開發豬用有效生物性疫苗佐劑之新穎平台

Novel platforms for the development of effectively biological vaccine adjuvants

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Development of vaccines often faces bottlenecks such as their efficiency limitations, as well as constrains and restrictions in producing appropriate antigens. For some vaccines which induce poor immune responses, more doses will be needed to increase their effectiveness. However, vaccine efficiency in relation to its cost appears to be determining factor for farmers' willingness to invest in it.

Porcine reproductive and respiratory syndrome virus (PRRSV) is the leading causative agent of swine disease which causes severe economic losses in global. Due to high transmission rate of PRRSV, prevention and control of disease within swine field rely mainly on vaccination. However, PRRS vaccines evoke relatively late yet weak humoral mediated immune (HMI) and cell-mediated immune (CMI) responses, providing limited protection against PRRSV infection. Thus, taking vaccine's cost-effectiveness into consideration, co-administration of effective adjuvant tend to be a potential alternative to overcome the weaknesses of current vaccines.

We have developed exciting novel biological adjuvant which showed improved results in triggering immune response with no side-effects when co-administered with PRRSV vaccine. Research team of sub-project 1 has engineered novel cytokines with increased bioactivity through our well-established computational and structural biotechnology platform. The recombinant cytokines were further encapsulated in alginate/chitosan microparticles using electro-spraying technique performed by team of sub-project 2. The bioactivity of microparticle-released cytokine evaluated *in vitro* was found higher than cytokine alone, supporting chitosan's biomaterial adjuvant characteristic. Cumulative release profiles of encapsulated cytokine were investigated and a sustain release of over 16 days was observed. This result suggests that prolongation of immune response may be achieved through this approach. Research team of sub-project 3 and sub-project 4 have performed clinical trials referring to European Pharmacopoeia (Ph. Eur) Reference Standards guidelines on data requirements for adjuvant in vaccine for veterinary use. SPF piglets vaccinated with cytokine or cytokine-loaded microparticles had significantly increased interferon-γ and PRRSV-specific antibodies (IgG) secretion. These supporting results concluded that this novel cytokine is an effective adjuvant that enhances swine immunity when co-administered with the PRRSV MLV vaccine.

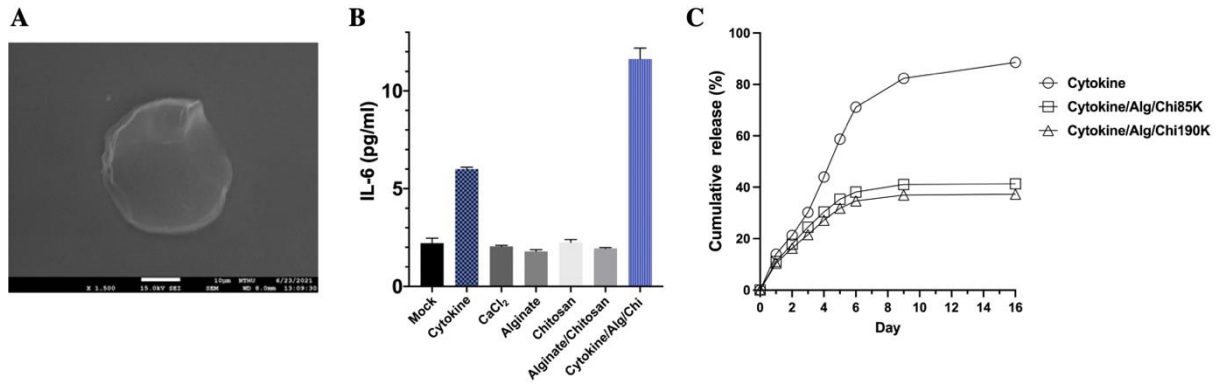

Figure 1: Microparticle-based delivery system. (A) TEM image of adjuvant microparticle prepared by encapsulating cytokine in alginate/chitosan microparticle. (B) Bioactivity evaluation of adjuvant on porcine fibroblast cell line. Cytokine/Alg/Chi (blue column) showed significant increase in bioactivity. (C) Cumulative release profiles of entrapped cytokine. Microparticles are able to release entrapped cytokine for at least 16 days in controlled manner.

