empty vector control treated mice had 100% death rate and developed severe clinical symptoms including paralysis and diarrhea. In addition, the virus load in DEF201-treated mice muscle tissue was significantly reduced as compared with empty vector control. Histopathology analysis further revealed that DEF201 prevented mice from developing severe tissue damage and inflammation. Post-treatment assay at 6h instead of 12h, offered full protection indicating that DEF201 could be used as an antiviral therapeutic in early stage EV71 infection. Furthermore, our study showed that DEF201 enhanced the neutralization ability of serum in EV71-vaccinated mice implying that DEF201 could promote the production of specific anti-EV71 antibodies

Conclusion

Single dose of DEF201 is highly efficacious as a prophylactic and therapeutic agent against EV71 infection in vivo