

OC14 & P05 - Synthesis and functions of symbiotic bacterial lipopolysaccharide partial structures

Atsushi Shimoyama¹, Keisuke Mizote¹, Tomoya Uto¹, Flaviana Di Lorenzo², Naoko Shibata³, Yukari Fujimoto⁴, Jun Kunisawa⁵, Hiroshi Kiyono⁶, Antonio Molinaro², Koichi Fukase^{1*}

¹Osaka University.

²University of Naples Federico II.

³Waseda University.

⁴Keio University. ⁵National Institute of Biomedical Innovation. ⁶The University of Tokyo.

ashimo@chem.sci.osaka-u.ac.jp

Lipopolysaccharides (LPS) are the major glycoconjugates in outer membrane of Gram-negative bacteria and activate innate immunity to induce strong inflammation. The terminal glycolipid called lipid A is the active principle of LPS. Low inflammatory LPS, lipid A, and their derivatives have been expected as immunoadjuvants for vaccines and agents for immunotherapy.

Alcaligenes sp. have been known as opportunistic pathogens. Kiyono et al. showed that *Alcaligenes faecalis* inhabits dendritic cells in human gut Peyer's patch, which plays an important role in immune response ^[1].

In this study, we isolated LPS from *A. faecalis* and found that its component is lipooligosaccharide (LOS) with shorter oligosaccharide. Interestingly, *A. faecalis* LOS was found to be promising immune adjuvant, since it showed very low toxicity and weak inflammatory activity but high potency of antibody induction ^[2]. These results suggested *A. faecalis* LOS is an important regulator for the gut immunity.

We then determined the chemical structure of LOS by using NMR and MS to be a glycolipid composed of nona-saccharide and multiple fatty acids (molecular weight: ca. 3,000, Fig. 1). Furthermore, we have accomplished the chemical synthesis of *A. faecalis* lipid A. Synthesized *A. faecalis* lipid A showed weaker IL-6 and IL-10 inducing activity than *E. coli* LPS with bell-shaped concentration-dependency. Interestingly, in the presence of *E. coli* LPS, *A. faecalis* lipid A promoted the production of anti-inflammatory IL-10 in a concentration-dependent manner. These results suggested that *A. faecalis* LPS/lipid A is associated with maintenance of homeostasis.

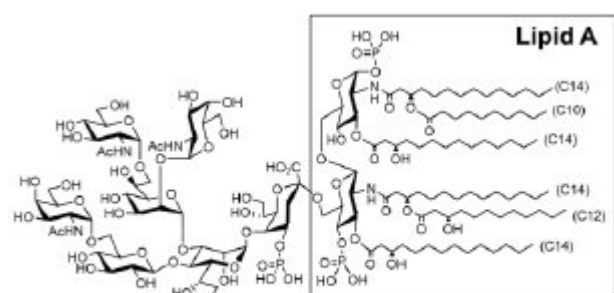


Fig. 1. *A. faecalis* LOS/lipid A

Reference

1. Obata, T., Kunisawa, J., Kiyono, H., et al. Proc. Natl. Acad. Sci. USA. 2010, 107, 7419-24.
2. Shibata, N., Kunisawa, J., Shimoyama, A., Fukase, K., Kiyono, H. et al. Mucosal Immunology 2018, 11, 693-702.