A Neonatal Murine Model of Coxsackievirus A6 Infection for Evaluation of Antiviral and Vaccine Efficacy

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Coxsackievirus A6 (CVA6) is one of the major pathogens associated with hand, foot, and mouth disease (HFMD). In the present study, we present a novel murine model to study CVA6 pathology that will be extremely useful in developing effective antivirals and vaccines to diminish the burden of HFMD-associated disease.

Using this model of CVA6 infection, we found that high levels of IL-6 were associated with severe viral pneumonia and encephalitis, as in an evaluation of antiviral efficacy *in vivo*, IL-6 had no protective effect and instead accelerated death in neonatal mice. We demonstrated that, as antiviral drugs, both gamma interferon and ribavirin played important protective roles in the early stages of infection, with increased survival in treated neonatal mice challenged with CVA6. Moreover, active and passive immunization with the inactivated vaccines and anti-CVA6 serum also protected mice against homologous challenge infections.

Fig. 1 Histopathologic and IHC analyses of tissues from CVA6-infected mice.

Fig.2 Expression of proinflammatory cytokines in mice infected with CVA6.

Fig.3 Therapeutic effect of the administration of CVA6 antiserum on neonatal mice

Immunization is considered to be the most effective tool with which to control HFMD epidemics. We have employed a clinical isolate to develop a CVA6 neonatal mouse model and this mouse model of CVA6 infection provides a reliable tool for anti-CVA6 drug screening and vaccine development to develop therapies and prophylactic approaches to reduce the morbidity and mortality associated with HFMD.

Fig.4 Examination of heterologous cross-protection of CVA6 antiserum.

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