Brown Adipose Tissue Cell Lines Derived from Protein-Tyrosine Phosphatase 1B Knockout Mice Reconstituted with Sumoylation Mutant PTP1B K4R

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Technology description

Since Protein-Tyrosine Phosphatase 1B (PTP1B), a non-receptor PTP, has emerged as a potential target for the treatment of obesity and type 2 diabetes, a number of academic and industry research laboratories focused on generating PTP1B-specific inhibitors. Currently, the cell-based platforms that could be utilized to test the specificity and efficiency of PTP1B inhibitors are not ideal. They are mostly fibroblast cells that do not respond to insulin appropriately and in a "physiological" manner.
To circumvent these problems, researchers at the University of California, Davis have developed a platform to test the effects of human PTP1B inhibition not only on insulin signaling, but also adipose differentiation and metabolic regulation. Primary brown adipose tissue (BAT) cells were derived from PTP1B knockout (KO) mice, immortalized, then retrovirally-reconstituted with either backbone vector (KO), human wild type PTP1B, "substrate-trapping" mutant PTP1B D181A, and sumoylation-resistant mutant PTP1B K4R. These pre-adipocytes could be induced to differentiate into fat cells enabling one to assess the effect(s) of PTP1B deletion and its mutants on insulin signaling, adipocyte differentiation and metabolic regulation. In addition, the substrate(s) of PTP1B that are mediating these effects could be easily identified.
Platform for testing the effects of human PTP1B inhibition on insulin signaling, adipose differentiation and glucose uptake.

Application area

Obesity
Diabetes Type 2

Advantages

These cell lines provide an excellent platform for cell-based high throughput screening for testing the efficiency and specificity of human PTP1B inhibitors. Since the differentiation and signaling in this cell system is very well characterized, their use to dissect the role of PTP1B inhibition in insulin signaling and metabolic regulation is greatly facilitated.

Institution

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