White Primary Human Pre-adipocytes can be Induced to Express UCP-1 and Transdifferentiate into Brown-like Adipocytes in-vitro

Bodo Ortmann1, Steffi Busch1, Tamara Grabeck1, Michael Töller1, Stephanie Nickles2, Minh Hong2

1. Lorenzo Cologne GmbH, 50299 Cologne, Germany. 2. Lonza Walkersville Inc., Walkersville, MD 21793, USA

1. Abstract

Brown adipose tissue (BAT) is dedicated to regulating body temperature in hibernating mammals and newborn humans. In the many mammalian species where brown adipocytes accumulate, fatty acids are degraded and energy is released as heat. This process called thermogenesis works by upregulating the mitochondrial electron transport chain from the production of ATP. Expression of the mitochondria’s inner membrane, uncoupling protein 1 (UCP1) bypasses the proton pump, allowing for the energy released by the breakdown of fatty acids to be used for propagation of heat rather than for ATP synthesis. This is achieved by the characteristic shape of intracellular lipid droplets. This process has been shown to be regulated by the PR domain containing protein PGC1α. The PGC1α gene is expressed in adipocytes and muscle cells, the former to white adipocytes and brite or beige adipocytes (intermediates of brown and white adipocytes). Beige adipocytes express the brown adipocytes marker UCP-1 (for actual concentrations see references listed at the end).

2. Materials & Methods

2.1. Differentiation into brown-like adipocytes

The differentiation was performed according to three different published protocols which differed in the various factors added to the cell culture and the regimes of incubation times and media changes. The differentiation was started by replacing culture medium with differentiation medium containing the following factors (for actual concentrations see references listed at the end).

Differentiation to brown-like adipocytes

1. Differentiation by protocol 1: Accumulated intracellular lipid is a marker of adipocyte differentiation. Only a portion of pre-adipocytes undergo differentiation to adipocytes by intracellular lipid droplet expansion. Micrograph images were taken of differentiated adipocytes stained with AdipoRed™ Assay at arbitrary shown positions in the wells of day 18 after start of differentiation.

2.2. Results

3. Conclusions

Subcutaneous and visceral human pre-adipocytes can be differentiated to “brown-like” adipocytes expressing the marker protein UCP-1.

Expression of UCP-1 can be induced by treatment with forskolin in undifferentiated pre-adipocytes.

If you have further questions or comments please contact Minh.Hong@lonza.com or Bodo.Ortmann@lonza.com

References


