

Adenovirus-Mediated gene transfer of SOCS-1 protects against acute lung injury

Narasaiah Kolliputi

Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, USA

Hyperoxia is a necessary part of treatment for patients with cardiovascular and pulmonary diseases. However, prolonged exposure to hyperoxia leads to acute lung injury (ALI), a devastating clinical problem involving key events of inflammation and cell death. Attenuating such inflammation and cell death may provide valuable insights for therapeutic intervention for ALI and the resolution of pulmonary diseases. Our long-term goal is to elucidate the regulatory signaling mechanisms in ALI as a necessary prerequisite to the development of therapeutic agents that will minimize lung damage by inhibiting cell death and inflammation. Inflammasome is a newly discovered molecular platform required for the activation and release of IL-1 β . IL-1 β is the most active cytokine in ALI patients. Recently it has been reported that reactive oxygen species (ROS) are required for purinergic P2X7 receptor (P2X7R)-mediated NALP3 inflammasome activation. Our previous results suggest that suppressor of cytokine signaling-1 (SOCS-1) functions as a negative regulator in ROS-induced apoptotic responses by inducing ASK-1 degradation. Thus, we hypothesized that the toxic effects of hyperoxia could be mediated by ASK-1-induced P2X7 mediated inflammasome and that the protective effects of SOCS-1 could be due, at least in part, to its ability to suppress inflammasome response. To test this, we administered SOCS-1 adenovirus (Ad-SOCS-1) into the lung and exposed mice to hyperoxia. Ad-SOCS-1 mice lived significantly longer in hyperoxia when compared to Ad-GFP controls. These findings suggest that SOCS-1 over-expressing mice are protected from hyperoxia-induced inflammation, which is associated with inactivation of inflammasome, thus demonstrating a critical role for SOCS-1 in inflammasome-mediated inflammation in ALI.

Biography

Narasaiah Kolliputi is an assistant professor at the University of South Florida. He graduated from Osmania University, India, where he received doctoral degree in biochemistry. He received his postdoctoral training in MGH at Harvard Medical School. His present work at USF involves elucidating translational strategies to attenuate acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). His research is funded by NIH RO1 and American Heart Association Scientist Developmental grants.

nkollipu@health.usf.edu