Nature Reviews Endocrinology | Published online 24 Mar 2017; doi:10.1038/nrendo.2017.34

ADIPOSE TISSUE

New route to functional human beige adipocytes

Activation of thermogenesis in beige adipose tissue has been proposed as a potential strategy to treat obesity and type 2 diabetes mellitus; however, implementation of this approach has been hampered by a limited supply of beige adipocytes for therapeutic screening. Now, in a new study published in *Diabetes*, investigators report an efficient, three-step, 20-day protocol for the generation of functional beige adipocytes from human induced pluripotent stem cells (hiPSCs).

In the first step, mesoderm differentiation was induced in hiPSC lines (reprogrammed from fibroblasts) on day 0 using bone morphogenetic protein 4 and activin A. In the second step (days 4–10), a mixture of insulin, isobutylmethylxanthine, dexamethasone and indomethacin was used to induce adipogenic differentiation. Last, in the third step (days 10–20), the hiPSC-derived adipocyte progenitors were cultured under conditions favouring adipogenic maturation.

The hiPSC-derived adipocytes exhibited a beige phenotype from day 4 onwards, as they had increased expression of *UCP1*, *PGC1A* and *PRDM16* (markers of beige and brown adipocytes) yet undetectable expression of *MYF5* and *ZIC1* (markers of mature brown adipocytes). Moreover, treatment of day-20 hiPSC-derived adipocytes with a cAMP analogue induced thermogenic gene expression (*PGC1A*, *PRDM16*, *PPARA* and *DIO2*) and shrinkage of lipid droplets, as well as increased mitochondrial content and oxygen consumption. *In vivo* functionality of the mature adipocytes was demonstrated by injecting 10 million day-18 cells into the backs of nude mice. After 30 days, the hiPSC-derived adipocytes had formed well-organized and vascularized adipose tissue that was responsive to β-adrenergic stimulation.

"Our model of human beige adipocyte development provides a new and scalable tool for disease modelling and therapeutic screening," write the authors.

David Holmes

ORIGINAL ARTICLE Guénantin, A.-C. *et al.* Functional human beige adipocytes from induced pluripotent stem cells. *Diabetes* https://doi.org/10.2337/db16-1107 (2017)