PID1 alters antilipolytic action of insulin and increases lipolysis via inhibition of the AKT/PKA pathway activation

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Purpose: The aim was to investigate the effect of phosphotyrosine interaction domain containing 1 (PID1) on insulin-induced activation of AKT (the protein kinase B)/protein kinase A (PKA)/hormone sensitive lipase (HSL) pathway and lipolysis.

Methods: Sprague–Dawley rats were fed either chow or high-fat diet (HFD). Levels of insulin, glycerol, free fatty acids (FFA) and PID1 expression were measured in the 2 groups. Further, we examined the role of PID1 in the regulation of AKT/PKA/HSL cascade and lipolysis in 3T3-L1 cell lines.

Results: Adipose tissue from HFD rats exhibited elevated PID1 expression, which showed a positive correlation with insulin levels and lipolysis. In 3T3-L1 adipocytes, we found that the antilipolytic effect of insulin is mediated by AKT and that phosphorylated AKT results in phosphorylation of PKA and HSL and suppresses glycerol release. However, PID1 over-expression resulted in increased release of glycerol and noticeable inhibition of AKT phosphorylation and phosphorylation of PKA/HSL. In contrast, PID1 knockdown inhibited lipolysis and activated phosphorylation of AKT, which resulted in dephosphorylation of PKA and HSL.

Conclusions: Our findings indicate that PID1 in adipose tissue increases lipolysis by altering the antilipolytic action of insulin. This suggests that PID1 may represent a new therapeutic target to ameliorate adipocyte lipolysis and hence to improve insulin sensitivity.