IL-7 Decreases Mortality and Protects Against T Cell Depletion During Sepsis

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INTRODUCTION: Sepsis affects greater than 750,000 patients in the US annually. Immune system dysfunction is integral to sepsis with extensive T cell apoptosis is a key characteristic. IL-7 is a cytokine central to T-cell development and homeostasis. The purpose of this investigation was to assess the role of IL-7 in a clinically relevant model of sepsis.

METHODS: We treated male C57BL/6 mice 6-8 weeks old with either 5 μg recombinant human IL-7 (rhIL7, Cytheris) or PBS control injected at time of sepsis induction.

RESULTS: To determine whether rhIL-7 treatment prevented T cell death during sepsis, we determined splenic T cell numbers. We observed increased CD4 and CD8 numbers in rhIL-7 treated mice as compared to wild type (WT) mice ($p < .01$). We further determined that expression of the anti-apoptotic molecule, Bcl-2, was significantly higher in T cells isolated from rhIL-7 treated mice. Finally, we isolated an increased percentage of activated T cells from the rhIL-7 treated mice.

These effects were associated with a significant improvement in survival in septic mice receiving rhIL-7. Additionally, serum levels of IL-6 were significantly increased in rhIL-7 treated as compared to wild type mice at 6 hours. We determined serum aspartate aminotransferase (AST) as a surrogate indicator of systemic tissue damage and found no differences between rhIL-7 treated and wild type mice.

We next assessed the immune competence of T cells. First, we found that septic mice that received rhIL-7 had improved host DTH response to antigenic challenge. Secondly, we found that isolated T cells from the IL-7 treated mice had increased *ex vivo* IFN-γ production. Finally, over the course of the first 24 hours after CLP, T cells from rhIL-7 treated mice had more sustained *in vivo* production of IFN-γ.

Lastly, we investigated whether rhIL-7 treatment mediated the host innate immune response. Here, we observed increased *in vivo* T cell production of IL-17, a cytokine involved in neutrophil recruitment and increased neutrophil recruitment and activation in the rhIL-7 treated mice.

CONCLUSION: Altogether, rhIL-7 treatment reverses the loss of critical immune effector cells and the subsequent compromised host defenses.