Abstract

Neuropeptide Y, a 36-amino acid residue polypeptide, distributed throughout the nervous system, acts on various immune cells in many organs, including the respiratory system. However, little is known about its role in the pathogenesis of pulmonary fibrosis. This study was performed to determine the effects of neuropeptide Y on pulmonary fibrosis. Neuropeptide Y-deficient and wild-type mice were intratracheally administered bleomycin. Inflammatory cells, cytokine levels, and morphological morphometry of the lungs were analyzed. Serum neuropeptide Y levels were also measured in idiopathic pulmonary fibrosis patients and healthy controls. Neuropeptide Y-deficient mice exhibited significantly enhanced pulmonary fibrosis and higher IL-1β levels in the lungs compared to wild-type mice. Exogenous neuropeptide Y treatment suppressed the development of bleomycin-induced lung fibrosis and decreased IL-1β levels in the lungs. Moreover, IL-1β neutralization in neuropeptide Y-deficient mice attenuated the fibrotic changes. Neuropeptide Y decreased IL-1β release, and Y1 receptor antagonists inhibited IL-1β release and induced epithelial mesenchymal transition in human alveolar epithelial cells. Patients with idiopathic pulmonary fibrosis had lower neuropeptide Y and greater IL-1β levels in the serums compared to healthy controls. Neuropeptide Y expression was mainly observed around bronchial epithelial cells in human idiopathic pulmonary fibrosis

lungs. These data suggest that neuropeptide Y plays a protective role against pulmonary fibrosis by suppressing IL-1β release and manipulating the neuropeptide Y-Y1 receptor axis could be a potential therapeutic strategy for delaying disease progression.

Keywords: idiopathic pulmonary fibrosis, neuropeptide Y, IL-1β, bleomycin, bronchial epithelial cells