ATS 2017 Highlights

Respiratory Structure and Function Early Career Professionals

Chantal Donovan, PhD

NHMRC Early Career Fellow
Priority Research Centre for Healthy Lungs
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More info on Chantal's research

Get to know members of the RSF Assembly

Is your research clinical, basic science or translational?

Basic Science.

Tell us about your research?

Our research is focused on understanding airway remodelling in lung diseases, notably chronic obstructive pulmonary disease (COPD), asthma and idiopathic pulmonary fibrosis (IPF). We have established novel mouse models of these diseases which we utilise to assess airway function using in vivo lung function mechanics, small airway function with precision cut lung slices, and molecular biology techniques, to assess novel targets and treatments for airway remodelling.

Where do you see yourself in 5 years?

In academia as a postdoctoral researcher.

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

RSF Assembly membership has been a fantastic way to network with other like-minded researchers. This has allowed me to enhance my scientific knowledge, strengthen collaborations and build an awesome network of friends worldwide.

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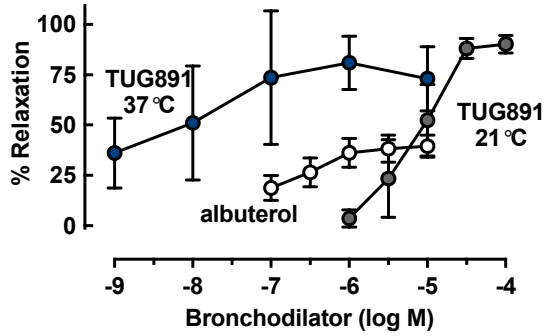

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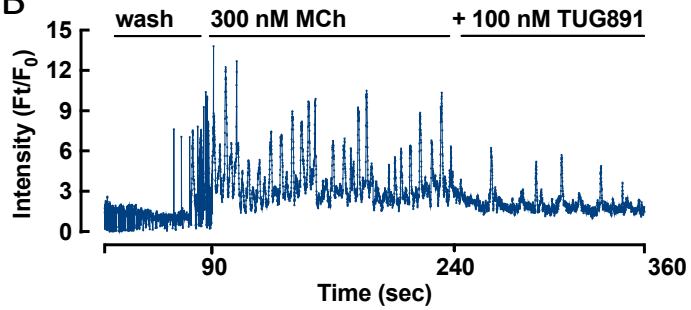

GPR120 agonist relaxes airway smooth muscle

RATIONALE: Small airways are a major site of airway obstruction in asthmatic and COPD patients. Novel bronchodilator agents targeting these airways are crucial to provide therapeutic alternatives when albuterol (ALB) is ineffective. The free fatty acid receptor 4(FFA4)/GPR120 has recently been identified in human and mouse lungs. TUG891 is able to activate GPR120, however its function in airway smooth muscle is unknown.

AIMS: To assess the effect of TUG891 on mouse small airways in precision cut lung slices (PCLS) and isolated trachea.

METHODS: Mouse PCLS were prepared for visualising changes in area of intrapulmonary airways (~200μm) by phase contrast microscopy and in calcium oscillations within airway smooth muscle cells using two-photon microscopy. Potential bronchodilator responses to TUG891 following methacholine (MCh) pre-contraction were compared with ALB. The effects of TUG891 on the increase in calcium oscillations induced by MCh were also tested. Mouse tracheal rings (2mm) were mounted in a myograph (37°C) for measurements of changes in MCh-induced tone to TUG891 and ALB.

RESULTS: TUG891 elicited concentration-dependent relaxation in PCLS. At 21°C, this occurred at μM concentrations (% relaxation: 100μM TUG891: 90.2±2.2 n=5)(Figure A). However at 37°C, TUG891 was over 100x more potent, eliciting 36.1±8.7% relaxation at 1nM and maximal relaxation at 1μM, and was 10x more potent than ALB at the same temperature. Calcium oscillations induced by 300nM MCh were inhibited by TUG891 over the same concentration range (Figure B). In mouse trachea, TUG891 elicited complete relaxation, but only at 100μM (n=4).

CONCLUSIONS: TUG891 is a potent bronchodilator, eliciting airway relaxation at nM concentrations at 37°C in PCLS, with higher potency than ALB. TUG891 appears to have a novel property of selectivity for small airways, since TUG891-mediated relaxation was only evident at μM concentrations in trachea. These data highlights that FFA4/GPR120 might represent a new target for treatment of obstructive airway diseases.

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