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Host Defense & Pathophysiology

Interleukin 7 immunotherapy improves host immunity and survival in a two - hit model of *Pseudomonas aeruginosa* pneumonia

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Abstract

Patients with protracted sepsis develop impaired immunity, which predisposes them to acquiring secondary infections. One of the most common and lethal secondary infections is *Pseudomonas aeruginosa* pneumonia. Immunoadjuvant therapy is a promising approach to reverse sepsis - induced immunosuppression and improve morbidity and mortality from secondary infections. Interleukin - 7 is an immunoadjuvant that improves survival in clinically relevant animal models of polymicrobial peritonitis and in fungal sepsis. This study investigated the effect of recombinant human interleukin - 7 (rhIL - 7) on survival in a 2 - hit model of sublethal cecal ligation and puncture followed by *P. aeruginosa* pneumonia. Potential immunologic mechanisms responsible for the rhIL - 7 putative beneficial effect were also examined, focusing on IL - 17, IL - 22, IFN - γ, and TNF - α, cytokines that are critical in the control of sepsis and pulmonary *Pseudomonas* infections. Results showed that rhIL - 7 was highly effective in preventing *P. aeruginosa*–induced death, i.e., 92% survival in rhIL - 7–treated mice versus 56% survival in control mice. rhIL - 7 increased absolute numbers of immune effector cells in lung and spleen and ameliorated the sepsis - induced loss of lung innate lymphoid cells (ILCs). rhIL - 7 also significantly increased IL - 17–, IFN - γ –, and TNF - α –producing lung ILCs and CD8 T cells as well as IFN - γ – and TNF - α –producing splenic T cell subsets and ILCs. Furthermore, rhIL - 7 enhanced NF - κ B and STAT3 signaling in lungs during sepsis and pneumonia. Given the high mortality associated with secondary *P. aeruginosa* pneumonia, the ability of rhIL - 7 to improve immunity and increase survival in multiple animal models of sepsis, and the remarkable safety profile of rhIL - 7, clinical trials with rhIL - 7 should be considered.

Citing Literature

Supporting Information