Spring 2018

The Role of Lipin 1 in Cardiac Metabolism and Function

Alison Swearingen
Washington University in St. Louis

The Role of Lipin 1 in Cardiac Metabolism and Function

Alison Swearingen

Mentor: Brian Finck

Lipin 1 is an intracellular protein that dephosphorylates phosphatidic acid (PA) to generate diacylglycerol, which is an important step in lipid metabolism. Exercise, which affects cardiac metabolism, has been shown to increase lipin 1 expression in mice, while heart failure or hypertrophy has been shown to cause decreased lipin 1 expression. We have hypothesized that accumulation of PA in failing heart contributes to cardiac hypertrophy and dysfunction, and thus, the overexpression of lipin 1 in failing hearts will alleviate cardiac dysfunction by reducing PA accumulation. To test this hypothesis, we generated transgenic mice with cardiac specific overexpression of lipin 1 (cs-lipin 1 OE) by using a cre-inducible transgene to examine the effects of this protein on cardiac metabolism and function. The cs-lipin 1 OE mice appear outwardly normal, and H&E staining did not show any architectural abnormalities or inflammatory infiltrates.

Additionally, echocardiographic studies revealed no functional abnormalities in the hearts of cs-lipin 1 OE mice compared to littermate control mice. However, the cs-lipin 1 OE mice have increased heart weight to body weight ratios and increased expression of several genes associated with ventricular hypertrophy at baseline. Following pressure overload on the heart, cs-lipin 1 OE mice have slightly decreased expression of some genes associated with hypertrophy compared to littermate control mice. The cs-lipin 1 OE mice show no change in heart function, architecture, or inflammation as measured by echocardiography and H&E staining when compared to wild type control mice following pressure overload. While contrary to our original hypothesis, these data provide novel evidence that lipin 1 may influence cardiac hypertrophy and function.