The Mucosal and Systemic Immune Responses Elicits by a CpG-adjuvanted Intranasal Enterovirus 71 Vaccine and Protects Mice against Lethal Challenge in Human SCARB2-transgenic Mice

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Background/Objective

Enterovirus 71 (EV71) is an etiologic agent responsible for seasonal epidemics of hand-foot-and-mouth disease and causes significant mortality among young children. Due to the high risk of poliomyelitis-like paralysis and fatal encephalitis, an effective vaccine to EV71 could potentially prevent virus-induced morbidity and mortality. Mucosal vaccines can efficiently induce secretory IgA at mucosal surfaces, thereby preventing or limiting infection at the site of virus entry. Since Toll-like receptor (TLR) ligands can act as both the systematic and mucosal adjuvants. CpG oligodeoxynucleotides (ODNs), resembling bacterial DNA, CpG could induce the innate immune response through activation of TLR9. We used CpG as adjuvants to study the EV71 mucosal vaccine.

Method

Each mouse was intranasal immunized at 0, 3, and 6 weeks. To evaluate the humoral immune responses, the anti-EV71 IgG and IgA were assay, and the neutralization test were detected. To evaluate the cellular immune responses, spleens were harvested to test the splenocyte proliferation and cytokines production. To confirm the neutralizing antibodies in protection, we used human SCARB2-transgenic mice to do the lethal challenge.

Result

Our datas showed that EV71-specific IgA and IgG titers of serum, nasal wash, BALF, and feces in EV71+CpG group was significantly higher than EV71 or PBS group. Furthermore, there were more EV71-specific IgA and IgG-producing cells in EV71 adjuvanted with CpG. In addition, T-cell proliferative responses, IFN-γ and IL-17 secretion were significantly increased when the EV71 was formulated with CpG. More importantly, these antibodies were able to neutralize the infectivity of EV71 (C2 genotype). They also could cross-neutralized B4 and B5 genotype of EV71 infection. In SCARB2-transgenic mice intranasal immunized with CpG-adjuvanted EV71 vaccine was able to resist the subsequent lethal challenge with EV71.

Conclusion

Our results indicate that CpG is an effective intranasal adjuvant for EV71 vaccine, and IL-17 played an important role in mucosal immunity.