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Title: LSC 2013 abstract - Host defense against pneumonia: The role of the leptin/neutrophil axis?

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Body: Rationale: Respiratory infections are an important trigger of COPD exacerbations and a major risk factor for Acute Lung Injury. We have shown that leptin is a key mediator of neutrophil recruitment to the injured lung. However, the importance of leptin in the neutrophilic response to respiratory infection remains unknown. We hypothesize that leptin contributes to development of pulmonary neutrophilia in pneumonia and that defective leptin signaling impairs this response. Methods: Leptin staining was performed in human and murine lung tissue infected with bacterial or H1N1-influenza pneumonia and controls by immunohistochemistry. BAL neutrophilia was determined 24h after murine E.coli infection and o.p. aspiration of recombinant leptin or buffer. Human blood- and murine bone marrow-derived neutrophils were examined for phosphorylation of STAT3, Erk, p38, Akt, and GSK-3β after leptin stimulation. Results: Human and murine pneumonia lung samples showed increased leptin staining compared to controls. BAL neutrophil levels in E.coli infected mice significantly increased at 24h in mice treated with leptin compared to controls, whereas in db/db mice, these levels were decreased. In human and murine neutrophils stimulated with leptin ex vivo, increases in P-p38, P-Akt, and P-GSK3β were observed, whereas no P-STAT3 or P-Erk was found, suggesting that neutrophils signal to leptin primarily through the short form of the leptin receptor (ObRa). Conclusion: Pulmonary leptin is induced in the infected lung and is effective in neutrophil recruitment to the lung following infection. This response is impaired in ObRb deficient mice. Yet, a paradox is suggested by evidence that neutrophil leptin-response is primarily through ObRa.