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Title: PBI-compound, a novel first-in-class anti-inflammatory/fibrotic compound, reduces bleomycin-induced pulmonary fibrosis by regulating inflammatory cytokines in bronchoalveolar fluid

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Body: Background: We recently reported that PBI-Compound demonstrated anti-inflammatory and anti-fibrotic activities in acute and chronic kidney disease models. Inflammatory cytokines play a key role in the pathogenesis of pulmonary fibrosis. Aims: To determine the effect of PBI-Compound on bleomycin-induced lung fibrosis at the pro-inflammatory/fibrotic cytokine level and histological lesions. Methods: C57BL/6 mice received bleomycin by intratracheal instillation on day 0, and then were treated with oral administration of PBI-Compound from day 7 to 21. Mice were euthanized on day 21 and protein level of IFN-γ, IL-1β and TNF-α was quantified in the bronchoalveolar lavage fluid (BALF). Results: The results show that intratracheal instillation of bleomycin induced a significant increase in CTGF, IL-1β and TNF-α in BALF. PBI-Compound treatment significantly decreased the amount of CTGF close to the level observed in the control group. IL-1β and TNF-α were also reduced by 20-30%. Regulation of these cytokines correlated with the histological observations from HEP and Masson's trichrome staining of the lung tissue. Bleomycin-induced widening and filling of alveolar spaces with collagen fibers indicated proliferative fibroblastic lesions that were significantly reduced with the oral treatment of PBI-Compound. Conclusions: The data suggests that treatment with PBI Compound may be beneficial in preventing the progression of lung injury by reducing tissue fibrosis and regulating key cytokines.