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**Title:** Transforming growth factor-beta1 (TGF- $\beta$ 1) expression is related to reticular basement membrane (Rbm) hypervascularity in smokers and COPD

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**Body:** Introduction: TGF-β1 is likely to play an important role in COPD airway pathology, including angiogenesis and epithelial mesenchymal transition (EMT), but it is relatively under-investigated in this condition. We have previously published that the Rbm is fragmented as a likely marker of active EMT and hyper-vascular in the airways of current smokers either with or without COPD. Objective: This study evaluated the status of TGF-β1 in endobronchial biopsies (ebb) from smokers with or without COPD. Methods: Ebb sections from 15 smokers with normal lung function (S-NLF), 19 current (CS) and 14 ex-smokers (ES) with COPD were immunostained for TGF-β1 and compared to 17 normal controls (NC). The percentage area of tissue and the number and area of vessels and also the percentage of vessels staining positively for TGF-β1 were compared between groups. Results: There were no differences between groups in epithelial TGF-β1 staining. TGF-β1 stained vessels in the Rbm were increased in S-NLF, CS-COPD and ES-COPD compared to NC, but especially so in CS-COPD [median (range) for number of vessels/mm Rbm 2.5 (0.0-12.7), 3.4 (0.0-8.1) and 1.0 (0.0-6.3) vs. 0.0 (0.0-7.0), p<0.05]. Percentage of vessels stained was also increased in these clinical groups compared to NC [median (range) for S-NLF 31% (0-121), for CS-COPD 40% (0-123) and for ES-COPD 22% (0-114) vs. H-N 0 % (0-26), p<0.05]. Conclusions: Vessel-associated TGF-β1 was increased in smokers and COPD, but especially in CS-COPD. This is likely to be relative to the pathogenesis of COPD; EMT, structural remodelling, angiogenesis and tumorigenesis.