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Murine airway bronchodilation via Proteinase Activated Receptor 2

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Hyper-reactivity, inflammation and hyperplasia/hypertrophy of airway smooth muscle (ASM) limit airflow and are key features of chronic obstructive pulmonary disease (COPD). Proteinase activated receptor 2 (PAR2) is a critical modulator of inflammatory responses in respiratory disease such as asthma, yet is reported to promote ASM relaxation. However, the role of ASM PAR2 in COPD is not well understood (Sokolova, E. et al. Pharmacol Ther. 2007; 115(1):70-83).

Our aim was to determine the presence and role of PAR2 in murine lung and ASM subjected to an oxidative stressor environment using both immunohistochemistry (IHC) and wire myography.

PAR2 was detected using APR-32 antibody (Alomone, Israel) on both murine airway and lung tissue, with clean isotype. Data presented as mean ± SEM.

An oxidative stressor environment increased trypsin-induced ASM relaxation in both bronchial (Oxidative 54.5±8.5 % vs. Control 35.1±3.7 %; n=6; p=0.05; paired t-test) and tracheal tissue (Oxidative 56.7±10.5 % vs. Control 30.3±2.9 %; n=6; p=0.052; paired t-test). This was PAR2 dependent, as relaxation to trypsin was virtually abolished in PAR2⁻/⁻ compared with WT tracheal (WT 56.7±10.5 % vs. PAR2⁻/⁻ 2.5±0.7 %; n=3-6; p<0.01; unpaired t-test) and bronchial tissue (WT 54.5±8.5 % vs. PAR2⁻/⁻ 2.3±0.9 %; n=3-6; p<0.01; unpaired t-test). Further confirmation of PAR2 dependent relaxation was achieved using a PAR2 specific peptide (2-FLIGRLO-NH₂).

In conclusion, this study confirms a functional PAR2 role in murine airway tissue; importantly, the role of PAR2 in mediating ASM relaxation appears to be enhanced in oxidative environments such as found in COPD. This may have important implications for future potential therapies.