CpG Oligodeoxynucleotides enhances both humoral and cellular immune responses against FMDV in mice

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Foot and Mouth Disease is one of the major contagious and devastating viral diseases which is caused by FMD virus (FMDV) of the cloven hoofed animals. FMD outbreaks all around the world caused serious economical losses during the last century. Conventionally, inactivated FMDV is the major vaccine component used to control or eradicate the disease. These vaccines have proven to be an important component of control and eradication of the disease so far. However due to difficulties to grow certain serotypes and subtypes in cell culture to get sufficient amount of antigen (Ag) for vaccine production and the lack of longevity and rapidity features of currently used vaccines, more rapid and potent vaccination strategies are urgently needed.

Synthetic oligodeoxynucleotides (ODNs) containing unmethylated CpG bases due to their high immunoadjuvant activity that promotes humoral and cell mediated immunity is receiving great attention. Several animal challenge studies and clinical trials indicated that co-administration of CpG ODNs with increased vaccine induced protection. The aim of this study is to develop CpG ODN adjuvanted FMD vaccine that confers long lasting immunity and better protection against the disease. 6-8 week old female BALB/c mice (8-10/group) were injected twice intraperitoneally at day=0 and 15 either with licenced monovalent vaccine or free FMDV serotype-O antigen were combined with CpG ODN (5ug/animal). Mouse sera were collected with 2 weeks intervals for 5 months. Serum O-specific total IgG, IgG1, IgG2a antibodies (Ab) and IFNγ levels were determined by ELISA. Neutralization levels of immune mouse sera were determined by FMD virus neutralization assay.

Our results indicated that formulations with CpG ODN were induced significantly higher levels of total IgG and IgG2a antibodies either over oil-emulsion formulated monovalent Serotype–O Ag or its free counterpart. Moreover, CpG ODN induced a robust Th1-biased immune response as evidenced by increased IgG2a/IgG1>1 ratio. This increased Ab milieu was persistent over a course of 5 months. The virus neutralization assays revealed that CpG ODN added treatment groups developed much higher neutralizing antibody titers compared to non-CpG formulations. Consistent with anti-FMD-Ab findings, virus neutralization titer levels and duration of neutralization were superior in CpG groups.

IFNγ is one of the major Th1 type cytokine which plays critical roles in the improvement of $CD8^+$ T-cell responses. It has been reported that IFNγ induced in vaccinated cattle is correlated with the animal's ability to control the replication of FMD virus. Since mice injected with CpG ODNs induced such high IgG2a/IgG1 ratios, we investigated whether CpG ODN including formulations can also induce cell-mediated immunity. As an indicator of cellular immune responses serum IFNγ levels of mice have been measured by ELISA. Our results revealed that 24h after injection CpG containing formulations induced 1,5 to 2 fold more IFNγ in serum which indicates the contribution of cell-mediated immune response

In summary, this study demonstrated that CpG ODN provided an Ag sparing effect while it achieved an enhancement both for humoral and cellular immune responses required to control better FMDV infection.