Zhilong Jiang et al., J Pulm Respir Med 2017, 7:2 (Suppl)
http://dx.doi.org/10.4172/2161-105X-C1-021

The distinct roles of circulating monocytes and alveolar macrophages in mouse model with acute lung injury

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Acute lung injury and acute respiratory distress syndrome (ALI/ARDS) are characterized with acute diffuse alveolar damage, influx of neutrophils and protein-rich exudates in the alveolar spaces. Circulating monocytes are activated and infiltrated into alveolar space to form alveolar macrophages, provide home defense against pathogen invasion and induce lung inflammation under the physiological and pathological conditions. Alveolar macrophages are heterogeneous types of cells. To clarify the distinct roles of circulating monocytes and alveolar macrophages, in this study we depleted circulating monocytes and alveolar macrophages respectively via intravenous and intratracheal administration of liposome clodronate into C57/B6 mice. Two days after cell depletion, the mice were intratracheal treated with LPS to establish ALI/ARDS mouse model. BAL and lung tissues were collected 2 days after LPS treatment for analysis of lung inflammation and cellular responses. We observed an elevated lung neutrophilia in BAL and lung tissues of mice treated with LPS alone as compared to the naïve control mice. However, the lung inflammation was significantly suppressed by pre-depletion of circulating monocytes in ALI/ARDS mouse model as compared to the mice treated with LPS alone. In contrast, the lung inflammation was significantly enhanced in the mice pre-depleted with alveolar macrophages as compared to the mice treated with LPS alone. The lung severity was positively correlated to the levels of MCP-1, IL-17, surfactant protein D (SP-D) and HMGB1. The results indicated the pro-inflammatory role of circulating monocytes, but anti-inflammatory role of alveolar macrophages in the LPS-induced ALI/ARDS mouse model. Blocking circulating monocyte homing into lung during LPS treatment via intraperitoneal administration of MCP-1 neutralizing antibody significantly suppressed the lung inflammation as compared to the IgG isotype antibody treated controls. In addition, we observed that resveratrol, an anti-oxidant as well as SIRT1 activator can suppress MCP-1 expression in bone marrow-derived macrophages (BMMs). Intraperitoneal adoptive transfer of the resveratrol-treated BMMs into LPS-treated mice significantly suppressed BMMs migration into lung and induction of lung inflammation in the mouse model. The immune suppressive effects were also achieved by intraperitoneally injection of resveratrol in mice with ALI/ARDS. In SOCS3 knock-out mice, we observed that SOCS3 deficiency up-regulated MCP-1 expression in the SOCS3 knock-out BMMs and lung tissues, the results were correlated to the enhanced lung inflammation as compared to the wild-type mice with ALI/ARDS. Thereby, molecular intervention of circulating monocyte function would be beneficial in the treatment of ALI/ARDS.

Biography

Zhilong Jiang is currently working in the Department of Pulmonary Medicine at Zhongshan Hospital, Fudan University, China. He holds PhD and MD degrees. He has joined the Airways Biology Initiative (ABI) in 2011 as a Postdoctoral Fellow in Dr. Haczku's Laboratory.

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