Peroxisome Proliferator-Activated Receptor β/δ does not regulate glucose uptake and lactose synthesis in bovine mammary epithelial cells cultivated *in vitro*

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Summary

The hypothesis of the study is that inhibition of PPARβ/δ increases glucose uptake and lactose synthesis in bovine mammary epithelial cells by reducing the expression of the glucose transporter mRNA destabilizer calreticulin. Three experiments were conducted to test the hypothesis using immortalized bovine mammary alveolar (MACT) and primary bovine mammary (PBMC) cells. In Experiment 1 the most effective dose to inhibit PPARβ/δ activity among two synthetic antagonists (GSK-3787 and PT-s58) was assessed using a gene reporter assay. In Experiment 2 the effect on glucose uptake and lactose synthesis was evaluated by measuring glucose and lactose in the media and expression of related key genes upon modulation of PPARβ/δ using GSK-3787, the synthetic PPARβ/δ agonist GW-501516, or a combination of the two in cells cultivated in plastic. In Experiment 3 the same treatments were applied to cells cultivated in Matrigel and glucose and lactose in media were measured. In Experiment 1 it was determined that a significant inhibition of PPARβ/δ in the presence of absence of fetal bovine serum was achieved with ≥ 1000 nM GSK-3787 but not significant inhibition was observed with PT-s58. In Experiment 2 inhibition of PPARβ/δ had no effect on glucose uptake and lactose synthesis but they were both increased by GW-551516 in PBMC. The mRNA abundance of PPARβ/δ target gene pyruvate dehydrogenase kinase 4 was increased but transcription of calreticulin was decreased (only in MACT cells) by GW-551516. Treatment with GSK-3787 did not affect the transcription of measured genes. No effects on glucose uptake or lactose synthesis were detected by modulation of PPARβ/δ activity on cells cultivated in Matrigel. The above data do not provide support the original hypothesis and suggest that PPARβ/δ does not play a major role in glucose uptake and lactose synthesis in bovine mammary epithelial cells.