lung, COPD and emphysema. Immunohistochemical findings were correlated with the clinical data.

Damaged alveolar walls formed distal alveolar distensions, which contained α-SMA-positive cells as well as occasionally tenascin-C and EDA-fibronectin. α-SMA-positive cells located in bronchi as foci of variable sizes. Tenascin-C expression in bronchi was analyzed as previously showing positivity a) in basal cells and basement membrane (BM), b) in basal cells plus BM plus stroma underneath BM, and c) in abovementioned areas plus widely in the stroma (2). Most of the bronchioles revealed positive cells for α-SMA, while the expression for tenascin-C and EDA-fibronectin was mainly negative. The number of α-SMA positive distal alveolar distensions was higher in non-smokers and normal lung than in smokers and COPD. The number of α-SMA positive foci in bronchi associated with obstruction. We concluded that α-SMA-positive distensions in alveolar walls might be involved in regenerative process of alveoli in normal and diseased lung. Moreover, foci of α-SMA positive cells in bronchial walls together with the excess of tenascin-C seemed to reflect remodelling process of large airways in COPD.

References
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ALTERED FIBROBLAST REPAIR FUNCTION IN COPD
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During wound healing processes fibroblasts accounts for wound closure by adopting a contractile phenotype and produce extracellular matrix (ECM) molecules. During normal wound healing the process is terminated when the wound has healed and the initial trigger disappears. However when the trigger persists, as is the case in COPD with the repeated exposure of cigarette smoke, the wound healing process becomes pathological and the fibroblast phenotype is likely to be altered. Our aim was to investigate the repair capability, defined as ECM production and contractility, in centrally (bronchial) and distally (alveolar) derived fibroblasts from severe COPD patients and control subjects.

The repair functions were different in centrally and distally derived fibroblasts from COPD patients compared to the corresponding cells from control subjects. Distally derived fibroblasts from COPD patients were more contractile and this was dependent on increased ROCK1 activity. In addition, these cells had enhanced production of the proteoglycan versican. Versican have been suggested to interfere with de novo synthesis of elastin and may thus be important in formation of emphysema. Centrally derived fibroblasts from COPD patients had a lower basal production of the basement membrane-stabilizing proteoglycan perlecan which may indicate alterations of the bronchial basement membrane in COPD. To summarize, our results suggest that fibroblasts from COPD patients have altered repair functions. Importantly, there was a difference in function between bronchial and alveolar fibroblasts which may reflect the different pathological processes in these sites.

MICROFIBRIL ASSOCIATED PROTEIN 4 (MFAP4) IS SUPPRESSED BY SMOKING AND ASSOCIATE TO DYSPNEA IN COPD PATIENTS
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Background: MFAP4 is a glycoprotein, co-localized with elastin and microfibrils in elastic fibres (Schlosser, Thomsen et al. (2006)). MFAP4 knock-out mice develop mild emphysema (not yet published data). We hypothesized that circulating MFAP4 reflects elastin degradation and can be used as a marker of emphysema severity.

Methods: Plasma levels of MFAP4 (pmMFAP4) were determined by Alphalisa® assay in 76 Danish COPD patients from the multicentre ECLIPSE study, (Vestbo, Anderson et al. (2008) 50 smokers and 54 non-smokers. Controls were healthy blooddonors. Associations between ln-transformed pmMFAP4 levels and clinical outcomes were assessed by Pearson product moment correlation test and multiple regression analysis. Age, gender, packyears and carbonmonoxide (as a indicator of current smoking) were included as covariates.

Results: Levels of lnMFAP4 were significantly lower in smokers (mean:364 ng/mL) than in non-smokers (471 ng/mL) and COPD patients (457 ng/mL). LnMFAP4 associated significantly with MMRC (Modified Medical Research Council score) in COPD patients (β: -0.09 p<0.05). There was a tendency of association between the composite BODE Index (BMI, Obstruction index, Dyspnea score and Exercise capacity), it was borderline significant when adjusting for covariates (β: -0.03 p<0.07). LnMFAP4 did not associate significantly with FEV1 (β: -0.02 p=0.24) or obstruction index (β: -0.04 p=0.13).

Conclusion: MFAP4 plasma levels are supressed by smoking, and are associated to dyspnea in COPD patients.

References

ASSESSMENT OF LOCAL INFLAMMATION IN THE LUNGS OF SMOKERS BY HRCT
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Smoking is the most important environmental risk factor for the development of COPD. Computer tomography (CT) imaging provides means of quantifying pulmonary structure and function. We hypothesized that the inflammation in smokers may be mirrored by an altered attenuation on high resolution CT (HRCT). Forty smokers with normal lung function (20 men, 20 women, age mean 54; range 45-65; 35±12 pack years, 40 healthy neversmokers, age 57 (45-65) and 40 patients with COPD, GOLD stage II, age 59 (45-65) (38±11 pack year, 31 current smokers and 9 exsmokers) underwent inspiratory HRCT scans . Values between -750 and -900 HU were considered as high attenuation areas and the percentage of the lung volume with this attenuation range was calculated. Bronchoalveolar lavage, BAL, was performed according to a standardized protocol. Cell concentration and differential cell counts in BAL fluid were recorded. The percentage of lung with high attenuation was increased in smokers (44±5.7; mean±SD) compared to neversmokers (38±5.6) and COPD exsmokers (33±4.5) (p<0.001 and p<0.05 respectively) indicating denser lungs in smokers. COPD current smokers (41±5.0) did not differ from that of smokers with normal lung function. A significant positive correlation (p<0.001) between cell concentration in BAL and HRCT areas with high density was found in current smokers. There was no significant correlation between cell concentrations in BAL and HRCT density in neversmokers and COPD exsmokers. Female neversmokers had denser lungs than males (40±1.3 vs 36±1.3, p<0.03). This was also the case for smokers with normal lung function (females 46±1.3 vs males 42±1.2; p<0.04).

The increased density in smokers compared to nonsmokers may mirror an inflammatory response induced by cigarette smoke and is correlated to current smoking status rather than smoking history. This hypothesis is strengthened by a positive correlation between lung attenuation and cell concentration in the lower respiratory tract. A gender difference was found suggesting a more intense inflammation in female smokers than in males.