

ATS 2018 Highlights

Respiratory Structure and Function Early Career Professionals

Get to know members of the RSF Assembly



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Is your research clinical, basic science or translational?

Basic and translational science.

Tell us about your research?

Our research is guided by three mutually reinforcing foci: i) patient oriented research on respiratory mucosal immunology, ii) small molecule drug discovery programs for commercialization opportunities, and iii) basic science characterization of the epithelial cell biology. Presently, the major focus of the Hirota Lab is on ABC Transporters in the respiratory mucosa.

Where do you see yourself in 5 years?

I aim to develop an internationally recognized translational research group studying respiratory mucosal immunology that is simultaneously a fertile environment to train the next generation of basic and translational respiratory researchers.

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

The biggest benefit of being an RSF member is interacting and collaborating with the high caliber of researchers on an annual basis through the ATS meeting.



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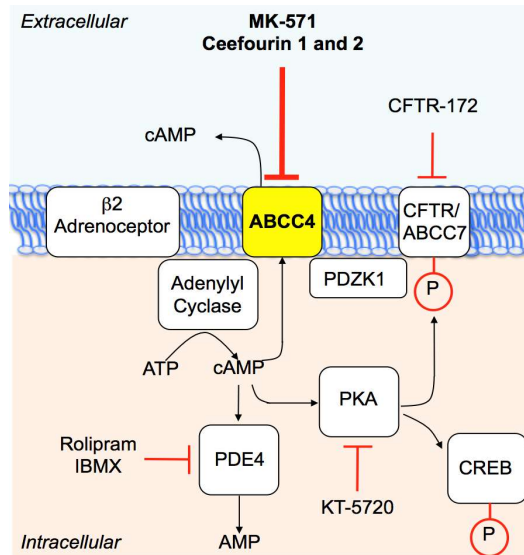
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Figure 1: Schematic detailing ATP Binding Cassette C4 (ABCC4) function as an extracellular cAMP transporter in human airway epithelial cells and interrelationship with cAMP signalling pathways. Inhibition of ABCC4 with pharmacological tools (MK-571, ceefourin 1/2) results in activation of intracellular protein kinase A, which can in turn phosphorylate and potentiate cystic fibrosis transmembrane conductance regulator (CFTR/ABCC7) and cAMP response element binding proteins (CREB).



Inhibition of ABCC4 potentiates combination beta agonist and glucocorticoid responses in human airway epithelial cells.

Objective: We have recently demonstrated that human airway epithelial cells express ABCC4 which functions as an extracellular transporter for cAMP. In chronic respiratory diseases, management practices include therapeutics that elevate intracellular cAMP. We hypothesized that inhibition of ABCC4 would augment cAMP-dependent signalling and glucocorticoid responses at the genomic and functional level, with direct implications for asthma management (**Figure 1**).

Methods: ABCC4 gene and protein expression was determined in situ in human lung samples and in vitro in human airway epithelial cells. ABCC4 gene expression was monitored following exposure to house dust mite, particulate matter, bacterial products, and viral mimic. Mechanistic in vitro experiments with human airway epithelial cells used pharmacological tools to inhibit ABCC4 and cAMP-dependent signalling and induce anti-inflammatory responses.

Results: No differences in ABCC4 gene and protein expression were observed in airway epithelial cells from healthy subjects and those with asthma. ABCC4 was not modulated by environmental exposures important in asthma pathogenesis. ABCC4 inhibition attenuates extracellular transport of cAMP, augments cAMP-dependent gene expression, and potentiates anti-inflammatory activities of combination β 2-agonist and glucocorticoid treatment.

Conclusion: Inhibition of ABCC4 in human airway epithelial cells prevents extracellular transport of cAMP and potentiates anti-inflammatory responses induced by combination β 2-agonist and glucocorticoid therapies.

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