Differential Inflammation Activation in M1 and M2a Pulmonary Macrophages

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Abstract

Macrophages are a key cell type in developing immune responses and preserving the integrity of the lung. Pulmonary macrophages are a heterogeneous population consisting of two major groups, the alveolar macrophages and the interstitial macrophages. Within each of these two groups there is a diverse array of subpopulations resulting from differences in activation pathways, phenotype, and function. Macrophage phenotypes can be identified by their expression of MHC class II, surface antigen expression, and protein substrates. By its ability to modulate immune responses, the pulmonary macrophage is a target for pathogenic microorganisms and plays a critical role in the pathogenesis of disease. Exposure of pulmonary macrophages to a variety of deleterious agents shifts the macrophage subpopulation has the highest inflammation driven by activation of the multi-protein complex called the inflammasome. We propose that the level of inflammation activation is distinct among separate subsets of pulmonary macrophages, and that there is a relationship between the level of inflammation activation and the role of Th2 immunity in pulmonary fibrosis. Based on these observations, we propose that the level of activation and IL-1β secretion in IL-4 treated macrophages when compared to untreated and IFN-γ treated controls. There seems to be a correlation between the level of inflammation activation and the role of Th2 immunity in pulmonary fibrosis.

Silicosis Model

Silica is a chronic inflammation and pulmonary fibrosis caused by inhalation of silica dust. The progression of the disease has been extensively studied and involves a shift in the immune response from Th1 to Th2 activation. In the silica model, changes in macrophage subpopulation have been previously shown (McMillan, 2009). Initially following silica inhalation there is a Th1 associated inflammation driven by activation of the multi-protein complex called the inflammasome and subsequent production of IL-1β. Cassel et al. (2006) proposed that the level of inflammation activation is distinct among separate subsets of pulmonary macrophages, and that there is a relationship between the level of inflammation activation and the role of Th2 immunity in pulmonary fibrosis.

Materials and Methods

Isolation of Pulmonary Macrophages

Water macrophages (AM) were isolated by whole lung lavage. Interstitial macrophages (IM) were isolated from collagenase-treated lungs and further isolated using Percoll gradient centrifugation for analysis of mRNA and IL-1β production. Flow cytometry analysis is used to collect data from the M1 macrophage population (GCD4). Cells harvested from the lungs were isolated using a rotor cell system (BD). Materials and Methods

Control

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