Nitric oxide in the pathogenesis of diffuse pulmonary fibrosis

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摘要.

Abstract

By studying the responses of nitric oxide in pulmonary fibrosis, the role of inducible nitric oxide synthase in diffuse pulmonary fibrosis as caused by lipopolysaccharide (LPS) treatment was investigated. When compared to rats treated with LPS only, the rats pretreated with 1400W (an iNOS-specific inhibitor) were found to exhibit a reduced level in: (i) NOx (nitrate/nitrite) production, (ii) collagen type I protein expression, (iv) soluble collagen production, and (iv) the loss of body weight and carotid artery PO2. In the pulmonary fibroblast culture, exogenous NO from LPS-stimulated secretion by macrophages or from a NO donor, such as DETA NONOate, was observed to induce the expression of TIMP-1, HSP47, TGF-β1, and collagen type I as well as the phosphorylation of SMAD-2. After inhalation of NO for 24 h, an up-regulation of collagen type I protein was also noted to occur in rat pulmonary tissue. The results suggest that the NO signal pathway enhanced the expression of TGF-β1, TIMP-1, and HSP47 in pulmonary fibroblasts, which collectively demonstrate that the NO signal pathway could activate the SMAD-signal cascade, by initiating a rapid increase in TGF-β1, thereby increasing the expression of TIMP-1 and HSP47 in pulmonary fibroblasts, and play an important role in pulmonary fibrosis.