No.	K25-3159	
Project Title	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)

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IMSUT International Joint Usage/Research Center Project <International>

Joint Research Report (Annual/Project Completion)

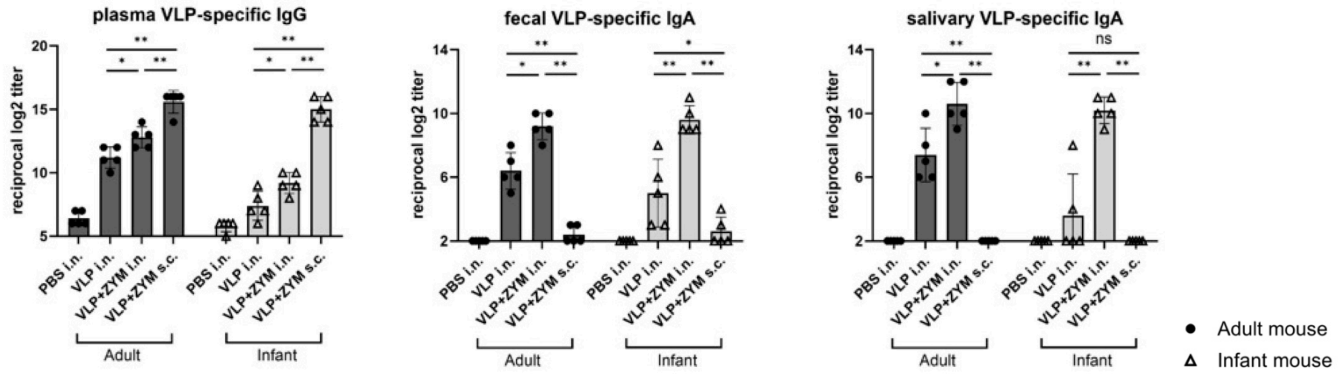
Annual Report

Report

Research Progress Report

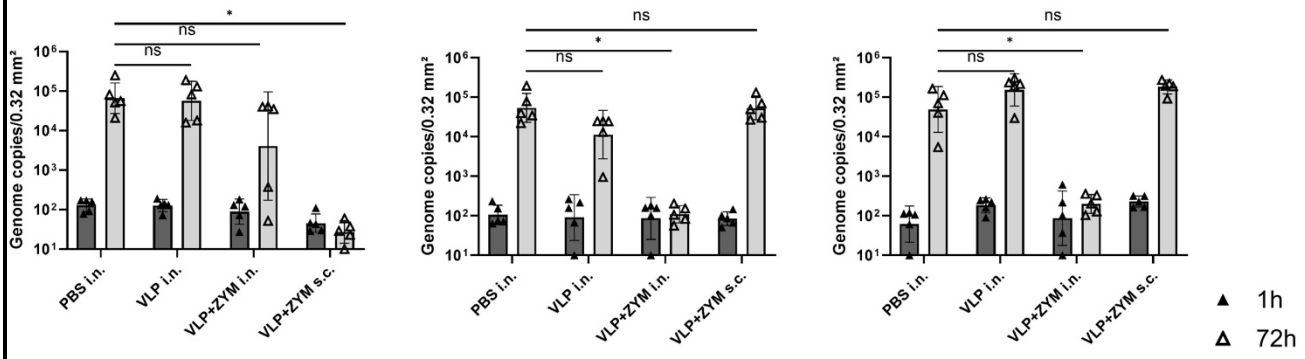
Using an infant murine model, we examined the effectiveness of an intranasal norovirus virus-like-particle (VLP) vaccine with zymosan as an adjuvant. Intranasal immunization of infant mice with VLPs alone induced mucosal and systemic VLP-specific immune responses that were substantially weaker than those of adults. In contrast, infant mice given minimum dose of intranasal VLP vaccine plus zymosan showed increased levels of salivary and intestinal VLP-specific IgA antibodies, as well as plasma VLP-specific IgG antibodies, at levels comparable to those in adults (Figure 1). Importantly, salivary and intestinal antibodies elicited by intranasal immunization with VLP vaccine plus zymosan effectively inhibited norovirus propagation in human-induced pluripotent stem (iPS) cell-derived intestinal epithelial cells. These findings suggest that intranasal norovirus VLP vaccine with zymosan is an effective mucosal vaccine candidate for infants. It may help reduce both the pain associated with injections and the number of immunizations infants need to achieve sufficient protective immunity against norovirus. Currently, we are conducting a study to elucidate the usefuleness of water-soluble beta-glucan (a major component of zymosan) as an intranasal vaccine adjuvant for the future clinical application of intranasal VLP vaccine in children.

Figure 1. VLP-specific immune response by intranasal VLP vaccine plus zymosan



Data are presented as means ± SD. Each experiment was performed in duplicate. (A–F) n = 5 per group. *P < 0.05; **P < 0.01, as determined by Tukey's test. ZYM, zymosan; i.n., intranasal immunization; s.c., subcutaneous immunization.

Figure 2. Saliva and intestinal wash fluid following intranasal immunization with virus-like particles plus zymosan inhibit norovirus propagation.



When the intestinal wash and saliva were evaluated, samples derived from infant mice intranasally immunized with VLP + zymosan (ZYM) effectively inhibited human norovirus propagation at 72h. Data are presented as means ± SD. Each

experiment was performed in duplicate. n = 5 per group. *$P < 0.05$; **$P < 0.01$ as indicated by Tukey's test. i.n., intranasal immunization; s.c., subcutaneous immunization