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temat: "***Identification of mechanisms remodeling mitochondria during adaptation of adipose tissue to changing ambient temperature.***

Identyfikacja mechanizmów remodelujących mitochondria podczas adaptacji tkanki tłuszczowej do zmiennych warunków temperaturowych*"*.

English Abstract

Brown adipocytes in white adipose tissue (brite cells) show features of being a valuable tool to combat obesity. Their appearance in white fat depots and ability to burn excess lipid stores depends on their induction in adults upon cold exposure or β3-adrenergic agonist stimulation and their disappearance in the absence of sympathetic stimulation. Although little is known about the mechanisms of their disappearance, we believe, that mechanisms regulating turnover of brite cells can have profound effects on the capacity of an individual for thermogenesis. Therefore, we investigated changes in markers of mitophagy, mitofusion/mitofission and apoptosis during the transition from brite-cell-induction to brite-cell-suppression. Additionally, we investigated involvement of PKA-AKAP1 interaction in white adipose tissue adaptation changes. Protein kinase A (PKA) is a key molecule, which executes events induced by adrenergic stimulation, while A-kinase anchoring protein 1 (AKAP1) tethers PKA activity on the surface of mitochondria. We designed an experiment to investigate involvement of AKAP1 in processes of mitophagy, mitofusion/mitofission and apoptosis in cold-induced remodeling of inguinal white adipose tissue. Mice of AxB8 and AKAP1-KO strain were kept for 15 days at 4^{o}C to cause induction of thermogenic program and then transferred to thermoneutrality (29^{o}C) to foster brite cells involution.

Studies utilizing AxB mice showed that brown adipocytes that developed in the inguinal white adipose tissue upon cold exposure reorganize their mitochondrial network when re-exposed to thermoneutrality. We observed a shift in balance between mitochondrial dynamic events

towards mitofission at 29^{o}C. Results of analysis of mitophagy markers were inconclusive due to high variance. We did not observe an activation of apoptosis in AxB8 mice based on cleavage of Procaspase3. A second experiment comparing changes in the levels of makers of mitochondrial remodeling in AKAP1-KO strain of mice demonstrated that anchoring of PKA by AKAP1 is not crucial for adaptation of white adipose tissue to ambient temperature. Mice deprived of AKAP1 protein did not differ in the profiles of levels of mitophagy and mitofiusion/mitofission markers from wild type mice. Conversely, AKAP1-KO mice had increased levels of Caspase3 and OPA1 short forms (implicated in apoptosis signaling), suggesting an anti-apoptotic role of AKAP1 during remodeling of white adipose tissue.