Adipocytes are coagulant active in a TF/FVIIa dependent manner but lipolysis is unaffected by TF/FVIIa

Authors:
D Eden¹, D Mokhtari², J W Eriksson², M Aberg¹, A Siegbahn¹, ¹Uppsala University, Department of Medical Sciences, Clinical Chemistry and Science for Life Laboratory - Uppsala - Sweden, ²Uppsala University, Department of medical sciences, Clinical diabetes and metabolism - Uppsala - Sweden,

Topic(s):
Lipids, Metabolism

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S131

Funding Acknowledgements:
Swedish heart and lung foundation, Swedish research council, Olle Engkvist foundation

Background/introduction

Tissue factor (TF) is the main initiator of blood coagulation and has been shown to promote diet-induced obesity, adipose tissue inflammation and insulin resistance in mice. Obese patients have increased expression of TF in their adipose tissue and also have increased rates of lipolysis resulting in elevated circulating fatty acids that contribute to inflammation and insulin resistance.

Purpose

We aimed to study which roles TF and its ligand coagulation factor VIIa (FVIIa) plays on a functional level, i.e. coagulation activity and lipolysis, in adipocytes using 3T3-L1- and human primary adipocytes as models.

Material and methods

TF protein levels were down-regulated in differentiated 3T3-L1 adipocytes using siRNA. The down-regulation was confirmed by western blot. The pro-coagulant properties of adipocytes were determined by a colorimetric FX-assay. Lipolysis was determined at basal levels and in response to isoproterenol and insulin and was measured as free glycerol in the cell media with a colorimetric method measuring absorbance. The effects on lipolysis were also determined after pre-stimulation with recombinant murine and human FVIIa (10nM, 30 min.) in 3T3-L1- and human primary adipocytes respectively.

Results

Transfection of 3T3-L1 adipocytes with TF siRNA was stable throughout all experiments and TF protein levels were significantly decreased with 85±4 % compared to cells transfected with unspecific siRNA. TF down-regulation in 3T3-L1 adipocytes resulted in a significant decrease in coagulation activity by 42% as compared to cells transfected with unspecific siRNA. The lipolysis was unaffected by depletion of TF in 3T3-L1 adipocytes on basal level and in response to isoproterenol and insulin. FVIIa pre-stimulation rendered no difference in the lipolysis rate in neither 3T3-L1- nor human primary adipocytes.

Conclusions

Down-regulation of TF in 3T3-L1 adipocytes significantly reduces FVIIa induced FXa generation. Neither stimulation with FVIIa nor depletion of TF altered isoproterenol induced lipolysis or insulin’s anti-lipolytic effect,
Adipocytes are coagulant active in a TF/FVIIa dependent manner but lipolysis is unaffected by TF/FVIIa signalling does not seem to be involved in the regulation of lipolysis.