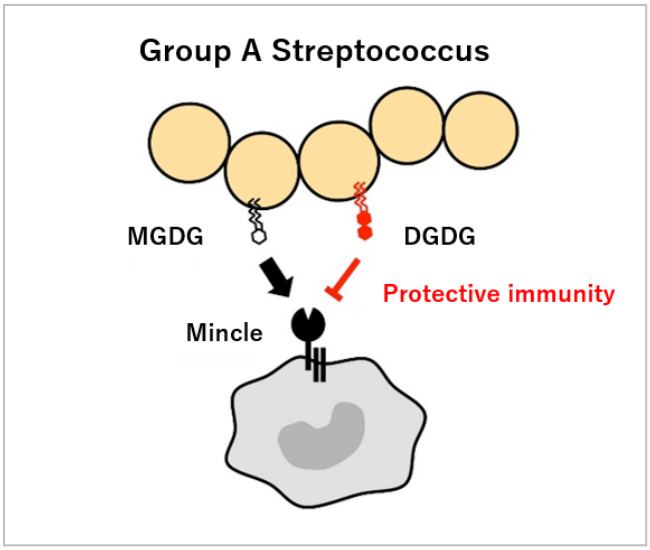
Lipoteichoic acid anchor triggers Mincle to drive protective immunity against invasive group A Streptococcus infection

Keywords: Innate immunity, Bacterial infection, C-type lectin receptors, Glycolipids

Group A Streptococcus (GAS) causes invasive streptococcal infections in humans, resulting high mortality. Thus, GAS is also known as “killer bacteria” or “flesh-eating bacteria”. However, the mechanisms by which the innate immune system recognizes GAS are not well understood.

Sho Yamasaki and his research group reported that the C-type lectin receptor macrophage inducible C-type lectin (Mincle) recognizes GAS and initiates anti-bacterial immunity. Gene expression analysis of myeloid cells upon GAS stimulation revealed the contribution of the caspase recruitment domain-containing protein 9 (CARD9) pathway to the anti-bacterial responses. Among receptors signaling through CARD9, Mincle induced the production of inflammatory cytokines, inducible nitric oxide synthase (iNOS) and reactive oxygen species (ROS) upon recognition of the anchor of lipoteichoic acid (LTA), monoglucosyldiacylglycerol (MGDG), produced by GAS. Upon GAS infection, Mincle-deficient mice exhibited impaired production of pro-inflammatory cytokines, severe bacteremia and rapid lethality. GAS also possesses another Mincle ligand, diglucosyldiacylglycerol (DGDG); however, this glycolipid interfered with MGDG-induced activation. These results indicate that Mincle plays a central role in protective immunity against acute GAS infection.



In this study, the authors showed that the innate immune receptor Mincle (macrophage inducible Ctype lectin) plays pivotal roles against invasive GAS infection through the recognition of monoglucosyldiacylglycerol (MGDG), a component of the lipoteichoic acid anchor.

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