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Evidence for impacts of Insulin-like growth factor binding proteins on glucose metabolism, independent of Insulin-like growth factor-1 binding

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Insulin-like growth factor binding proteins (IGFBPs) play important roles in modulating the metabolic effects of insulin-like growth factor-1 (IGF-1). However, several *in vitro* and *in vivo* studies have also demonstrated the IGF-1 independent actions of IGFBPs on metabolism. The aim of this study was to investigate the effects of IGFBP-2 and IGFBP-3 on glucose uptake in two different *in vitro* models (3T3-L1 adipocytes and C2C12 myotubes) independent IGF-1 binding. Treatment of 3T3-L1 adipocytes and C2C12 myotubes with recombinant human IGFBP-2 (rhIGFBP-2) resulted in a significant increase in basal glucose uptake (54±14 %, P<0.05; and 12±3.7%, P<0.05 respectively). This increase was inhibited by wortmannin, a phosphoinositide 3-kinase (PI3K) inhibitor. The levels of P-Akt (Ser 473) were elevated in rhIGFBP-2 treated cells as compared to controls (3.8 folds, P<0.01 in 3T3-L1 adipocytes and 1.9 folds, P<0.01 in C2C12 myotubes). When 3T3-L1 adipocytes and C2C12 myotubes were treated with recombinant human IGFBP-3 (rhIGFBP-3), both basal (22±2.5 % and 25±8.5% respectively) and IGF-1 stimulated (203±8.5% and 50±13% respectively) glucose uptake were decreased significantly (P<0.05). During the experiment, the IGF-1 independent effects of IGFBPs were always controlled with IGF-1 analogues that are unable to bind IGFBPs. In conclusion, rhIGFBP-2 stimulates basal glucose uptake in 3T3-L1 adipocytes and C2C12 myotubes, whereas rhIGFBP-3 itself seems to inhibit basal glucose uptake. In contrast to the reduction in IGF-1 induced glucose uptake by rhIGFBP-3 that is not solely mediated by binding to IGF-1, rhIGFBP-2 did not impact the IGF-1 induced glucose uptake. The stimulatory effect of rhIGFBP-2 on basal glucose uptake in these cell culture models seems to involve the PI3K signalling pathway. Further mechanistic studies are required to address the mechanism by which these IGFBPs exert their effect on glucose metabolism in these cellular models.

Biography

Biruhalem Assefa has Bachelor in pharmacy from Jimma University, Jimma, Ethiopia in 2007, Master degree in Molecular Medical Biology from Örebro University, Örebro, Sweden in 2012 and is a PhD candidate in Endocrinology (medicine) in DFG funded graduate college 1208/2 at Charite-Universitat medizin Berlin, Berlin, Germany since October 2012.

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