



Category: Molecular Genetics

Arginylation regulates adipose tissue development and function via modulating PPAR γ expression

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Abstract

Arginylation, a poorly understood post translational modification mediated by ATE1 known to regulate protein activity and stability [1]. Unconditional deletion of Ate1 results in embryonic lethality and postnatal whole body deletion of Ate1 in mouse results in adipose tissue dysfunction i.e. loss of visceral fat, exhibit higher metabolic rate and resistant to diet induced obesity [2]. Adipose tissue dysregulation leads to various life threatening diseases like obesity, diabetes, cardiovascular defects and cancer [3, 4]. Current study is undertaken to understand the role of protein arginylation in adipose tissue development and function. Our initial investigation showed an increase in ATE1 protein expression with progression of adipogenesis in 3T3L1 preadipocyte differentiation. Further, treatment of these cells with ATE1 inhibitors, tannic (10 μ M) acid and merbromin (75 μ M) suppressed lipid accumulation in 3T3L1 cell significantly. Gene expression analysis shows inhibition of peroxisome proliferator activated receptor gamma (PPAR γ) 1 and PPAR γ 2 expression in 3T3L1 cells differentiated in presence of ATE1 inhibitors. PPAR γ is a key transcription factor of adipogenesis and plays crucial role in induction of various adipogenic genes which contributes to lipid formation. The mRNA level of PPAR γ associated genes glucose transporter 4 (GLUT4), fatty acid binding protein 4 (FABP4) and perilipin (pln1) were found to be downregulated by ATE1 inhibitors, hence results into decrease in lipid accumulation. As PPAR γ found to be a target for ATE1 inhibitors, PPAR γ 1 was overexpressed in Ate1 knockout (KO γ 1) and wild type mouse embryonic fibroblast (MEF) cells. Expression of PPAR γ 1 was found to be significantly low in KO γ 1 as compared to its wild type counterpart at transcript level. Interestingly inhibition of PPAR γ 1 expression in absence of arginylation becomes more profound at protein level. Low level of PPAR γ 1 impedes adipogenesis when KO γ 1 cells were induced to differentiation with poor induction of GLUT4, lipoprotein lipase and FABP4. Current study provides a new protein arginylation dependent adipogenic pathway which promotes adipogenesis by promoting PPAR γ .

References

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