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THE ROLE OF LIPIN 1 IN CARDIAC METABOLISM AND FUNCTION

Alison Swearingen

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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. While contrary to our original hypothesis, these data provide novel evidence that lipin 1 may influence cardiac hypertrophy and function.