

## Engineering Fat Cell Fate to Fight Obesity and Metabolic Diseases

Shingo Kajimura, Ph.D.  
University of California, San Francisco  
UCSF Diabetes Center and Department of Cell and Tissue Biology  
skajimura@diabetes.ucsf.edu

All mammals harbor two types of adipose tissues that serve distinct physiological functions: white adipose tissue (WAT) and brown adipose tissue (BAT). WAT functions mainly in the storage of excess energy, while BAT specializes in dissipating energy in the form of heat and functions as a defense against hypothermia and obesity. Since adult humans possess significant amounts of active BAT depots and its mass inversely correlates with adiposity, BAT plays an important role in human obesity and energy homeostasis.

New evidence suggests two types of thermogenic adipocytes with distinct developmental and anatomical features: classical brown adipocytes and beige adipocytes. Classical brown adipocytes are located mainly in dedicated BAT depots of rodents and infants. Beige adipocytes, on the other hand, reside mainly in subcutaneous WAT where they arise postnatally in response to certain external cues, such as chronic cold exposure and long-term treatment with PPAR- $\gamma$  agonists, a process often referred to as the “browning” of WAT. Importantly, adult human BAT appears to be mainly composed of beige-like adipocytes, making this cell type an attractive therapeutic target for obesity and obesity-related diseases, such as insulin resistance and type2 diabetes. I will review recent progress in the molecular control of brown and beige adipocyte development and discuss emerging questions, with a special emphasis on adult human BAT.

Keywords: Obesity, brown and beige adipocytes, glucose homeostasis

Recent publications:

1. Shinoda K., Lijjten I. H.N., Hasegawa Y., Hong H., Sonne S. B., Xue R., Chondronikola M., Kim M., Cypess A.M., Tseng Y., Nedergaard J., Sidossis L.S., & Kajimura S. (2015). Genetic and functional characterization of clonally-derived adult human brown adipocytes. *Nature Medicine* doi: 10.1038/nm.3819.
2. Galmozzi A., Sonne S.B., Keylin S., Hasegawa Y., Shinoda K., Lijjten I., Chang J.W., Sharp L.Z., Cravatt B. F., Saez E., & Kajimura S. (2014). ThermoMouse: an *in vivo* model to identify modulators of UCP1 expression in brown adipose tissue. *Cell Reports* S2211-1247.
3. Ohno, H., Shinoda, K., Ohyama, K., Sharp, L.Z. & Kajimura, S. (2013). EHMT1 controls brown adipose cell fate and thermogenesis through the PRDM16 complex. *Nature* 504(7478):163-7. PMC3855638
4. Ohno, H., Shinoda, K., Spiegelman, B.M. & Kajimura, S. (2012). PPAR $\gamma$  agonists induce a white-to-brown fat conversion through stabilization of PRDM16 protein. *Cell Metabolism* 15(3), 395-404. PMC3410936