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Non-Trainee

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Basic Science

Abstract Title

EpOMEs and DiHOMEs require TRPA1 and/or TRPV1 to induce calcium flux in human airway smooth muscle

Background

Oxylipins are bioactive lipid mediators found throughout the lung. Classical oxylipins such as the prostaglandins, thromboxanes, and leukotrienes are capable of promoting Airway Smooth Muscle (ASM) contraction or relaxation. Most lung derived oxylipins remain unexplored in the context of ASM contractility. We have previously shown that oxylipins EpOMEs and DiHOMEs initiate a rise in intracellular calcium (Ca^{2+}) in ASM. Previous research suggests these oxylipins activate the Ca^{2+} channels 'TRPA1' and 'TRPV1' in neuronal tissue. These channels are abundant in ASM and may be activated in a similar manner.

Objective

Therefore, we hypothesize that EpOMEs and DiHOMEs use TRPA1 and TRPV1 channels to induce transient Ca^{2+} changes in ASM.

Methods

Senescence-resistant human ASM were incubated with Ca^{2+} binding indicator dye (Fluo-4) and fluorescence was measured. ASM were pre-incubated with either DMSO (vehicle), HC-030031 (TRPA1-inhibitor), AMG 517 (TRPV1-inhibitor) or Gadolinium (cation channel blocker) for 1 hour. $10\mu\text{M}$ of 9, 10-EpOME, 12,13-EpOME, 9,10-DiHOME, or 12,13-DiHOME were injected, and fluorescence was measured in triplicate wells. Data is presented as $\Delta\text{F}/\text{F}_0$ and analyzed via One-Way ANOVA with Dunnet's post-test versus vehicle, significance set at $p < 0.05$.

Results

HC-030031 caused a significant 66% reduction in 9,10 EpOMEs Ca^{2+} response. AMG 517 was capable of significantly reducing 12,13 EpOMEs response by 80% while HC-030031 significantly augmented 12,13 EpOMEs response by 61%. AMG 517 and HC-030031 reduced 9,10 DiHOMEs response significantly by 79% and 46%, respectively. HC-030031 was capable of significantly reducing 12,13 DiHOMEs response by 65%.

Conclusion

EpOMEs and DiHOMEs require TRPA1 and/or TRPV1 to induce Ca^{2+} flux in ASM. EpOMEs and DiHOMEs are abundant in the lung and may initiate ASM contraction and airway narrowing through Ca^{2+} mechanisms. Future studies are required to understand the contractile abilities of EpOMEs and DiHOMEs and determine if they are detrimental in human airways, especially in obstructive disease like asthma.

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