Modulating Endogenous CD4+ T cell Restoration Following Sepsis

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Background

The phenomenon of sepsis often leaves surviving patients with detrimental immunosuppressive sequelae resulting in nosocomial infections. These secondary infections following the acute phase of sepsis kill more than 200,000 hospitalized patients annually. Although survivors retain total lymphocyte cell counts after several weeks, the efficacy of the adaptive immune system is impaired. A significant influence on this impairment can be contributed to the changing profile of the CD4+ T cell population in a given system. While definitive causative agents have not been identified, reactive oxygen species and metabolic stress are candidates when considering contributors to this lymphopenic state. The surviving CD4+ populations undergo homeostatic proliferation to restore bulk numbers, however, the diversity in the repertoire of TCRs can decrease dramatically. Additionally, remaining cells can enter an energizing state where effector functions and phenotype plasticity can be limited. With newly acquired deficits in CD4+ responses, patients are left susceptible to a variety of bacterial and viral infections. Many interleukins are critical for T cell development and proliferation. IL-2 has already been implemented in treating patients with severely compromised T cell function. These interleukins may also have the potential to assist T cells rebounding from a septic environment.

Hypotheses

1) Cytokine therapy (e.g., IL-2 or IL-7) after sepsis augments CD4+ T cell recovery and function.
2) CD4+ T cells reactive to intestinal flora expand following sepsis.

Methods

![Diagram showing experimental setup and data analysis for cytokine therapy and gut flora antigens stimulation.]

Cytokine Therapy

![Diagram illustrating cytokine therapy effects on CD4+ T cells and gut flora.

Gut Flora Antigen Stimulation

![Diagram showing gut flora antigen stimulation effects on immune response.

Summary of Findings

1) IL-2 and IL-7 complex treatments enhance numerical recovery of bulk CD4+ T cells.
2) Enhancement of antigen-specific CD4+ splenocyte recovery from sepsis using interleukin therapy is cytokine selective.
3) Variability in gut microbiota influences the recovering capacity of antigen-specific T cell populations after sepsis.

Acknowledgements and References

1. Griffith Laboratory
2. The Center for Immunology, University of Minnesota
3. Summer Research Program in Infectious and Immune Disease
4. Dana Nudler, M.D.
5. V.A. Hospital, Minneapolis, MN

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