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Title: Adiponectin acts as an anti-inflammatory cytokine on human lung macrophages

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Body: Adiponectin (APN) is an adipokine, mostly released by adipocytes, involved in the inflammatory status observed in obese subjects. Lung macrophages were isolated from tissues obtained after surgical resection for cancer. Macrophages were treated with LPS (10 ng/ml), Poly I:C (10 µg/ml) and IL-4 (10 ng/ml) in presence or not of APN (3-10-30 µg/ml). LPS and Poly I:C are agonists that guide macrophages towards an M1-classical state of activation while IL-4 promotes an M2-alternative state. Cytokines were measured by ELISA in supernatants after 24 hours culture. In addition APN was measured in supernatants of lung parenchymal explants after 24h culture. Results were obtained from preparations on 4-9 different patients. APN concentration-dependently reduced LPS-induced release of CCL2, CXCL10, CCL4 and CXCL1; the reduction with APN 10µg/ml was respectively -73±11%, -61.5 ±16%, -56±7% and -68±8.5 %. Similarly, APN 10 µg/ml reduced Poly I:C-induced release of CCL2, CXCL10, CCL4 and CXCL1, respectively : -64.4±10%, -78±8%, -84±9% and -44.4±8.4% Finally, APN also decreased IL4-induced release of M2 cytokines: CCL13 (-96±1%) and CCL18 (-77.4±3.6%). Otherwise, the basal concentration of APN in lung parenchymal supernatants was 144±30 ng/ml corresponding to an estimated concentration of 43.2 µg/ml of interstitial tissue. This measure was not modulated by LPS. APN, at concentrations close to that in lung parenchyma, was able to reduce cytokine production in human lung macrophages stimulated either by LPS, Poly I:C or IL4, suggesting that APN may be involved in the regulation of lung inflammation.