TEMPERATURE
2017, VOL. 4, NO. 2, 126–127
https://doi.org/10.1080/23328940.2017.1317380

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FRONT MATTER: LETTER

Brown fat in obesity: Uncoupling protein-1 versus thermogenic activity

Letter on: Romanovsky AA. Award-winning papers published in Temperature in 2014. Temperature 2016;3:8-10. PMID: 27227086; doi:10.1080/23328940.2016.1151295.

There has been a resurgence of interest in brown adipose tissue (BAT) since the re-discovery of this tissue in adult humans. The renewed interest in BAT has also been bolstered by its potential for therapeutic targeting for obesity. In a recent editorial,[1] a call was issued for an explanation to reconcile apparently paradoxical observations concerning BAT during obesity. A fundamental observation that has focused attention on BAT as a therapeutic target for obesity is that obese humans have lower levels of metabolically active BAT compared with lean individuals. In apparent contrast, diet-induced obese rodents have elevated levels of uncoupling protein 1 (UCP-1) compared with lean rodents, suggesting that BAT in rodents is more active during obesity. How can these observations be reconciled?

The pedestrian interpretation that there is a species difference, with obese humans having impaired activation of BAT and obese rodents having elevated activation of BAT can be dispelled since sympathetic activation of BAT is impaired in obese rats.[2] Instead, at the crux of the apparent paradox is the erroneous interpretation that expression of UCP-1 is a reliable "readout" of BAT activation. In fact, expression of UCP-1 mRNA and protein levels of UCP-1 are not reliable indices of BAT activation, since they can be dissociated from activation of BAT.[3] The role of BAT in the metabolism of fat (the lack of which contributes to the accumulation of adiposity) would be determined primarily by the long-term interplay between the amount of sympathetic activation of this tissue and the thermogenic capacity of this tissue (largely determined by UCP-1 expression). Acceptance of this reconciliation raises further questions, such as, how the sympathetic activation of BAT during cold-exposure is impaired in rats chronically consuming a high-fat diet. Understanding the mechanisms underlying the impairment of sympathetic activation of BAT during obesity will provide a foundation for therapeutic approaches to increase metabolism of adipose tissue and combat obesity. Another important question is how UCP-1 can be upregulated in BAT when the sympathetic activation of this tissue is impaired or absent. Insights may be gleaned by inspection of physiologic states that parallel this condition. In this regard, the state of BAT in obese rats on a high-fat diet closely parallels that of a hibernation state. During hibernation UCP-1 is upregulated, even though BAT thermogenesis is decreased.[4] More intriguing still, the accumulation of excess adipose tissue is required for hibernation.[5] Investigation of the physiologic mechanisms underlying the regulation of BAT during high-fat diet and during hibernation will provide important insights into these phenomena that could uncover novel therapeutic targets for obesity.

References

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