

Salmonella Outermembrane Remodeling and Innate Immune Responses

○ Kiyoshi Kawasaki (National Institute of Infectious Diseases)

Salmonella typhimurium remodels its outer membrane, including the lipid A component of lipopolysaccharide, to survive within animals. Activation of the sensor kinase PhoQ by host environments, promotes synthesis of enzymes that deacylate, palmitoylate, hydroxylate and attach aminoarabinose to lipid A, which is known as endotoxin. Deacylated- and/or palmitoylated-lipid A species were generated, and we examined their ability to induce cellular signaling through Toll-like receptor 4. The ability was reduced by the modifications, suggesting that the modifications are beneficial for bacteria to evade from host recognition.

The *Salmonellae* lipid A 3-*O*-deacylase PagL, is an outer membrane protein whose expression is regulated by PhoQ. Upon PhoQ-activation, 3-*O*-deacylated lipid A species were not detected in *S. typhimurium* despite induction of the PagL expression. In contrast, strains defective for aminoarabinose modification of the outer membrane demonstrated in vivo PagL activity, indicating that this membrane modification inhibited PagL enzymatic activity. Since not all lipid A molecules are modified with aminoarabinose upon PhoQ-activation, these results suggested that PagL enzymatic deacylation was post-translationally inhibited by membrane environments sequestering PagL from its substrate or altering its conformations. PagL-dependent deacylation was detected in sonically disrupted membrane and membrane treated with octylglucoside, suggesting that damages of intact membrane releases PagL from the post-translational inhibition.