OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Clinical & Cellular Immunology

October 22-24, 2012 DoubleTree by Hilton Chicago-Northshore, USA

The ubiquitin-proteasome system regulates lung inflammation by targeting IL-33 receptor ST2L stability

Yutong Zhao
University of Pittsburgh, USA

Acute lung injury is characterized as acute respiratory failure resulting from acute pulmonary inflammation. Cytokine release and cytokine-mediated signaling contribute to pathogenesis of lung inflammatory diseases. Ubiquitin-proteasome system regulates turnover of majority of intracellular proteins. Here, we show a new orphan protein that exhibits the prototypical behavior of a SCF E3 ligase subunit; termed FBXL19 (F-box protein 19, SCF^{FBXL19}) regulates lung inflammation and injury. ST2L, a receptor of IL-33, is instable in response to IL-33 treatment. IL-33 induces ST2L ubiquitination and degradation in the proteasome system. FBXL19 targets ST2L and mediates ST2L ubiquitination and turn over. Lysine 326 within ST2L is an ubiquitin acceptor site and lysine 326 mutant of ST2L enhances its stability. IL-33-ST2L pathway plays a critical role in LPS-induced lung injury. To investigate the effect of FBXL19 in LPS-induced lung injury, we expressed a FBXL19-tdTomato fluorescence fusion protein or a lenti-control-tdTomato in mice and in vivo expression of these constructs in lung tissue was analyzed by fluorescence scanning. TUNEL assays show that FBXL19 over-expression in mice blocked LPS intratracheal challenge-induced cell death. Further, FBXL19 administration effectively attenuated LPS-induced pulmonary inflammation histologically, alveolar protein leak, and reduced IL-6 and TNFα levels in BAL fluid. These results suggest that FBXL19 exhibits an anti-inflammatory property and protects against LPS-induced lung inflammation and injury via targeting IL-33-ST2L pathway.

Biography

Zhao received his M.D. in Dalian Medical University and Ph.D. in Gifu University, School of Medicine in Japan. Zhao had been trained as pulmonary fellow in Johns Hopkins University and was promoted to a junior faculty in Johns Hopkins University and the University of Chicago. Currently, Zhao is an Associate Professor in the University of Pittsburgh. His research focuses on the role of lysophospholipids in airway inflammation and remodeling. Zhao has recently developed a new field in the role of ubiquitin-proteasome system in regulation of lung inflammation. Zhao has around 50 publications, including a recent article published in Nature Immunology.

zhaoy3@upmc.edu