BIOCHEMISTRY 640

(Biomembranes Discussion Group)

Wednesday, February 7, 2018

Room 4-70 Medical Sciences Building

4:00 PM

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"SERCA2b and RyR2 mediate thermogenesis of beige fat via Ca^{2+} cycling"

Brown adipose tissue (BAT) is part of the adipose organ whose primary function is thermoregulation of the organism by non-shivering thermogenesis. Thermogenesis is achieved by the leakage of protons across the inner membrane in mitochondria along its concentration gradient by Uncoupling Protein 1 (UCP1). Beige adipocytes are inducible fat cells in white adipose tissue (WAT) which play a role in whole body metabolism as well as thermogenesis. Since beige adipocytes have comparable expression of UCP1 and thus thermogenesis in these cells is thought to be mechanistically similarly to BAT.

In this article the role of UCP1 on beige adipocyte thermogenesis was explored by monitoring body temperature of transgenic mice under chronic cold conditions. The transgenic mice either expressed *Prdm16* (a gene that promotes beige adipocyte biogenesis), lacking UCP1 (*Ucp1*$^{-/-}$), or both (*Prdm16*-Tg x *Ucp1*-/-). It was found that regardless of UCP1 expression, if *Prdm16* was expressed the mice maintained body temperature, therefore UCP1 necessary for the thermogenic function of beige fat. Interestingly RNA sequencing and further experiments with *Prdm16*-Tg x *Ucp*$^{-/-}$ mice revealed that thermogenic function of beige adipocytes are maintained through a ATP-dependent Ca^{2+} cycling via ryanodine receptor 2 (RyR2) and sarco/endoplasmic reticulum Ca2+-ATPase 2b (SERCA2b). Stimulation of Ca^{2+} cycling in the absence of UCP1 was also found to enhance glycolysis, tricarboxylic acid metabolism, and pyruvate dehydrogenase. This result implies that beige adipocytes may be a promising target for obesity and diabetic pharmaceuticals.

Article:
Ikeda, K., et al. (2017) UCP1-independent signaling involving SERCA2b-mediated calcium cycling regulates beige fat thermogenesis and systemic glucose homeostasis. *Nature Medicine,* 23(12), 1454-1465. doi:10.1038/nm.4429