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Title: Cigarette smoke extract and TGF-β_1 induce distinctive expression of extracellular matrix protein genes in human airway smooth muscle cells

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Body: Introduction: The increased thickness of airway wall in COPD is related to the abnormal deposition of extracellular matrix (ECM) proteins. Cigarette smoking and TGF-β_1 are likely involved in the pathological progress. This study aimed to compare the ECM protein gene expression in COPD and non COPD airway smooth muscle (ASM) cells stimulated by cigarette smoke extract (CSE) or TGF-β_1. Methods: Human ASM cells obtained from smoking donors with (n=3) or without COPD (n=3) were stimulated with 5% CSE or 10ng/ml TGF-β_1. RNA lysates were collected and pooled then 84 ECM and adhesion molecule related genes were examined by real time PCR. Data were normalized to 18S rRNA and expressed as fold change compared with control. A cut off of 2 fold was used to indicate up-regulation. Results: In ASM cells 70 genes can be detected at basal condition. TGF-β_1 up-regulated 27 of these genes in COPD ASM cells, and 28 genes in non-COPD ASM cells. CSE up-regulated 44 and 36 of the 70 genes in COPD and non COPD ASM cells, respectively. Among the genes up-regulated by CSE, 5 genes (collagen type I, V, VIII, XV, and thrombospondin 2) were expressed more than 1.5 times higher in COPD than non COPD ASM cells. In contrast, 6 genes (matrix metalloproteinases 1, 12, 14, ADAM metalloproteinases with thrombospondin type 1, 8, and selectin L) were at least 1.5 times lower in COPD than non COPD ASM cells. Conclusions: Overall CSE up-regulated more ECM protein genes than TGF-β_1. In particular, collagen genes were up-regulated to a greater extent in COPD versus non-COPD ASM cells. However, CSE induced matrix metalloproteinase genes had impaired up-regulation in COPD cells.