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TNF-a increases transcription of Gai-2

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Keywords

[Actinomycin D](#), [cyclohexamide](#), [G protein](#), [mRNA](#), [smooth muscle](#), [TNF-a](#)

Context

Tumour necrosis factor (TNF)-a, a proinflammatory cytokine that is produced in the lung, is found in increased amounts in the airways of symptomatic patients with asthma. TNF-a is thought to play a role in increasing airway smooth muscle tone and reactivity. It has been previously shown that TNF-a upregulates $G_{\alpha i-2}$ in various cell types, although the mechanism of TNF-a-induced increases in $G_{\alpha i-2}$ protein levels is unknown. In this report, the mechanism of TNF-a-mediated upregulation of $G_{\alpha i-2}$ in human airway smooth muscle cells is investigated.

Significant findings

Treatment with TNF-a increased $G_{\alpha i-2}$ protein abundance in human airway smooth muscle cells. The increase was not due to a change in viability, cell number, or alterations in protein half-life. Rather, TNF-a increased the steady-state level of $G_{\alpha i-2}$ mRNA. The authors conclude that upregulation of $G_{\alpha i-2}$ mRNA levels was due to an increase in transcription alone and not due to an increase in mRNA half-life. They did not rule out the possibility that other mechanisms that regulate protein level, such as translational efficiency, mRNA splicing, or other intracellular signalling pathways could be involved.

Comments

The authors now add $G_{\alpha i-2}$ to the growing list of signalling proteins that are regulated by TNF- α . TNF- α increases $G_{\alpha i-2}$ protein abundance secondary to increasing $G_{\alpha i-2}$ mRNA transcription. In airway smooth muscle, TNF- α impairs β -adrenoceptor-mediated airway smooth muscle relaxation and enhances methacholine airway responses. An increase in $G_{\alpha i-2}$ -mediated inhibition of adenylyl cyclase and subsequent decrease in cellular cAMP levels leading to impaired smooth muscle cell relaxation could account for these effects. This study elucidates the mechanism of TNF- α -mediated regulation of a specific G protein and its potential effect on airway smooth muscle cell tone.

Methods

Immunoblot analysis, RNA extraction, ribonuclease protection assay

Additional information

References

1. Hotta K, Hirshman CA, Emala CW: TNF- α increases transcription of $G_{\alpha i-2}$ in human airway smooth muscle cells. *Am J Physiol Lung Cell Mol Physiol.* 2000, 279: 319-325.