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Angiotensin-converting enzyme-2 within the lung in health and disease

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Introduction: Recently there has been renewed interest in the peptides of the renin-angiotensin system (RAS) and particularly the pro-and anti-inflammatory properties of angiotensin II and angiotensin–(1-7) in cardiovascular diseases. Abnormal inflammation is also present in obstructive lung diseases but little is known about the role of RAS in this disease. We investigated the expression of the RAS pathway within the lungs of subjects with and without chronic obstructive pulmonary disease (COPD).

Method: Surgically resected human lung tissue from COPD patients (age 71.8±1.7 $FEV_1/FVC < 0.62±0.01$ 3F/9M)) and patients without COPD (age 66.8±2.0, $FEV_1/FVC < 0.79±0.02$, 7F/6M) were dissected, acetone-fixed and embedded in glycol methacrylate resin for immunohistochemistry. No subjects were prescribed steroid treatment. Serial 2μm sections of lung parenchyma were stained with antibodies to angiotensin-converting enzyme-2 (ACE-2) and angiotensin-converting enzyme (ACE). Serial sections were also stained for $CD68^+$ to identify macrophages and EN4 to locate endothelial cells.

Results: Preliminary data suggests that ACE-2 staining in the distal lung appeared to be in the alveolar macrophages. Co-localization studies using sequential sections indicate 77.4±9.2% and 68.5±8.2% of ACE-2 expressing cells/mm^2 were macrophages in the subjects with and without COPD. In a subpopulation of subjects prescribed angiotensin-converting inhibitors (ACEi), ACE-2 positive cells/mm^2 in both COPD (Median {IQR}= 9.2 {0.9-68.23}) and no COPD groups (3.3 {1.4-48.8}) were higher in number compared in subjects not prescribed ACEi both in COPD (0.8{0.0-7.9}) and no COPD groups (1.6{1.0 -11.3}). ACE was localised to blood vessels only. The mean percentage of ACE positive vessels/EN4 stained vessels ranged from 94.4-102.4% in the distal lung of all subjects. Subjects prescribed ACEi did not differ in percentage of ACE vessels stained.

Conclusions: ACE-2 and ACE protein expression within the lung is mainly located in alveolar macrophages and blood vessels in the distal lung, respectively. Subjects prescribed ACE inhibitors seem to have increased ACE-2 expression human lungs however preliminary data suggests there are no differences between subjects with or without COPD.