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Title: Role of midkine in idiopathic pulmonary fibrosis

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Body: Background: Midkine (MK) is a multi-functional heparin-binding growth factor, and previous studies have shown that MK regulates cell growth, survival and migration. MK is reported to be up-regulated in proximal tubular epithelial cells by oxidative stress, suggesting its critical roles in the pathogenesis of kidney injury. In skin fibroblasts, MK is demonstrated to stimulate collagen expression and glycosaminoglycan synthesis. Although these facts suggest the important roles of MK in tissue injury and repair processes, the role of MK in pulmonary fibrosis has not been clarified. The goal of this study was to determine if MK plays an important role in the pathogenesis of idiopathic pulmonary fibrosis (IPF). Methods: We analyzed the concentration of MK in serum of 28 patients with IPF and 10 healthy volunteers (HVs), and compared to several clinical parameters in patients with IPF. Results: The concentration of MK in serum was significantly higher in patients with IPF than HVs (1730.7 + 140.4 vs 1009.6 + 209.0 pg/ml, $p < 0.05$). In patients with IPF, serum levels of MK had no correlation with serum biomarkers such as KL-6 and SP-D, or parameters of pulmonary function test. However, there was a significant correlation of the concentrations of MK in serum with the number of neutrophils and eosinophils in bronchoalveolar lavage fluid. Conclusion: These findings suggest the possible role of MK in the pathogenesis of IPF.