CALIFORNIA STATE SCIENCE FAIR
2010 PROJECT SUMMARY

Name(s)

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Project Number

S0413

Project Title

The Role of Bone Morphogenetic Protein Receptor 2 in the Assembly of Elastin Fibers

Abstract

Objectives/Goals

Pulmonary arterial hypertension (PAH) is characterized by progressive loss of vessels in the lungs. The pathology of the disease includes over-proliferation of smooth muscle cells and degradation of elastin fibers. Mutations in bone morphogenetic protein receptor-2 (BMPR2) have been observed in 20% of idiopathic clinical cases of the disease. BMPR2 has been shown to inhibit proliferation of smooth muscle cells and associate with heightened elastase activity. The goal of this study was to determine if the downregulation of the BMPR2 gene may play a direct role in elastin fiber assembly in vivo.

Methods/Materials

BMPR2 was deleted in vascular smooth muscle cells of mice. Mice were genotyped to identify wild-type and knockout adult mice. Breeding was setup based on these genotyping results. Distal blood vessels within fixed, transverse lung tissue of newborn mice were qualitatively characterized via light microscopy. Greater lung vessels were quantifiably studied using the BioQuant Image Analysis system. Adult mice tissue from normoxic and hypoxic mice were compared quantitatively as well.

Results

Knockout mice had visibly indistinct and disrupted elastin laminae when compared to wild-type mice via light microscopy. Quantitative investigation suggested that the thickness of elastin laminae was significantly diminished in newborn ($P < 0.0001$) and adult hypoxic ($P < 0.0001$) knockout mice.

Conclusions/Discussion

These results indicate that the absence of BMPR2 signaling has a negative effect on the assembly of elastin fibers in pulmonary vasculature. Although hypoxic conditions decrease the breakdown of elastin, adult hypoxic knockout mice still demonstrate diminished elastin laminae thickness. Moreover, the growth to adulthood does not seem to trigger elastin assembly. The results conclude that the knockout of BMPR2 may induce PAH because it effectively diminishes elastin fiber assembly.

Summary Statement

This study sought to demonstrate that the knockout of bone morphogenetic protein receptor 2 may lead to diminished elastin fiber assembly, which may be a cause of pulmonary arterial hypertension.

Help Received

Used lab equipment and conducted experiments at Stanford University under the supervision and leadership of Dr. Lingli Wang