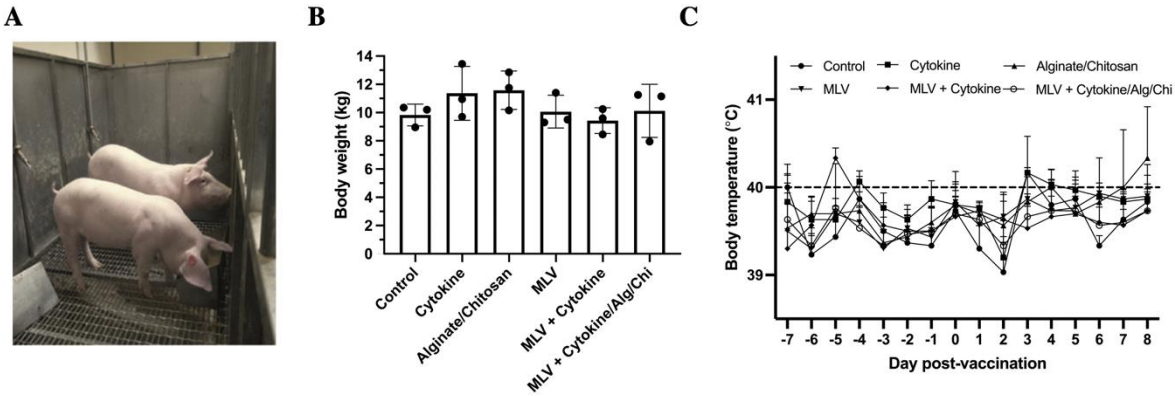

Figure 3: Safety evaluation of adjuvant in PRRSV vaccine. (A) SPF piglets fed in negative pressure barn for viral-challenge studies. (B) Body weight and (C) body temperature of piglets were recorded. No significant difference was observed, conforms to safety regulations of adjuvant.

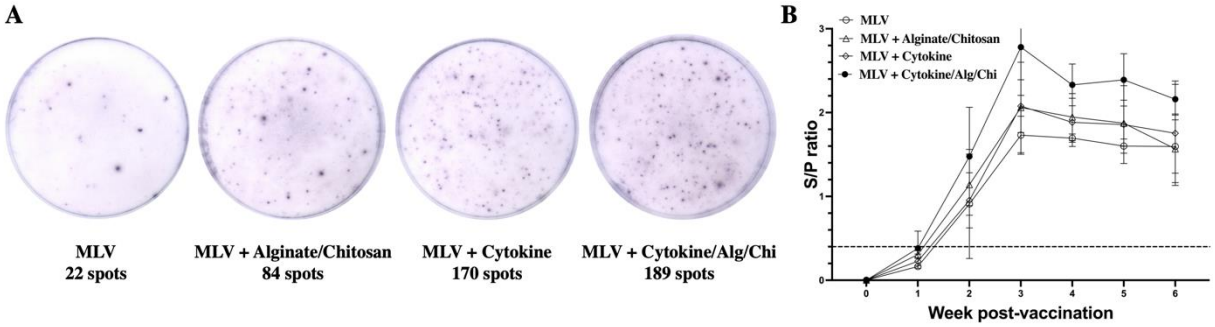

Figure 2: Evaluation of humoral and cellular immune responses of novel adjuvant in PRRSV MLV vaccine. (A) Splenocytes were harvested and infected with PRRSV Taiwan strain 109-929. IFN-γ ELISpot assay was performed to assess PRRSV-specific CMI. (B) PRRSV-specific antibody titers (S/P ratio) were carried out by ELISA. These results showed that co-administration of novel adjuvant significantly enhanced swine's CMI and HMI, particularly observed in microparticle form.

Reference

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[2] Alginate-coated chitosan nanoparticles act as effective adjuvant for hepatitis A vaccine in mice. International journal of biological macromolecules. 2020;152:904-912.