NLRP3-deficient mice have enhanced neutrophil apoptosis and suppressed inflammatory response to hyperoxia-induced acute lung injury

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Inspiration of high concentration of oxygen, a therapy for acute lung injury (ALI) could unexpectedly lead to reactive oxygen species (ROS) production and hyperoxia-induced acute lung injury (HALI). Nucleotide-binding domain and leucine-rich repeat PYD containing protein 3 (NLRP3) senses the ROS, triggering inflammasome activation and interleukin-1beta (IL-1β) production and secretion. However, the role of NLRP3 inflammasome in HALI is unclear. The aim of this study is to determine the effect of NLRP3 gene deletion on inflammatory response and cell death in the lungs of hyperoxic mice. In this study, WT and NLRP3−/− mice were exposed to 100% O2 for 48-72 hrs. Bronchoalveolar lavage (BAL) fluid and lung tissues were examined for proinflammatory cytokines and lung inflammation. Conditioned media from NLRP3 silenced THP-1 cells were added to human neutrophils to examine neutrophil survival and apoptosis. Results showed that Hyperoxia induced lung pathological score were suppressed in NLRP3−/− mice when compared to WT mice. Hyperoxia-induced recruitment of inflammatory cells and elevation of IL-1β, TNFα and MCP-1 are attenuated in NLRP3−/− mice. NLRP3 deletion decreased lung epithelial cell death, caspase-3 levels and suppressed NFκB levels when compared to wild type controls. Neutrophils co incubated with NLRP3 silenced THP-1 conditioned medium displayed enhanced neutrophil apoptosis when compared to controls. Taken together, this research demonstrates for the first time that NLRP3-deficient mice have enhanced neutrophil apoptosis and a suppressed inflammatory response to HALI.

Biography

Narasaiah Kolliputi is an Assistant Professor and Division Director of Research Education for Division of Allergy and Immunology at the Morsani College of Medicine. He is working on translational strategies to attenuate oxidative stress mediated acute lung injury (ALI). He received his postdoctoral training in the Massachusetts General Hospital, Harvard Medical School. He is currently serving as a grant reviewer for the National Institute of Health, Department of Defense and American Heart Association Grants. He is an Associate Editor for Frontiers in Respiratory Pharmacology, Frontiers in Oxidant Physiology, Frontiers in Non-coding RNA and Guest Associate Editor for Frontiers in Physiology, Editorial Board Member for Translational Medicine, Virology & Mycology and Journal of Biocatalysis & Biotransformation. His research is currently funded by NIH RO1 grant and American Heart Association.

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