leptin resistance, and body weight in the periphery and the brain. In the hypothalamic arcuate nucleus (ARC) of the brain, Sirt1 increases in the obese state and acts to promote weight gain as well as insulin and leptin resistance by increasing the orexigenic neuropeptides Agouti-related protein (AgRP) and neuropeptide Y (NPY), and in a distinct set of ARC neurons, by decreasing POMC and thus its anorexigenic derivative alpha-melanocyte stimulating hormone (alpha-MSH) (1). Sirt1's actions on these neuropeptides are mediated at least in part by the deacetylation of the transcription factor forkhead box O1 (FOXO1). Another mechanism by which Sirt1 regulates body weight appears to be through mediating changes in the synapses of these neuropeptide-producing ARC neurons. For example, a previous study demonstrated that Sirt1 inhibition with the specific Sirt1 inhibitor, Ex-527, decreased AgRP-NPY inhibitory synaptic input on POMC neurons, which suggests that the obesity-induced increase in ARC Sirt1 would increase AgRP-NPY inhibition of POMC neurons thus promoting weight gain (2). The present study investigated how Sirt1 regulates synapses specifically in POMC-producing N43-5 neurons. Results reveal that inhibition of Sirt1 with Ex-527 significantly increased the presynaptic marker Synapsin 1 (Syn1) in N43-5 neurons. Furthermore, we investigated whether the Sirt1 target, FOXO1, mediates these synaptic changes. FOXO1 overexpression significantly decreased Syn1 and transfection of mutant FOXO1 significantly increased Syn1. Overall, our results suggest that Sirt1 regulates synapses of POMC neurons and does so in a manner that differs from Sirt1's regulation of AgRP-NPY neuronal synapses. Future work will elucidate the mechanisms and consequences of Sirt1 and FOXO1 regulation of POMC neuron synapses under different nutritional conditions *in vitro* and *in vivo.*

(1) Cyr, N. E., Steger, J. S., Toorie, A. M., Yang, J. Z., Stuart, R., Nillni, E. A. (2014). Central Sirt1 Regulates Body Weight and Energy Expenditure Along With the POMC-Derived Peptide α-MSH and the Processing Enzyme CPE Production in Diet-Induced Obese Male Rats, *Endocrinology, 155*(7), 2423–2435.

(2) Dietrich, M. O., Antunes, C., Geliang, G., Liu, Z., Borok, E., Nie, Y., . . . Horvath, T. L. (2010). Agrp neurons mediate Sirt1's action on the melanocortin system and energy balance: Roles for Sirt1 in neuronal firing and synaptic plasticity. *The Journal of Neuroscience, 30*(35), 11815–11825.

Adipose Tissue, Appetite, and Obesity

NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Skeletal Muscle Stromal Cells Derived From MuRF1 Knockout Mice Are Resistant to Adipogenesis

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Background: Intramuscular adipose tissue has been found to contribute to muscle dysfunction and is associated with a sedentary lifestyle, aging, and glucocorticoid treatment. Muscle ring finger 1 knockout (MuRF1 KO) mice have been shown to be protected from muscle loss following disuse, aging, and glucocorticoid treatment. In this study we used *in vitro* techniques to determine if MuRF1 KO muscle stromal cells are resistant to adipogenesis. **Methods:** Stromal cells were isolated from skeletal muscle tissue of MuRF1 KO and wild type mice. These cells were expanded in culture until 70–90% confluent, then differentiated in either a myogenic media formulation (myogenic cultures) or an adipogenic media formulation (adipogenic cultures). Gene expression was analyzed by qRT-PCR, protein content was measured by bicinchoninic acid assay, and triglyceride content was analyzed by colorimetric assay. We also analyzed isolated stromal cells, which had not been expanded in culture, by flow cytometry to identify myogenic satellite cells (SCs) and fibro-adipogenic progenitors (FAPs). **Results:** Wild type adipogenic cultures had higher expression of *Trim63,* the gene encoding MuRF1, when compared to wild type myogenic cultures. Adipogenic cultures had higher expression of adipogenic programing and lipid handling genes than myogenic cultures. These adipogenic cultures also had higher triglyceride content than myogenic cultures. The expression of adipogenic programing genes and lipid handling genes were lower in cultures derived from MuRF1 KO mice compared to wild type derived cultures; however, there was no statistically significant difference in the triglyceride content between the two genotypes. Analysis of stromal cell populations by flow cytometry indicated no difference in the FAP:SC ratio between wild type and MuRF1 KO mice. **Conclusions:** These results indicate that although there are no differences in the ratio of FAPs to SCs in wild type and MuRF1 KO mice, the MuRF1 KO cultures appear to be resistant to adipogenesis. The mechanism behind this resistance to adipogenesis remains to be elucidated.

Adipose Tissue, Appetite, and Obesity

NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Spexin as a Satiety Factor in Mouse via Regulatory Actions Within the Hypothalamus

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Spexin (SPX) is a pleiotropic peptide with highly conserved protein sequence from fish to mammals and its biological actions are mediated by GalR2/GalR3 receptors expressed in target tissues. Recently, SPX was found to be a novel satiety factor in fish models but whether the peptide has a similar function in mammals is still unknown. Using the mouse as a model for mammalian species, the functional role of SPX in feeding control and the mechanisms involved were investigated. After food intake, serum SPX could be up-regulated in mice with parallel elevations of transcript expression and tissue content of SPX in the glandular stomach but not in other tissues examined. As revealed by immunostaining, food intake also intensified SPX signals in different cell types within the gastric mucosa of glandular stomach. Furthermore, IP injection of