

IL-17 producing Gamma Delta T-cells in Pathophysiology of Sepsis and ARDS

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It is well established that the development of pulmonary complications (ALI, ARDS), sepsis, and multiple organ dysfunction syndrome (MODS) hampers the recovery of patients with severe traumatic injuries. While current evidence suggests that the activation of a pro-inflammatory cascade plays an important role in these pathogenic processes, the identification of a specific causative mediator has been elusive. In murine models, gamma delta T-cells have been shown to play an intricate role in the inflammatory response secondary to sepsis, burns, and trauma. Gamma delta T-cells, along with NK cells and a novel T-cell response, the Th-17 response, produce a newly discovered cytokine, IL-17. The Th-17 response in particular has been shown to be a major mediator in non-traumatic lung diseases as well as multiple inflammatory diseases. With the recent discovery of this novel effector cytokine, IL-17, and the early data suggesting that the cells responsible for its production are up regulated following trauma, there is the potential for further categorizing the biologic mechanism(s) leading to sepsis and ARDS.

We hypothesize that those patients with traumatic injury and the subsequent development of ARDS will have an increased Th-17 cytokine response both systemically and locally. To study this, 25 subjects from the SICU who have severe traumatic injury and potential pulmonary complications (undergoing bronchoscopy for clinically indicated reasons) will be enrolled and both their pulmonary and systemic immune cell responses will be analyzed with regard to the Th-17 response and other inflammatory makers. This will be done by flow cytometric analysis of immune cells and cytokines isolated from bronchoalveolar lavage fluid and peripheral blood drawn at the time of bronchoscopy. Also, 10 normal volunteers will have their systemic immune cell profile similarly analyzed.

Early preliminary data suggests that those with critical illness have a more heterogeneous Th-17 immune cell profile suggesting a dysregulation of an otherwise tightly controlled cell population. By utilizing the discoveries provided by animal models and further investigation into local and systemic cytokine profiles in human trauma victims, the information gained holds promise in the development of unique therapeutic modalities for the treatment and prevention of ARDS following traumatic injury.