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ALTERED ISLET FUNCTION MAY PROMOTE A LEAN PHENOTYPE IN TAFAZZIN DEFICIENT MICE

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Background:

Barth syndrome (BTHS) is a rare x-linked genetic disease. Mutations occur in the gene tafazzin which causes the content and molecular structure of cardiolipin to be altered in the inner mitochondrial membrane. A well-established characteristic of BTHS is growth deficiency. Previous evaluations of individuals with BTHS have indicated low-mean body weights.

Objective:

In this study, we utilized a mouse model with an inducible tafazzin shRNA knock-down to investigate the *in vivo* effects of tafazzin deficiency on weight gain.

Methods:

We have utilized isolated pancreatic islets to measure insulin secretion rates, total insulin levels and oxygen consumption rates.

Results:

Previously, we have established that tafazzin knock-down mice were lean and maintained insulin sensitivity compared to the obese insulin resistant control litter mates. We have now determined that tafazzin protects against elevation in islet insulin content and loss of glucose-induced insulin secretion which are often associated with obesity-induced insulin resistance. We have ascertained that the quantity of beta-cells was similar between genotypes. However, insulin secretion during basal conditions was reduced from islets isolated from tafazzin knock-down mice. As a result, tafazzin knock-down mice exhibited significantly reduced basal insulin plasma levels. Preliminary data suggests that mitochondrial oxygen consumption is elevated due to increased heat production in islets lacking tafazzin.

Conclusion:

Our experiments indicate that tafazzin may have a role in regulating islet beta-cell function. These data also suggest that mice deficient in tafazzin may gain less weight, in part, by reducing basal insulin levels.