

Poster Prize of the Day of BioMedical Research 2024
Best Preclinical Project

Characterization of the role of Gas6 protein in sepsis as a basis for a novel therapy

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Sepsis is a life-threatening organ dysfunction currently lacking effective therapeutic options. Evidence on the high plasma concentrations of growth-arrest specific gene 6 (Gas6), correlate this protein with disease severity and organ dysfunction in septic patients. Here, we investigated Gas6's role in sepsis using two experimental models: endotoxemia and polymicrobial peritonitis, focusing on survival outcomes and inflammatory responses. Gas6 rescue activities were assessed in endotoxemia model with *WT* mice, where we did not observe septic symptoms or death when recombinant Gas6 (rGas6) was administered at 0.5h before and 12h, 24h post LPS injection. We further assessed rGas6 effect *in vitro* in bone marrow-derived macrophages (BMDMs) stimulated with LPS. Gas6 deficient BMDMs exhibited increased TNF-alpha and IL-6 release post-LPS stimulation, which was mitigated by rGas6 supplementation, restoring the inflammatory profile to normal level. Our findings suggest Gas6 protects against sepsis-induced mortality, at least in part by modulating inflammatory cytokine production in macrophages. Future investigations will explore the immunomodulatory effects of Gas6 in more detail and the potential of Gas6 agonists to treat sepsis.