Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Seminar

Targeting sepsis-induced acute lung injury by modulating the Calcineurin-NFATc3 pathway in pulmonary macrophages

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Specific therapies targeting cellular and molecular events of sepsis induced Acute Lung Injury (ALI) pathogenesis are lacking. We have identified a pivotal role for Nuclear Factors of Activated T cells (NFATc3) in regulating macrophage function during sepsis induced ALI. Lipopolysaccharide from E. coli activated NFATc3 in pulmonary macrophages leading to upregulation of different inflammatory genes. NFATc3 deficient mice showed decreased neutrophilic lung inflammation, improved alveolar capillary barrier function, arterial oxygen saturation and survival benefit when subjected to sepsis. Passive adoptive transfer of NFATc3 deficient macrophages in to the lungs of clodronate liposome treated wild type mice conferred protection against LPS induced ALI. Furthermore, GFP-VIVIT over expression plasmid which inhibits NFAT activation, effectively attenuated sepsis induced lung injury. As cellular uptake and binding affinity of VIVIT is low, we have developed cell permeable calcineurin peptide inhibitors that are highly potent. The cell permeable calcineurin inhibitors effectively reduced sepsis induced inflammatory cytokines and pulmonary edema in mice. Currently, we are evaluating the efficacy of calcineurin peptide inhibitors in different mouse models of acute lung injury.

Tuesday, Jan 8th 2019

11:30 AM (Tea/Coffee at 11:00 AM)

Auditorium, TIFR-H