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Targeting the MetAP2 Pathway in Pulmonary Arterial Hypertension

Pulmonary hypertension (PH) is characterized by elevation in pulmonary arterial pressures leading to hypoxemia and right ventricular dysfunction. While idiopathic pulmonary arterial hypertension is rare, PH complicates and worsens the prognoses of many pulmonary and systemic diseases including chronic obstructive pulmonary disease, pulmonary fibrosis, human immunodeficiency virus, systemic sclerosis, and liver cirrhosis. We have previously found that pharmacologic inhibition of MetAP2 with fumagillin decreases pulmonary fibrosis in mice injured with bleomycin. We have also found that fumagillin prevents the development of PH in monocrotaline-injured rats. In this study, we will determine if fumagillin can attenuate both pulmonary fibrosis and PH in animal models of secondary pulmonary hypertension. The ultimate goal of our work is to uncover novel therapeutic approaches to PH.