

ABSTRACT


TGF-β1 Induces HASM Cell Shortening and Airway Hyperresponsiveness Through a Smad3-Dependent Signaling Pathway

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TGF-β1 and Human Airway Smooth Muscle (HASM) Cell Excitation-Contraction (E-C) Coupling

- The link between AHR and airway structural alterations in asthma is poorly understood.
- TGF-β1: an important mediator of airway structural alterations – signals through Smad3 and Smad4-dependent (and – independent pathways.
- TGF-β1 may modulate Ca2+-dependent E-C coupling pathways in HASM cell shortening and AHR.

HYPOTHESIS

TGF-β1 signaling induces AHR by directly modifying Ca2+-dependent or Ca2+-sensitization pathways in HASM cell E-C coupling.

Smad3 Knockdown Decreases TGF-β1-Induced HASM Cell Shortening and ROCK Activation

Figure 1 – TGF-β1 and Human Airway Smooth Muscle (HASM) Cell Excitation-Contraction (E-C) Coupling

Figure 2 – TGF-β1 augments hPCLS bronchoconstriction and AHR

Figure 3 – TGF-β1 Induces HASM Cell Shortening Through a ROCK-Dependent, RhoA-Independent Pathway

Figure 4 - Smad3 knockdown decreases TGF-β1-induced MLC phosphorylation and AHR.

Summary

- TGF-β1 induces hPCLS bronchoconstriction and AHR.
- TGF-β1 augments basal and agonist-induced HASM cell shortening and MLC phosphorylation via TIR.
- TGF-β1 induces HASM cell shortening through a ROCK-dependent, RhoA-independent pathway.
- Smad3 knockdown decreases TGF-β1-induced HASM cell shortening and ROCK activation.

Significance

- TGF-β1 may induce AHR through Smad3-dependent ROCK activation.
- TGF-β1 release following repeated airway injury-repair may lead to increased bronchodilator tone and sustained airway hyperresponsiveness.
- Further elucidation of this pathway may lead to the development of novel therapeutic targets for moderate and severe persistent asthma.

References


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