

A form of autophagy triggers lipolysis in adipocytes exposed to a mitochondrial uncoupling

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Obesity is characterized by an excessive triacylglycerol accumulation in white adipocytes. Various mechanisms allowing the regulation of triacylglycerol storage and mobilization by lipid droplet-associated proteins as well as lipolytic enzymes have been identified. Increasing energy expenditure by inducing a mild uncoupling of mitochondria in adipocytes might represent a putative interesting anti-obesity strategy [1] as it reduces the adipose tissue triacylglycerol content by stimulating lipolysis through yet unknown mechanisms, limiting the systemic adverse effects of adipocyte hypertrophy.

The methodology used 3T3-L1 fibroblasts that were exposed to a mild uncoupling of mitochondria triggered by carbonyl cyanide-p-trifluoromethoxyphenylhydrazone FCCP or dinitrophenol (DNP) and several biochemical assays and techniques of microscopy were used to monitor mitochondria uncoupling-induced lipolysis assessed by glycerol release.

Main results revealed that mitochondrial uncoupling-induces lipolysis but does not involve lipolytic enzymes such as hormone-sensitive lipase (HSL) and adipose ATGL [2]. Enhanced lipolysis relies on a form of autophagy as lipid droplets are directly captured by endolysosomal vesicles. These organelles might thus physically interact with each other. In addition, lysosomal poisoning and inhibition of microautophagy by valinomycin inhibit lipolysis.

In conclusion, a new mechanism of triacylglycerol breakdown was identified in adipocytes exposed to mild uncoupling that provides new insights on the biology of adipocytes dealing with mitochondria forced to dissipate energy.

References :

[1] De Pauw A, Tejerina S, Raes M, Keijer J, Arnould T. Mitochondrial (dys)function in adipocyte (de)differentiation and systemic alterations. *Am J Pathol.* 2009;175(3):927-39.

[2] Demine S, Tejerina S, Bihin B, Thiry M, Reddy N, Renard P, Raes M, Jadot M, Arnould T. Mild mitochondrial uncoupling induces HSL/ATGL-independent lipolysis relying on a form of autophagy in 3T3-L1 adipocytes. *J Cell Physiol.* 2018

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