

## Role of Adrenomedullin in LPS-mediated lung injury

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Acute Respiratory Distress Syndrome is a life-threatening disease characterized by diffuse lung injury that leads to respiratory failure and death. Among various endogenous protective peptides, adrenomedullin (AM) has been demonstrated to play a major role. The aim of our study was to assess the significance of AM in the complex pathophysiological cascade underlying lipopolysaccharide (LPS) mediated inflammatory response. In the first set of our experiments we showed that LPS induced a significant increase in the activation of the mitogen-activated protein kinase (MAPK) transduction signals in epithelial respiratory cells. In particular, our results showed a time and dose dependent activation of ERK and JNK pathways. No significant changes were observed for p38MAPK phosphorylation. Luminex analysis further confirmed the significant increase of IL-6 release along with a significant increase of MCP-1, VEGF and IL-8. Pre-treatment of cells with AM (0.5 and 1 ng/ml) showed that AM was able to prevent JNK and ERK phosphorylation. Such effect turned into a significant reduction of IL-6 and TNF- gene transcription and induction of heme oxygenase-1 (Hsp32). Taken all together our data suggest that AM may play a major role in reducing LPS mediated inflammatory response by reducing the activation of MAPK signal transduction pathway.

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### Keywords

Acute Respiratory Distress Syndrome, adrenomedullin, lipopolysaccharide, Hsp32, MAPK, p38MAPK.