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MProtection of Sepsis by Immunomodulator Polysaccharide PG via Regulation of Inflammation Signals

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Polysaccharide *Panax ginseng* (PG), an acidic polysaccharide prepared from *Panax ginseng*, demonstrated multiple immunomodulatory effects in previous studies. This study was conducted to elucidate the antiseptic mechanism induced by polysaccharide PG (0.0005 mg/mouse) in mice infected with *Staphylococcus aureus*. When mice were treated with polysaccharide PG before the bacterial challenge with *S. aureus*, they were highly protected from sepsis-induced death. This survival benefit was associated with enhanced bacterial clearance from circulation, spleen and kidney. The numbers of *S. aureus* recovered from polysaccharide PG-treated mice were considerably lower than those recovered from nontreated mice. The phagocytic activity of polysaccharide PG-treated macrophage against *S. aureus* was considerably enhanced. However, the synthesis of inflammatory cytokines, such as tumor necrosis factor (TNF) -α, interleukin (IL)-1β, IL-6, interferon (IFN)-γ, IL-12, and IL-18, was significantly downregulated at the early phase of sepsis in mice that were treated with polysaccharide PG before the bacterial challenge. The expression of Toll-like receptors (TLRs), including TLR2, TLR4, and TLR9, as well as the adaptor molecule MyD88, was considerably reduced in peritoneal macrophages that were treated with polysaccharide PG before a subsequent contact with *S. aureus*.

Similarly, the expression of phospho-JNK1/2, phospho-p38 MAPK, and NF-κB was decreased in the same culture system. These results illustrate that the antiseptic activity of polysaccharide PG can be attributed to enhanced bacterial clearance, and reduced pro-inflammatory cytokines via the TLR signaling pathway.

These data indicated that polysaccharide PG protected mice from *S. aureus*-induced sepsis at an early phase and the enhancement of antimicrobial activities at subsequent phases of infection through the suppression of acute inflammatory responses and the TLR signaling pathway.