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**Title:** Selective endothelin-A receptor blockade attenuates bleomycin-induced pulmonary inflammation and fibrosis in mice

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**Body:** Pulmonary fibrosis is a progressive disorder leading to respiratory failure. Endothelin-1 (ET-1) is a potent vasoconstrictor, and inducer of fibrocyte and smooth muscle proliferation but its role in pulmonary fibrosis is still under investigation. We aimed to investigate the effect of selective ET-1 A (ETA) receptor blockade in the pathogenesis of pulmonary fibrosis. Adult male C57BL6 mice (4 groups; n=6-10/group) were injected intratracheally with bleomycin sulfate (BLM; 2mg/mL) or saline. Treatment with the specific ETA receptor inhibitor sitaxentan at 15mg/kg/day through drinking water, or with H2O, started one day prior to BLM injection. Mice were sacrificed at day 7, 14 and 21 post BLM, after evaluation of lung mechanics. Bronchoalveolar lavage fluid (BALF) and lung tissue samples were obtained. BLM exposure caused: i) a deterioration of lung elastance and compliance, ii) lung histological injury, and iii) increased cellularity and protein content in BALF, at all time points. Sitaxentan administration had no effect in naive mice, while in BLM-treated mice it improved lung mechanics, attenuated lung pathology and BALF pleiocytosis at all time points, and decreased BALF protein content at day 21. BLM increased tissue collagen deposition at day 21 from 200.5±18.7 (controls) to 294.4±29.8 μg/mL, denoting fibrosis, while sitaxentan administration decreased it to 219.4±5.6 (Mean±SEM; $p<0.05$ by ANOVA). In conclusion, prophylactic specific ETA receptor blockade preserves lung function, reduces airspace inflammation and lung pathology, and prevents collagen deposition in our model. ETA receptor inhibition may be a promising approach to the treatment of pulmonary fibrosis.