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Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

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Title: LSC 2012 abstract – TGFβ1 compensates cigarette smoke induced disruption of tight junctions in the bronchial epithelium

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Body: Rationale: The airway epithelium protects the body from inhaled insults, such as smoke, or allergens. The integrity of this epithelial barrier is crucial for bronchial homeostasis. COPD and asthma have been associated with defective airway barrier function. Tight junctions (TJ) represent the major junctional components, determining the permeability of an epithelial sheet. Cigarette smoke extract (CSE) has been described to impair TJ integrity. The aim of this study was to investigate if CSE also promotes EMT in human bronchial epithelial cells (HBEC), thereby contributing to small airway diseases. Methods and results: Normal HBECs (16HBE) underwent EMT-like processes in response to TGFβ1 treatment, as characterized by elevated mesenchymal markers (FN1, SNAI1, or ZEB1). Epithelial junctional markers (e.g. CDH1, JAM1, or ZO1) were upregulated or unaltered upon TGFβ1 stimulation. 16HBE cells do not change morphological or migrational upon TGFβ1 treatment, as demonstrated by IF or live imaging. CSE downregulated TJ-associated protein expression and destabilized TJ, as observed by IF. Combined long-term treatment (7 days) of 16HBE cells with TGFβ1 and CSE resulted in restored mRNA and protein levels of TJ proteins. This was accompanied by altered MAP kinase signaling. Conclusion: TGFβ1 and CSE resulted in EMT-like changes in HBECs. CSE induced TJ disruption, which was compensated by TGFβ1 through modified signaling processes. Thus, TGFβ1 could serve as a protective factor for bronchial epithelial cell homeostasis.