Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol10Issue2abst040P.pdf

The Transient Receptor Potential Ankyrin 1 channel localized to non-neuronal airway cells promotes non-neurogenic inflammation.

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The transient receptor potential ankyrin 1 (TRPA1) channel, localized to airway sensory nerves, has been proposed to mediate airway inflammation evoked by allergen and cigarette smoke (CS) in rodents, *via* a neurogenic mechanism. However the limited clinical evidence for the role of neurogenic inflammation in asthma or chronic obstructive pulmonary disease raises an alternative possibility that airway inflammation is promoted by non-neuronal TRPA1. By using Real-Time PCR and calcium imaging, we found that cultured human airway cells, including fibroblasts, epithelial and smooth muscle cells express functional TRPA1 channels. By using immunohistochemistry TRPA1 staining was observed in airway epithelial and smooth muscle cells in sections taken from human airways and lung and from airways and lung of wild-type, but not TRPA1-deficient mice. In cultured human airway epithelial and smooth muscle cells and fibroblasts, acrolein and CS extract evoked IL-8 release, a response selectively reduced by TRPA1 antagonists. Capsaicin, agonist of the transient receptor potential vanilloid 1 (TRPV1), a channel co-expressed with TRPA1 by airway sensory nerves, and acrolein or CS (TRPA1 agonists), or the neuropeptide substance P (SP), which is released from sensory nerve terminals by capsaicin, acrolein or CS), produced neurogenic inflammation in mouse airways. However, only acrolein and CS, but not capsaicin or SP, released the keratinocyte chemoattractant (CXCL-1/KC, IL-8 analogue) in bronchoalveolar lavage (BAL) fluid of wild-type mice. This effect of TRPA1 agonists was attenuated by TRPA1 antagonism or in TRPA1-deficient mice. In conclusion, our results demonstrate that, although either TRPV1 or TRPA1 activation causes airway neurogenic inflammation, solely TRPA1 activation orchestrates an additional inflammatory response which is not neurogenic. This finding suggests that non-neuronal TRPA1 in the airways is functional and potentially capable of contributing to inflammatory airway diseases.