Development of Next Generation Vaccines with High Efficacy and Safety by Utilizing the Excellent Adjuvant Effect of Synthetic *Alcaligenes* Lipid A

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Abstract

Adjuvant are substances administered together with antigens in order to enhance vaccine effectiveness. We developed a new glycolipid adjuvant, lipid A from *Alkaligenes faecalis,* which is a symbiotic bacterium in Peyer's patch. We achieved the chemical synthesis of *A. faecalis* lipid A and demonstrated that the synthetic lipid A shows effective immune activation in both mucosal and systemic immunity without excessive inflammation. The intranasal vaccine containing this adjuvant induced the excellent protective effect against pathogens in a mouse model.

Background & Results

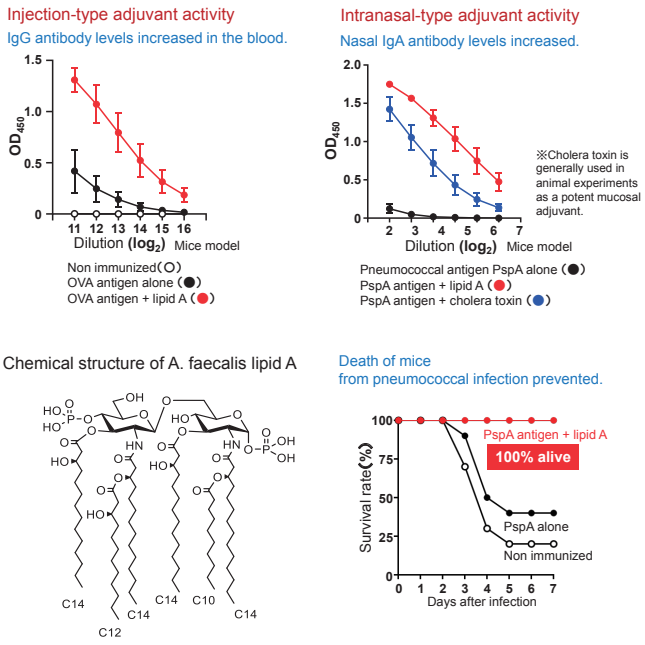
The importance of vaccines has been reaffirmed by the outbreak of new coronavirus infections. The challenges and efforts have been needed to develop vaccines, which are both safe and effective, against emerging and reemerging infectious diseases. To this end, it is necessary to develop excellent adjuvants that can optimize the effectiveness of vaccines. Until now, aluminum salts have been widely used as vaccine adjuvants. Recently, GSK developed a monophosphorylated lipid A (MPL), which is a non-toxic form of a bacterial-derived glycolipid termed lipid A, as an excellent adjuvant. MPL has been used in vaccines against viruses such as human papillomavirus (cervical cancer prevention vaccine).

Since mucosal surfaces are the most important portals of entry for pathogens, mucosal vaccines, which effectively enhance mucosal immunity as well as systemic immunity, are the next target for the vaccine development. However, effective and safe adjuvants for mucosal vaccines have not yet been developed. We developed a new mucosal vaccine adjuvant, lipid A from *Alcaligenes faecalis*, which symbiotically lives inside the intestine-associated lymphoid tissues, Peyer's patches. A. *faecalis* lipid A moderately activates mucosal and systemic immunity without inducing excessive inflammation. The research group established the chemical synthesis of A. *faecalis* lipid A and demonstrated that the synthetic lipid A effectively activates both mucosal and systemic immunity. Vaccines containing *A. faecalis* lipid A adjuvant effectively induced the antigen-specific immune response without causing adverse reactions such as inflammation. The intranasal vaccine consisting of pathogen antigen and *A. faecalis* lipid A showed excellent protection against pathogens in a mouse model.

Significance of the research and Future perspective

Since antigens alone do not effectively confer immunity, the addition of adjuvants is necessary to increase the efficacy of vaccines. However, it is not easy to develop adjuvants that are both effective and safe. The immunomodulating feature of commensal *Alcaligenes faecalis* that resides in lymphoid tissues inspired the use of *Alcaligenes* lipid A as a safe vaccine adjuvant. The chemically synthesized *Alcaligenes* lipid A enhances systemic and mucosal immunity to antigens without excessive inflammation. *Alcaligenes* lipid A can be applied to the development of various types of vaccines in the future.

Remarkable adjuvant effect of lipid A
from symbiotic bacterium *Alcaligenes faecalis*;
available for both injectable and intranasal vaccines



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Keyword adjuvant, vaccine, mucosa, immunity, antigen