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Adipogenic effect of calcium sensing receptor activation

Pia Villarroel · Marcela Reyes · Cecilia Fuentes · María Pia Segovia · Nicolás Tobar · Elisa Villalobos · Jorge Martínez · Eric Hugo · Nira Ben-Jonathan · Mariana Cifuentes

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Abstract We established that human adipose cells and the human adipose cell line LS14 express the calcium-sensing receptor (CaSR) and that its activation induces inflammatory cytokine production. Also, its expression is enhanced upon exposure to obesity-associated proinflammatory cytokines. We have thus proposed that CaSR activation may be associated with adipose dysfunction. Here, we evaluated a possible effect on adipogenesis. We induced adipose differentiation of primary and LS14 human preadipocytes with or without the simultaneous activation of CaSR, by the exposure to the calcimimetic cinacalcet. Activation of the receptor for 24 h decreased by 40 % the early differentiation marker CCAAT/enhancer-binding protein β. However, upon longer-term (10 day) exposure to the adipogenic cocktail, cinacalcet exerted the opposite effect, causing a dose–response increase in the expression of the mature adipose markers adipocyte protein 2, adiponectin, peroxisome proliferator-activated receptor γ, fatty acid synthase, and glycerol-3-phosphate dehydrogenase. To assess whether there was a time-sensitive effect of CaSR activation on adipogenesis, we evaluated the 10 day effect of cinacalcet exposure for the first 6, 24, 48 h, 6, and 10 days. Our observations suggest that regardless of the period of exposure, 10 day adipogenesis is elevated by cinacalcet. CaSR activation may interfere with the initial stages of adipocyte differentiation; however, these events do not seem to preclude adipogenesis from continuing. Even though adipogenesis (particularly in subcutaneous depots) is associated with insulin sensitivity and adequate adipose function, the implications of our findings in visceral adipocytes, especially in the context of inflamed AT and overnutrition, remain to be established.

Keywords Calcium sensing receptor · Adipogenesis · Adipose differentiation · Adipocyte

Abbreviations

aP2	Adipocyte protein 2
CaSR	Calcium sensing receptor
CEBPβ	CCAAT/enhancer-binding protein β
FASN	Fatty acid synthase
GPD	Glycerol-3-phosphate dehydrogenase
LPL	Lipoprotein lipase
PPARγ	Peroxisome proliferator-activated receptor γ
TBS	Tris-buffered saline

Introduction

Research in recent years has underscored the relevance of adipose tissue expandability to maintain a functionally healthy adipose tissue [1]. Preadipocyte differentiation into mature adipocytes is key for this process. Dysfunctional adipogenesis may be one of the consequences of a proinflammatory environment in adipose tissue, which has been extensively associated with obesity and its cardiometabolic consequences [2, 3].

Adipocyte differentiation is a complex sequential process influenced by a vast number of factors [4, 5]. The

P. Villarroel · M. Reyes · C. Fuentes · M. P. Segovia · N. Tobar · E. Villalobos · J. Martínez · M. Cifuentes (✉)
Institute of Nutrition and Food Technology (INTA), Universidad de Chile, El Líbano 5524, Macul, 138-11 Casilla, Santiago, Chile
e-mail: mcifuentes@inta.uchile.cl

E. Hugo · N. Ben-Jonathan
Department of Cancer and Cell Biology, College of Medicine, University of Cincinnati, 3125 Eden Avenue, Cincinnati, OH 45267-0521, USA

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