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Title: The role of ATP and purinergic-receptor- signalling in the pathogenesis of ALI/ARDS

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Body: Background: This study examined the role of extracellular ATP in recruiting inflammatory cells to the lung after induction of injury with lipopolysaccharide (LPS). Extracellular ATP serves as a danger signal to alert the immune system of tissue damage by acting on P2X or P2Y receptors. Acute lung injury (ALI) is characterized by rapid alveolar injury inflammation, cytokine induction, neutrophils accumulation and vascular leakage leading to lung oedema. Here we show that endogenous pulmonary ATP levels are increased in a mouse model of acute lung injury (ALI). ATP neutralization or specific/unspecific P2R-blockade markedly reduced LPS-induced lung injury. Aims: Investigate if extracellular ATP plays a role in the LPS mediated inflammation Methods and Results: To address this hypothesis, we used a murine model of LPS-induced ALI. These studies revealed that intrapulmonary application of ATP/ADP hydrolyzing enzyme apyrase or specific/unspecific P2R-Antagonists prior (prophylactic) or 24 hours after (therapeutic) LPS instillation decreased neutrophil trafficking into the lungs, pro-inflammatory cytokines levels in bronchoalveolar lavage fluid. Conclusion: Finally we can show that apyrase or antagonists can reduce and prevent LPS induced lung inflammation. This is a projection of a new therapeutical form, what can fully develop.