WHITE-TO-BROWN ADIPOSE TRANSDIFFERENTIATION, IS THERE A ROLE FOR GENISTEIN?

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Adipocytes can be classified as white and brown adipocytes; white adipocytes store energy-providing lipids and form WAT (white adipose tissue), brown adipocytes form BAT (brown adipose tissue) and do not store energy but rather dissipate it by producing heat. The adipose organ undergoes whitening and browning depending on the increase/decrease of UCP1-expression (uncoupling protein 1). Browning could represent a new target of anti-obesity strategies and PPARs (peroxisome proliferator activating receptor) agonists have been suggested as browning agents.

Genistein is an isoflavone that binds to the estrogen receptor beta (ERβ), and can also acts as a natural ligand of PPARs, was tested as a browning agent to induce white-to-brown adipocyte transdifferentiation.

3T3-L1 cells were differentiated into adipocytes under appropriate culturing conditions. Cells were treated with different concentrations of genistein: 10,50,100 and 200µM for up to 48hrs. At the end of genistein treatment, lipid accumulation was evaluated by oil-red-O staining and total mRNA was used to determine by qPCR the expression of the browning specific genes: UCP-1, PPARs (□ and □), the transcriptional regulator PRDM16, and Dio2 (encoding for Type 2 iodothyronine deiodinase (D2).

The results on oil-red-O staining demonstrated that after 24 and 48hrs genistein reduced the accumulation of lipids in treated cells, compared to controls at all tested doses. Accordingly, genistein (at the dose of 50µM) caused a significant increase ($p<.0001$ vs CTRL, each gene) in the expression of all browning specific genes, at 24hrs. On the contrary the expression of PPARɣ was not increased by genistein as compared to control cells. Even at 48hrs the expression of all genes was increased significantly at the dose of 200µM ($p<.0001$ vs CTRL, each gene), while the PPARɣ expression was not increased at any dose. These results suggest that genistein caused the white-to-brown adipose differentiation in a PPARɣ-independent manner, likely stimulating PPAR-□ and the estrogenic receptors. Even if preliminary these results further suggest that genistein might be considered as a browning agent.