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Abstract (see notes to authors)

PROTEINASE ACTIVATED RECEPTOR 2 (PAR2) MODULATION OF MURINE AIRWAY FUNCTION

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Hyperactivity, 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 key modulator of inflammatory responses in respiratory disease such as asthma, and promotes ASM relaxation. However, the role of the receptor in ASM in conditions such as COPD is not well understood[1].

The aim of this study was to use immunohistochemistry and an *ex vivo* murine airway myograph assay to confirm the presence in murine lung of PAR2 as a functional airway modulator.

PAR2 (detected using Alomone APR-32 antibody) was present on both murine airway and lung tissue. Following exposure to a disease relevant challenge (oxidative stress), PAR2 activation with trypsin (10 U ml^{-1}), was observed to induce a higher relaxation in airway segments pre-contracted with acetylcholine (1 µM) using wire myography. Specifically, tracheal segments subjected to oxidative stress showed a significantly higher percentage relaxation (mean ± SEM; 53.8%±10.3%) compared with control (30.8%±7.9%; *p=0.05; n=4)*. A higher percentage relaxation was also observed in bronchial segments (oxidative 55.1%±10.7% vs. control 33.9%±1.2%; *p=0.07; n=4)*. The trypsin-induced relaxation was confirmed to be PAR2-dependent since relaxation to trypsin was significantly reduced in tracheal and bronchial tissue derived from PAR2-knockout mice.

Taken together this data confirms that PAR2 is present and suggests the receptor contributes functionally to the modulation of ASM tone in mice.

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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