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Title: A possible therapeutic agent for pulmonary fibrosis: Antibody against integrin α8β1

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Body: Integrins are transmembrane receptors that modulate multiple cellular behaviors. One member of this family, the integrin αvβ6, has been also shown to activate the pro-fibrotic growth factor, TGF-β, in the extracellular space, and to play an important role in pulmonary fibrosis. A monoclonal antibody targeting this integrin is currently in phase 2 clinical trials for treatment of pulmonary fibrosis. However, αvβ6 is restricted in its expression to epithelial cells, so inhibition of this integrin might not modulate the behavior of pathological fibroblasts that are not in contact with epithelial cells. For example, anti-αvβ6 blocking antibody did not attenuate liver fibrosis induced by CCl_4. We have targeted the α8β1 integrin, that is expressed on activated fibroblasts and reported that anti-integrin α8β1, inhibited liver fibrosis induced by either CCL_4 or bile duct ligation (Nishimichi, N. et al. Am J Respir Crit Care Med 2012; 185: A1949). We now extend these findings to pulmonary fibrosis. In this study, we treated mice with intratracheal bleomycin and then with either. 10 mg/kg anti-α8β1 antibody or saline i.p. every 3 days from day 0 to day 21 after bleomycin instillation. On day 21, lung specimens from antibody-treated mice showed reduced fibrosis by H.E. and Masson's trichrome staining compared to mice treated with saline control. α-SMA and collagen type I gene expression and hydroxyproline content were also lower in the antibody-treated mice than control mice. Antibody treatment also protected the mice from body weight loss. These results suggest that anti-integrin α8β1 antibody could be a new therapeutic agent for pulmonary fibrosis.