

ATS 2018 Highlights

Respiratory Structure and Function Early Career Professionals



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Contact Brenda

Get to know members of the RSF Assembly

Is your research clinical, basic science or translational?

Basic and translational science.

Tell us about your research?

I recently found that TRPA1 agonists cause bronchodilation in human and animal models of asthma. Interestingly, the mechanisms responsible for TRPA1-induced relaxation appear to vary with the cause of bronchoconstriction. These findings provide insights into mechanisms of airway hyperreactivity. My ultimate goal is to identify novel therapies for asthma.

Where do you see yourself in 5 years?

In the next 5 years, I see myself working as an independent physician-scientist at an academic institution, with a research emphasis on mechanisms of airway hyperreactivity and a clinical emphasis on obstructive lung disease.

What do you find is the major benefit of RSF Assembly Membership?

As an early career investigator, the primary advantages of being an ATS RSF member are the intellectual and collaborative connections I make with other researchers. The feedback I have received from assembly members has been invaluable for driving my work forward. I continue to be inspired and challenged by the mentors I have found in RSF, and I hope to one day follow in their footsteps.

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If you or someone you know would like to be featured as an ATS RSF ECP please email Jade Jaffar (j.jaffar@alfred.org.au)



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TRPA1 relaxes histamine and methacholine contracted airways through complementary mechanisms.

Background: Multi-target approaches may improve bronchodilator efficacy.

Stimulation of transient receptor potential ankyrin-1 (TRPA1), a ligand-gated cation channel, causes vasodilation via multiple pathways. TRPA1 is expressed on many cell types and its vasodilatory effects are the result of pathways induced by each. Because TRPA1 is expressed on airway epithelial cells, airway smooth muscle cells, and pulmonary sensory nerves, I reasoned that stimulation of TRPA1 would induce bronchodilation via multiple, complementary mechanisms.

Methods: Isolated guinea pig tracheas, mouse tracheas, and post-mortem human trachealis muscle strips were suspended in an organ bath and contracted with methacholine, histamine, or potassium chloride. Contraction strength was measured with a force transducer. Airways were then treated with increasing doses of the TRPA1 agonist allyl isothiocyanate (AITC). Epithelium was removed from some airways prior to contraction.

Results: AITC relaxed pre-contracted human, mouse, and guinea pig tracheal segments in vitro (Figure, Top panel). Tracheas from mice lacking TRPA1 did not relax when treated with AITC. In methacholine contracted airways, relaxation required airway epithelium, whereas in histamine contracted airways, relaxation was epithelium-independent (Figure, Bottom panel).

Conclusions: AITC relaxed pre-contracted tracheal smooth muscle in a TRPA1-dependent manner. TRPA1 stimulation relaxed both histamine and methacholine contracted airways via prostaglandins. In addition, stimulation of TRPA1 generated a separate epithelium-derived factor that was specifically required for relaxation of methacholine contracted tissue. These studies demonstrate that TRPA1 stimulation relaxes bronchoconstriction via multiple mechanisms that target specific contractile pathways.

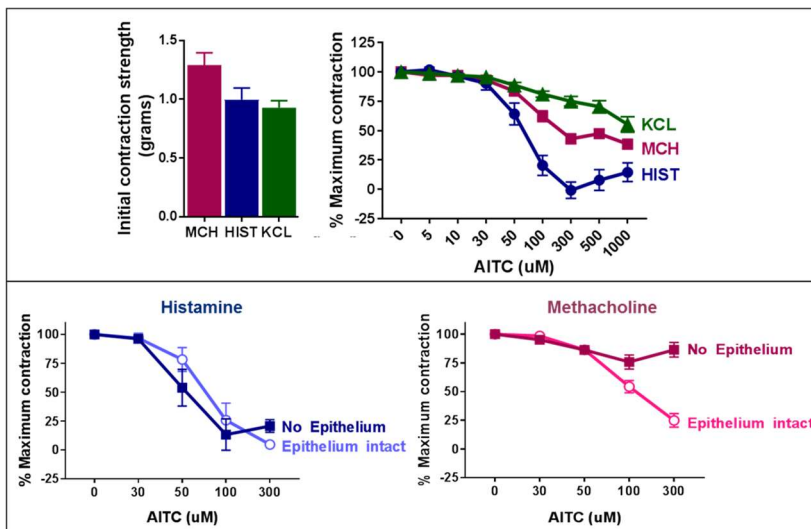


Figure. (Top panel) Allyl isothiocyanate (AITC)-relaxed pre-contracted human, mouse, and guinea pig tracheal segments in vitro. **(Bottom panel)** Effect of airway epithelium on relaxation.

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