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Funded by: Life Sciences Undergraduate Research Opportunity Program

Intrapulmonary expression of PPAR in a rat model of pulmonary hypertension

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Activation of peroxisome proliferator-activated receptor-gamma (PPARγ) inhibits vascular smooth muscle proliferation and neointimal formation associated with pulmonary hypertension. Recently, our laboratory developed a model of pulmonary hypertension incorporating both pnuemonectomy (PNX) of the left lung and exposure to monocrotaline (MCT) in rats. Together, PNX and MCT caused inflammation and vascular remodeling within the right lung including smooth muscle proliferation and neointimal formation. Therefore, we tested the hypothesis that PNX/MCT dual insult induces pulmonary hypertension by decreasing PPARγ expression. METHODS: Sixteen rats were randomly divided into four groups: 1) PNX/MCT, 2) PNX/Phosphate Buffer Solution (PBS), 3) Sham Surgery (SS)/MCT, and 4) SS/PBS. Seven days after surgery, we injected the animals with either monocrotaline (60 mg/kg, s.q.) or PBS. Three weeks after those injections, right ventricular systolic pressures (RVSP) were measured. Lung tissue was harvested for analysis of PPARγ protein expression and histopathology. Right ventricular to left ventricular plus septum ratios (RVR) were also determined. RESULTS: PNX/MCT animals exhibited higher RVSPs and RVRs than the other treatment groups. Also, morphometric analysis revealed medial hypertrophy and neointimal formation within the resistance vessels of PNX/MCT rat lungs. In our study, neither PNX nor MCT alone had an effect on intrapulmonary expression of PPARγ protein. Surprisingly, however, the dual insult induced PPARγ expression ($P<0.002$). We speculate that PPARγ protein may be up regulated as a consequence of the pnuemonectomy-monocrotaline dual insult and that down-regulation of this protein is not mediating the vascular remodeling of our model.