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研究課題名	Development of mucosal vaccines designed for infant based on the understanding of the infantile nasopharyngeal and gut mucosal immune system	
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(Form 2-2)

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IMSUT International Joint Usage/Research Center Project <International>

Joint Research Report (Annual/Project Completion)

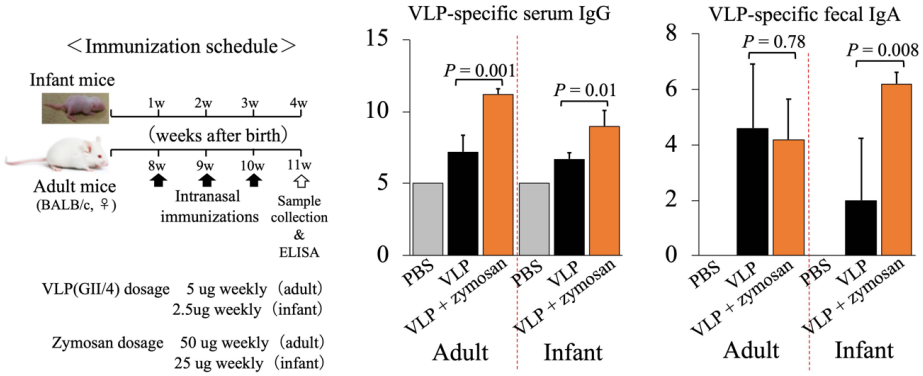
Annual Report

Report

Development of nasal norovirus vaccine for the children

We examined the effectiveness of nasal immunization of virus-like particle (VLP) derived from Norovirus (GII.4) with or without zymosan as an adjuvant in infantile and adult BALB/c mice. As a result, VLP-immunized infantile mice weakly induced VLP specific fecal IgA compared with those of VLP-immunized adult mice (Figure 1). On the other hand, nasal immunization of VLP with zymosan effectively enhanced the induction of VLP-specific fecal IgA compared with those of adult mice. These results demonstrated that zymosan can be used as the mucosal vaccine adjuvant especially for children. We will elucidate the mechanisms of zymosan-induced enhancement of infantile mucosal immunity and will develop effective nasal vaccines using zymosan as an adjuvant against various mucosal infections (e.g. Norovirus and RS virus) for children.

Figure 1. Zymosan effectively enhances induction of VLP-specific fecal IgA in infant mice.



Cationic nasal vaccine against RSV infection

Respiratory syncytial virus (RSV) is a leading cause of upper and lower respiratory tract infection, especially in children and the elderly. Various vaccines containing the major transmembrane surface proteins of RSV (proteins F and G) have been tested; however, they have either afforded inadequate protection or are associated with the risk of vaccine-enhanced disease (VED). Recently, F protein–based maternal immunization and vaccines for elderly patients have shown promising results in phase III clinical trials, however, these vaccines have been administered by injection. Here, we examined the potential of using the ectodomain of small hydrophobic protein (SHe), also an RSV transmembrane surface protein, as a nasal vaccine antigen (Figure 2). A vaccine was formulated using our previously developed cationic cholesteryl-group-bearing pullulan nanogel as the delivery system, and SHe was linked in triplicate to pneumococcal surface protein A as a carrier protein (Figure 2). Nasal immunization of mice and cotton rats induced both SHe-specific serum IgG and mucosal IgA antibodies, preventing viral invasion in both the upper and lower respiratory tracts without inducing VED. Moreover, nasal immunization induced greater protective immunity against RSV in the upper respiratory tract than did systemic immunization, suggesting a critical role for mucosal RSV-specific IgA responses in viral elimination at the airway epithelium. Thus, our nasal vaccine induced effective protection against RSV infection in the airway mucosa and is therefore a promising vaccine candidate for further development.

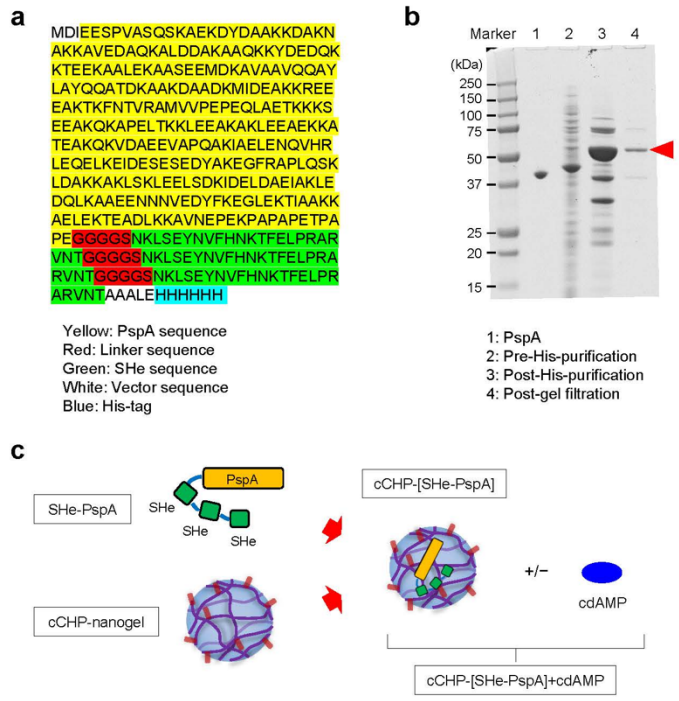


Figure 2.

The pancreas contains exocrine glands, which release enzymes (e.g., amylase, trypsin, and lipase) that are important for digestion and islets, which produce hormones. Digestive enzymes and hormones are secreted from the pancreas into the duodenum and bloodstream, respectively. Growing evidence suggests that the roles of the pancreas extend to not only the secretion of digestive enzymes and hormones but also to the regulation of intestinal homeostasis and inflammation (e.g., mucosal defense to pathogens and pathobionts). Organ crosstalk between the pancreas and intestine is linked to a range of physiological, immunological, and pathological activities, such as the regulation of the gut microbiota by the pancreatic proteins and lipids, the retroaction of the gut microbiota on the pancreas, the relationship between inflammatory bowel disease, and pancreatic diseases. We herein discuss the current understanding of the pancreas-intestinal barrier axis and the control of commensal bacteria in intestinal inflammation (Figure 3).

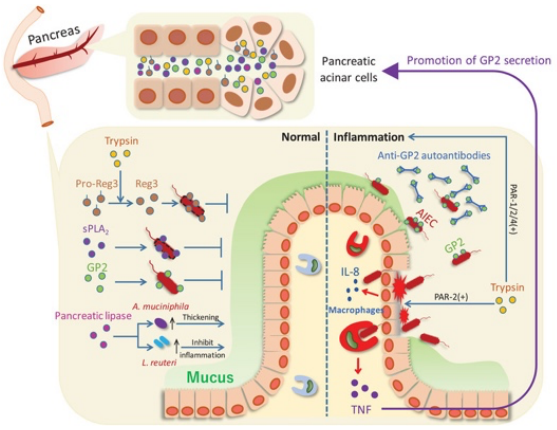


Figure 3.