A narrow spectrum kinase inhibitor, RV1729, induces bronchodilation of human small airways and rescues agonist-induced desensitization of the β₂ adrenoreceptor (β₂AR).

Cynthia J. Koziol-White¹, Jie Zhang¹, Edwin Yoo¹, Gaoyuan Cao¹, Catherine E. Charron², Christopher S. Stevenson²,³, and Reynold A. Panettieri Jr.¹

¹Rutgers Institute for Translational Medicine and Science, Rutgers University, New Brunswick, NJ; ²RespiVert Ltd., LBIC, London; ³Respiratory Discovery, Immunology Therapeutic Area, Janssen Pharmaceuticals, London

**Abstract**

**Roles for PI3K in allergic airways disease and β₂ adrenoreceptor function**

- Modulates mucus production, inflammatory cell influx to the lungs, degranulation of mast cells, and remodeling of the airways in a murine model of allergic airways disease.
- Inhibition of PI3K p110δ and γ attenuates allergen-induced airway hyperresponsiveness.
- PI3K p110 isoforms modulate vascular smooth muscle contractile signaling and shortening.
- RV1729 is a PI3K p110δ and γ inhibitor.

**Hypothesis**

**Selective inhibition of PI3K p110 δ and γ reverses agonist-mediated bronchoconstriction and modulates tachyphylaxis of the β₂-AR.**

**A model of airway dilation in human precision cut lung slices (hPCLS)**

Figure 1. Schematic of lung slice generation, measurement of bronchodilatation and bronchoconstriction of human small airways in precision cut lung slices.

**PI3K inhibition partially rescues formoterol-mediated hyporesponsiveness of human small airways to β₂AR agonist-induced dilation**

![Graph of Bronchodilation (%) vs Concentration (M) for various dilators and inhibitors](image)

**References**


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