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Enhanced airway smooth muscle relaxation 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[1].

Our aim was to determine the presence and role of PAR2 in murine lung and ASM subjected to oxidative stress 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.

Oxidative stress increased trypsin-induced ASM relaxation in both bronchial and tracheal tissue. This was PAR2 dependent, as relaxation was significantly reduced in $PAR2^{-/-}$ compared with WT tracheal (mean ± SEM; WT 53.4±13.4 % vs. $PAR2^{-/-}$ 2.5±0.8 %; *p=0.02; n=3-4*) and bronchial tissue (WT 56±13.3 % vs. $PAR2^{-/-}$ 2.3± 0.9 %; *p=0.02; n=3-4*).

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.

1. Sokolova E, Reiser G. A novel therapeutic target in various lung diseases: Airway proteases and protease-activated receptors. Pharmacol Ther. 2007;115(1):70–83.

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