SPRING 2021

Biochemistry and Molecular Biology Brown Bag Series

Alexandra Brown

M.S. Student

"Effects of Lipin1 Upregulation on the Diaphragm in the mdx Mouse"

Tuesday, April 13, 2021

11:00 AM

Please contact x3249 if you would like to attend but did not receive an emailed link.

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

Effects of Lipin1 Upregulation on the Diaphragm in the *mdx* Mouse

Duchenne Muscular Dystrophy (DMD) is an X-linked recessive disorder that is characterized by severe and progressive muscle wasting. This disease is caused by a mutation in the largest known human gene which encodes the protein Dystrophin. Dystrophin is critical for maintaining the structural stability of muscle cells during contraction. Mutations to the dystrophin gene result in myocyte membrane instability, contributing to the structural deterioration of the muscle tissue. Respiratory failure is a hallmark of DMD and is often the main cause of death. In Duchenne Muscular Dystrophy, the progressive deterioration of the respiratory muscles contributes to respiratory failure. Previous studies have shown that necroptosis mediates the cell death in dystrophin-deficient limb muscles, however the mechanism of cell death affecting the diaphragm in DMD has yet to be uncovered.

Currently there is no cure for Duchenne Muscular Dystrophy and gene therapy approaches are limited by the sheer size of the dystrophin gene which spans across 2,200 kb. Previous data generated from the laboratory has shown that the *mdx* mouse (used to model DMD) displays a reduced expression of Lipin1. Lipin1 is a phosphatidic acid phosphatase (PAP), which catalyzes the conversion of phosphatidic acid (PA) to diacylglycerol (DAG), a reaction important for membrane phospholipid and triacylglycerol synthesis. Preliminary data suggests overexpression of Lipin1 in skeletal muscle reduces the expression of necroptotic proteins in the diaphragm. Further investigation is required to identify the mechanism of cell death affecting the *mdx* diaphragm, and to determine if Lipin1 overexpression can ameliorate respiratory dysfunction in the *mdx* mouse model.