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Title: LSC 2013 abstract - Activin-A is up-regulated in severe asthma and is associated with angiogenesis

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Body: Background: Activin-A (Act-A) is a cytokine belonging to the TGF- β superfamily. Our group has shown that Act-A suppresses mouse allergic responses; however its effects on human asthma remain unknown. Objectives: Determine Act-A expression in the serum (steady-state and during exacerbation), in bronchoalveolar lavage (BALF) and bronchial tissue of healthy controls (CTRL) and asthmatics with mild-moderate (MMA) and severe asthma (SA), identify its cellular sources, examine its signaling mediators' expression and investigate possible correlations with disease severity and airway remodeling. Methods: Act-A expression was quantified in BALF (ELISA), bronchial tissue (IHC) and serum obtained from CTRL (n=41), MMA (n=48) and SA (n=26). Act-A signaling (ActRIIA, ALK4, pSMad2/3) and remodeling markers (RBM thickness, goblet cell hyperplasia, angiogenesis) were also assessed (IHC/IF/Confocal). In vitro cultures (HPMECs) and angiogenesis models (V2A kit) were used to assess the role of Act-A in angiogenesis. Results: Act-A levels were significantly increased in the serum, particularly during exacerbations, as well as in BALF and bronchial tissue of asthmatics, especially in the subepithelium of SA. T cells, neutrophils, mast cells, macrophages and endothelial cells expressed Act-A. ActRIIA, ALK4 and pSMad2/3 expression was downregulated especially in SA. Regarding remodeling, subepithelial Act-A expression correlated with tissue angiogenesis and Act-A/ALK4 were co-expressed in endothelial cells pointing to active signaling. Preliminary in vitro experiments suggest a pro-angiogenic role for Act-A. Conclusions: Our data suggest that Act-A plays a crucial role in the inflammatory and angiogenetic processes in asthma.