Toxicants, salicylic acid and toluene diisocyanate, enhance carbachol-induced bronchoconstriction in human precision-cut lung slices (hPCLS)

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Abstract

Toxicants and inflammatory mediators (e.g., diisocyanates) are occupational and environmental toxins that induce asthma. Despite the prevalence of asthma, the mechanisms linking the inflammatory mediator with the toxicant to the final pathophysiological outcome are only partially understood. Salicylic acid (SA) is an irritant and a component in various consumer products available to the market, a feature we investigated. To determine if SA enhances asthma by increasing cellular-induced airway narrowing, human respiratory epithelial cells (hPCLS) were treated with SA, followed by brief exposure to diisocyanate (TDI). SA enhanced agonist-induced [Ca^{2+}]_{i} mobilization in HASM cells, whereas TDI marginally enhanced basal MYPT1 phosphorylation in HASM cells. This work is supported by Research Institute for Fragrance Materials (RIFM), NIH Training Grant T32-ESS019851 & P30-ESS01358 (CEET, University of Pennsylvania).

Hypothesis

Toxicants salicylic acid (SA) and toluene diisocyanate (TDI) modulate ASM cell shortening to elicit AHR

Toxicant-induced AHR

- Toxicants from household environment exacerbate asthma
- Salicylic acid (SA) is an irritant found in cosmetic products and toluene diisocyanate (TDI) is a respiratory sensitizer found in plastics.
- We determined the effects of SA and TDI on airway narrowing and pro-contractile signaling in ASM.

Significance

Salicylic acid-induced AHR is mediated through altered contractile signaling in HASM cells. The smooth muscle-centric signaling can be a novel therapeutic target for toxicant-induced AHR

References