



Prolactin regulatory element-binding protein is involved in suppression of the adiponectin gene in vivo

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Abstract

Purpose Prolactin regulatory element-binding protein (PREB), a member of the WD-repeat protein family, has been recognized as a transcriptional factor that regulates prolactin promoter activity in the anterior pituitary of rats. PREB is expressed not only in the pituitary but also in various other tissues, including the adipose tissue. Previous studies have shown that PREB acts as a transcriptional regulator and suppresses the expression of the adiponectin gene in cultured 3T3L1 preadipocytes. The aim of this study was to further examine the potential role of PREB in adipose tissue in vivo.

Methods Transgenic mice that overexpressing PREB (PREB transgenic mice) were generated. Insulin resistance was evaluated in PREB transgenic mice using glucose and insulin tolerance tests. Adiponectin expression in the adipose tissue was examined by western blot analysis and quantitative polymerase chain reaction (qPCR). The expression levels of stearoyl-CoA desaturase (Scd) and adiponectin receptor 2 (ADIPOR2) were quantified by qPCR.

Results Glucose and insulin tolerance tests revealed insulin resistance in PREB transgenic mice. Serum adiponectin and leptin concentrations were decreased. Adiponectin gene expression was decreased in the adipose tissue, which was confirmed by the downregulation of the adiponectin-dependent hepatic Scd gene and upregulation of the ADIPOR2 gene in the liver of PREB transgenic mice. We also found that pioglitazone, an agonist for the peroxisome proliferator-activated

receptor- γ , improved the insulin resistance in the PREB transgenic mice after a 10-day feeding period.

Conclusions These results demonstrated that PREB might contribute to the regulation of adiponectin gene expression in vivo.

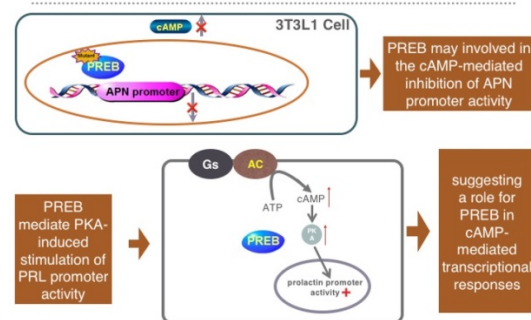
Keywords PREB · Adiponectin · Adipose tissue · Diabetes · Insulin resistance

Introduction

The prolactin regulatory element-binding protein (PREB) gene encodes a 1.9-kb mRNA, which is translated into a transcription factor that binds to and activates the basal prolactin promoter [1, 2]. The primary sequence of the PREB protein contains two potential transregulatory PQ-rich domains and three regions that are highly similar to the WD repeat, thus making it a member of the eukaryotic family of WD-repeat proteins. Members of this ever-expanding family of proteins are involved in multiple cellular functions, including signal transduction, RNA processing, cytoskeletal assembly, and vesicle trafficking [3]. The PREB protein has similarities to a subset of proteins belonging to the WD-repeat family of proteins, which play a role in gene regulation. Although PREB is ubiquitously expressed in humans, its expression levels vary greatly among tissues, with very high levels detected in the pituitary gland, pancreas, adrenal gland, and adipose tissue [4–6].

Adiponectin (APN), also called GBP28, apM1, AdipoQ, and Acrp30, is a 244-amino-acid-long polypeptide and is recognized as an adipocytokine that is highly specific to adipose tissue; it is also secreted into circulating blood and influences systemic metabolism [9]. Previous studies reported that APN acts as an anti-diabetic and anti-atherosclerotic molecule

POSSIBLE MECHANISM



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