Miglitol upregulates uncoupling protein 1 (UCP1) by enhancing β3-adrenergic signaling in mature brown adipocytes of rat.

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**Background**

We previously reported that miglitol, an alpha-glucosidase inhibitor (α-GI), increases energy expenditure by enhancing β3-adrenergic signaling of brown adipose tissue (BAT) and reduces obesity in high fat diet-induced obese mice (Figure1-6, Table1) (Nutrition & Metabolism 2014 Mar 26;11(1):14. doi: 10.1186/1743-7075-11-14). However, this report did not describe the mechanism by which miglitol enhances β3-adrenergic signaling. Miglitol, unlike other α-GIs, enters the circulation. We hypothesized that miglitol directly enhances β3-adrenergic signaling.

**Objective**

To determine whether miglitol has a direct effect on β3-adrenergic signaling in rat mature brown adipocytes (rBAC).

**Materials and Methods**

We cultured rat brown adipocytes with a culture kit (Takara, Japan). After the cells finished maturing, we added medium containing miglitol with or without a β3-adrenergic agonist (CL316,243). After 24 h, the cells were harvested. We used quantitative real-time PCR to determine the expressions of two genes involved in BAT thermogenesis: peroxisome proliferator-activated receptor gamma coactivator 1α (PGC1α) and uncoupling of protein 1 (UCP1).

**Results**

**Figure 1.** Miglitol decreased body weight gain in high fat diet-induced obese mice.

**Figure 2.** Miglitol increased oxygen consumption in high fat diet-induced obese mice.

**Figure 3.** Interscapular BAT temperature in HFM mice was significantly higher than in HF mice.

**Figure 4.** Miglitol enhanced the gene and protein expressions of UCP1 in HFM mice.

**Figure 5.** Miglitol enhanced β3-adrenergic signaling in BAT of HFM mice.

**Figure 6.** β3-adrenergic agonist induced greater amount of cAMP and PKA protein in HFM mice than HF mice.

**Figure 7.** Effect of miglitol alone on the expressions of PGC1α and UCP1 in rBAC.

**Figure 8.** Effect of miglitol plus β3-adrenergic agonist on the expressions of PGC1α and UCP1 in rBAC.

**Conclusion**

Miglitol increased the sensitivity of β3-adrenergic receptor in rat mature brown adipocytes. This suggests that miglitol entered the circulation and directly enhanced β3-adrenergic signaling of BAT in rodents.

We have nothing to disclose.