Nature Reviews Endocrinology **11**, 383 (2015); published online 19 May 2015; doi:10.1038/nrendo.2015.86

BASIC RESEARCH

FGF-21 antiobesity action independent of UCP1 and WAT browning

Fibroblast growth factor 21 (FGF-21) can induce weight loss and improve glucose homeostasis, which is correlated with increased expression of uncoupling protein 1 (UCP1) and browning of white adipose tissue (WAT). However, in a new study, investigators find that the antiobesogenic effect of FGF-21 does not require UCP1 or the generation of brown adipocytes in WAT, but might be the result of increased energy expenditure.

The team housed lean and diet-induced obese mice at 21 °C or 30 °C to assess if the action of FGF-21-Fc (an FGF-21 analogue) is temperature dependent. After 15 days of treatment with FGF-21-Fc both sets of mice had notable decreases in weight and improved glucose tolerance, regardless of temperature. However, only lean mice kept at 21 °C showed any significant browning of WAT, indicating that this FGF-21 action is indeed temperature dependent.

Intriguingly, the same beneficial effects of FGF-21-Fc were observed in UCP1 knockout mice. These data indicate that while FGF-21 can elicit changes in UCP1 expression, the uncoupling mechanism does not mediate any antiobesity effects. Of note, administration of FGF-21-Fc increased energy expenditure without affecting food intake in *Ucp1*$^{-/-}$ mice, which might account for the weight loss. Consistent with this finding, expression of the mitochondrial gene, *Ppargc1,* was increased in the WAT of *Ucp1*$^{-/-}$ mice.

Although FGF-21 induces browning of WAT, the investigators note that this process itself does not lead to weight loss. This finding challenges the concept that therapies inducing browning of WAT might be used as antiobesity agents.

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Original article Véniant, M. M. *et al.* Pharmacologic effects of FGF21 are independent of the "browning" of white adipose tissue. *Cell Metab.* **21**, 731–738 (2015)