

"Epithelial to mesenchymal transition in the airway epithelium from copd patients: correlation to disease severity"

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Abstract

Rationale: In chronic obstructive pulmonary disease (COPD), epithelial changes and subepithelial fibrosis are salient features in the airways. Epithelial to mesenchymal transition (EMT) has been suggested in COPD, mainly in alveolar epithelial cells. Objectives: To evaluate the presence of EMT in the airways and primary air-liquid interface cultures of bronchial epithelial cells (ALI-HBEC) from COPD patients, as compared to controls. Methods: Surgical lung tissue of COPD and control patients (n=49) and ALI-HBEC cultures (n=57) were assessed for EMT markers by immunohistochemistry, western blot and real-time qPCR. Mesenchymal functionalities of ALI-HBEC were assayed through fibronectin release and wound repair. Measurements and main results: The bronchial epithelium from COPD patients, as compared to non-smokers and smokers without COPD, showed increased vimentin expression in large (p=0.002 for severe COPD versus non-smokers) and small airways correlated with airway obstruction (FEV1...

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EPITHELIAL TO MESENCHYMAL TRANSITION IN THE AIRWAY EPITHELIUM FROM COPD PATIENTS: CORRELATION TO DISEASE SEVERITY

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Background

Chronic obstructive pulmonary disease (COPD) is associated with structural changes notably of the respiratory epithelium¹. Epithelial to mesenchymal transition (EMT) has been suggested in COPD, mainly in alveolar epithelial cells.^{2,3}

Objectives

To address EMT in the airway epithelium from COPD patients as compared to controls.

Methods

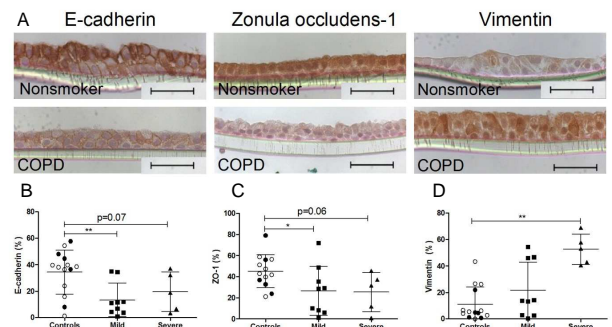
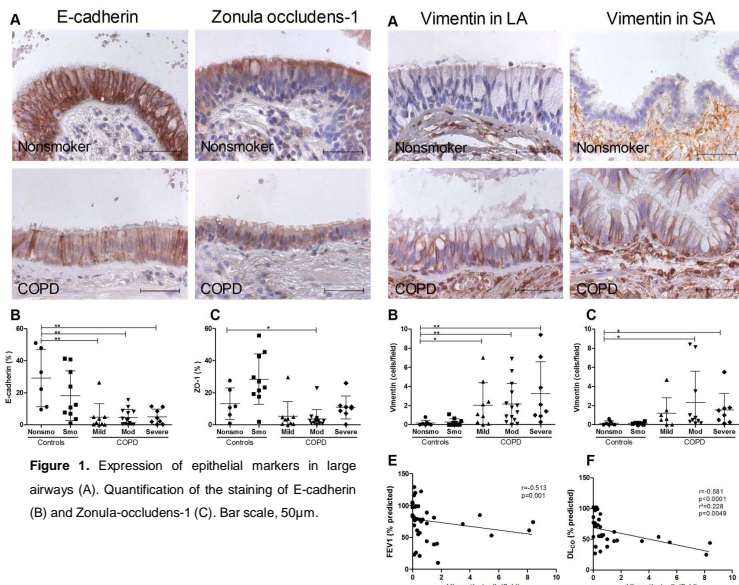
Surgical lung tissue of 52 control patients and COPD patients undergoing surgery for solitary pulmonary nodule and primary human bronchial epithelial cultures of 64 patients were assessed for EMT markers by immunohistochemistry.

Mesenchymal features were evaluated through fibronectin release and wound repair assays.

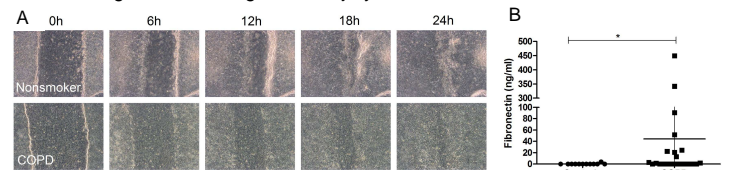
Results

The bronchial epithelium from COPD patients showed decreased epithelial markers (E-cadherin, ZO-1) and increased vimentin expression in large and small airways, which correlated with impairment in lung function.

COPD bronchial epithelium displayed similar features (upregulated vimentin, decreased E-cadherin/ZO-1) *in vitro*, which were also correlated to lung function.



COPD ALI-HBEC released increased amounts of fibronectin and displayed reduced migration following wound injury.



Conclusions

The bronchial epithelium from COPD patients displays EMT features in lung tissue, which correlates to disease severity and which are recapitulated in primary cultures upon ALI conditions. We propose that this abnormal epithelial programming contributes to peribronchial fibrosis in COPD.

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