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Morphological characterization of a dietary challenged Sirtuin 1 heterozygous mice

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Sirtuin 1 (SIRT1), a member of the silencing information regulator 2 enzymes called sirtuins, is emerging as a master-regulator of metabolic functions like energy balance, mitochondrial health, browning of white adipose tissue, lipolysis. To best characterize its role in obesity, we analysed metabolic and morphological changes induced in SIRT1 heterozygous mice (HET) [1] by a high fat diet (5.4 Kcal/g from fatlard TD03584-Envigo) in comparison with C57BL6/J mice. Male C57BL6/J (WT) and HET mice received a standard maintenance diet (SD) (2.9 Kcal/g) or a high fat (HF) diet for 16 weeks from 12 to 28 weeks of age. Hepatic and epididymal white adipose depot (eWAT) reactions to the obesogenic diet were focused on hypoxia, inflammation, and endoplasmic reticulum stress. At euthanasia, blood was collected and the liver and eWAT removed for morphological analysis. WT HF and HET HF groups positively correlated with glucose intolerance, hepatomegaly and adipogenesis when compared with SD groups. Remarkably hepatosteatosis, fibrosis and inflammation were exacerbated in HET HF. Oxidative damage and abnormal lipogenesis were confirmed by elevated 4HNE and SREBP1 expressions. Hepatic mitochondria revealed myelinic figures and abnormal ER-mitochondria juxtapositions in HET HF [2]. eWAT adipocytes showed reduced perilipin but strong TNF-alpha and GRP78 signals in crown-like structures. In conclusion, HET HF mice might represent an intriguing animal model to best understand the complex pathogenesis of obesity and related disorders.

References

[1] Xu et al. (2010) Lack of Sirt1 activity leads to liver steatosis in the Sirt1$^{+/-}$ mice: a role of lipid mobilization and inflammation. Endocrinology 151: 2504-2514.
[2] Stacchiotti et al. (2016) Hepatic macrosteatosis is partially converted to microsteatosis by melatonin supplementation in ob/ob mice non alcoholic fatty liver disease. PlosOne 11: e0148115.

Keywords

Sirtuin 1, perilipin, lipid droplets, ER stress, mitochondria, TEM