19-HETE causes airway smooth muscle relaxation via cAMP production

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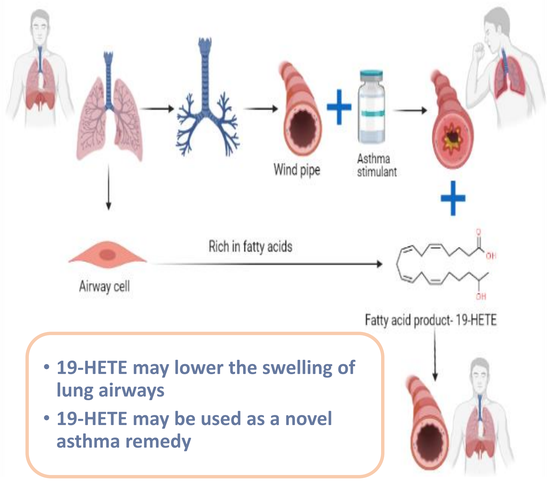
INTRODUCTION

- Asthma exacerbations, triggered by excessive inflammation and airway narrowing, causes significant childhood morbidity and mortality.
- β-agonists promote bronchodilation, can be futile due to deprivation of β-adrenergic receptor sensitivity.
- Hydroxyeicosatetraenoic acids (HETEs) are an abundant class of lipid mediators (oxylipins) in the airways.
- However, current knowledge on HETEs in the context of airway smooth muscle (ASM) physiology and asthma is scarce.
- Here, we hypothesize that **19-HETE causes ASM relaxation by promoting cAMP production in ASM cells.**

AIM

To investigate the role of HETEs in regulating ASM contractility.

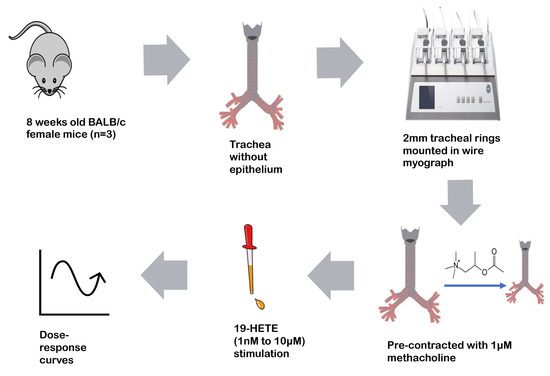


METHODS

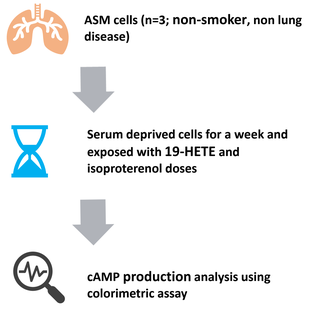
Lung oxylipin quantification

HETE production in primary cultured ASM cells (non-smokers, no lung disease, n=3) was quantified with HPLC-MS/MS.

ASM contractility: murine tracheal myography



cAMP estimation in stimulated ASM cells



Statistical analysis

Data is presented as mean +/- SD. Three-parameter dose-response curves were constructed using Graphpad Prism.

RESULTS

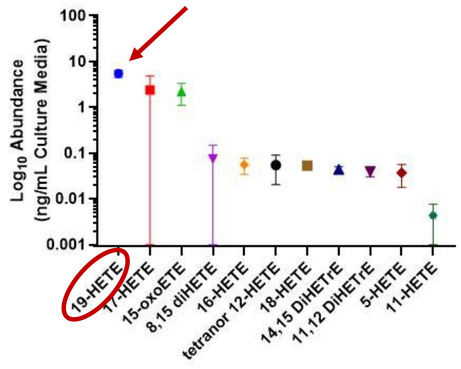


Fig. 1 **Hydroxyeicosatetraenoic** acids abundance in ASM

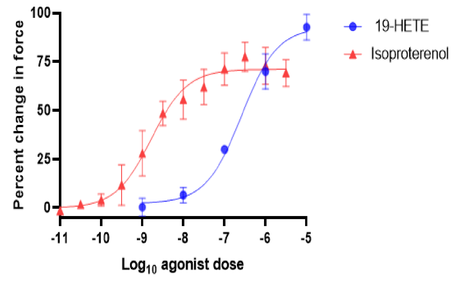


Fig. 2 Percent **change** in force with 19-HETE (0.01, 0.1, 1, and 10uM) doses

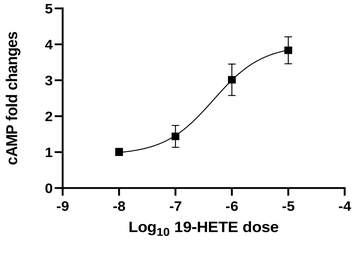
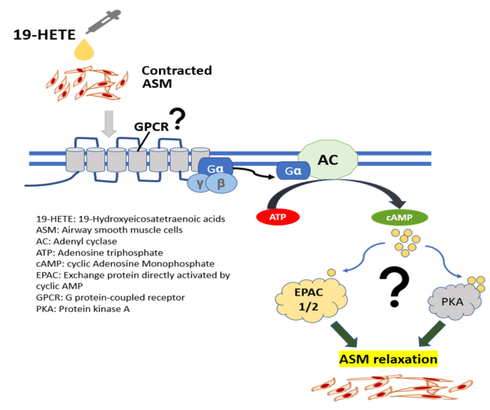


Fig. 3 Fold **increase** in cAMP with the respective 19-HETE doses

FUTURE DIRECTION

To identify the enzymes and inhibitors involved in 19-HETE stimulated cell cAMP downstream signalling pathway.



CONCLUSION

- 19-HETE is the **most abundant** HETEs in lung ASM.
- 19-HETE (1uM) stimulated murine trachea demonstrated **equivalent bronchorelaxation to isoproterenol** (1uM).
- ASM relaxation in 19-HETE exposed cells occur via **dose-dependent increase in cellular cAMP** with a maximal fold induction at 10μM.

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