Use of Recombinant Adenovirus Vectored Mouse IFN-α (mDEF201) to Mitigate Chikungunya Virus Infection in BALB/c Mouse Model

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Background/Objective

Chikungunya virus (CHIKV) is a mosquito-borne pathogen that is responsible for numerous large and geographical epidemics, causing millions of cases. However, there is no vaccine or therapy against CHIKV infection available on the market. Interferon-alpha (IFN-α) is an innate immune response protein that is involved in antiviral response during viral infection. Herein we demonstrated the use of an adenovirus vectored mouse IFN-α gene (mDEF201) as a prophylactic and treatment in a CHIKV-infected BALB/c mouse model.

Method

6 day-old BALB/c mice were pre- or post-treated intranasally with single dose of DEF201 at 5X10^7 PFU/animal and challenged with lethal dose of CHIKV. The survival rate, clinical symptoms and body weight were monitored for 14 days post challenge. Serum and multiple organs were harvested for viral load quantification from day 1 to 7 post challenge. Muscle and liver tissues were analysed for rescue of tissue tropism upon mDEF201 treatment at 7 days post challenge.

Result

Complete survival protection was observed in mice upon a single dose of mDEF201 administration 1 days prior to challenge, and no toxicity, as indicated by unaffected body weights of these treated mice. Viral load in the serum and multiple organs were significantly reduced upon mDEF201 administration, as compare to empty plasmid placebo set, in a dose dependent manner. Histological studies on mice tissue tropisms due to CHIKV infection also revealed that mDEF201 could significantly reduce the tissue morphological abnormities, mainly muscle fibre necrosis and infiltration of various immune cells. In addition, administration of mDEF201 at 6 hours post challenge also showed promising inhibitory effect against viral replication and dissemination.

Conclusion

Single-dose of intranasal administration with mDEF201 as a prophylactic or therapeutic agent against CHIKV is highly protective to BALB/c mouse in vivo.