Small Molecule Glycomimetics Enhance Adipogenesis and Glucose Uptake in Adipocytes

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**Background & Aim**

Adipose tissue is an endocrine organ that functions as a crucial integrator of glucose homeostasis. Adipocytes, the primary cell type of adipose tissue, are emerging drug target for the treatment of obesity and obesity-mediated metabolic syndrome. Small molecule glycomimetics are an untapped source of novel therapies for obesity and diabetes. The current study aims to scrutinize the effect of newly synthesized small molecule glycomimetics on adipogenesis and glucose uptake in 3T3-L1 adipocytes.

**Methods**

Seven small molecule glycomimetics were synthesized in our laboratory and their effects on adipocyte differentiation and glucose uptake were investigated. 3T3-L1 cells were treated with the glycomimetics during the differentiation process. Fully differentiated 3T3-L1 adipocytes were used to determine the effect of glycomimetics on glucose uptake and the underlying mechanism(s).

**Results**

1. Glycomimetics enhance adipocyte differentiation of 3T3-L1 cells via up-regulation of PPAR\(\gamma\) and its target genes/proteins C/EBP\(\alpha\) and aP2.

2. Glycomimetics increase glucose uptake and enhance GLUT4 translocation in differentiated adipocytes.

3. Glycomimetics increase the phosphorylation of IRS-1, PI3K, Akt, PKC\(\zeta\), AMPK\(\alpha\), TBC1D1 and TBC1D4.

4. Glycomimetics up-regulate PPAR\(\gamma\), adiponectin, FAS, ACC, FABP-4, SREBP-1c and GLUT4 mRNA expression in 3T3-L1 adipocytes.

**Conclusions**

Our novel small molecule glycomimetics promote adipocyte differentiation through increased expression of PPAR\(\gamma\). These glycomimetics activate multiple signaling pathways, and enhance GLUT-4 translocation and glucose uptake. These exciting effects could be the basis of the pharmacological benefits of a new class of targeted therapeutic drugs, benefiting diabetes patients.