ABSTRACT SUBMISSION

Title: PCSK9 EXPRESSION IS REGULATED BY PRO-INFLAMMATORY CYTOKINES AND ADIPOKINES IN HEPG2 CELLS

Abstract No. 0023

Title PCSK9 EXPRESSION IS REGULATED BY PRO-INFLAMMATORY CYTOKINES AND ADIPOKINES IN HEPG2 CELLS

Objectives

Clinical, genetic and experimental evidence indicates that proprotein convertase subtilisin/kexin 9 (PCSK9) may be either a cause or an effect of metabolic syndrome (MetS). We have recently demonstrated that PCSK9 is regulated by pro-inflammatory cytokine TNF-α in a SOCS3-dependent manner (Ruscica et al., JBC, 2016). Thus, the present work aimed to further extend this observation and studied the possible molecular mechanisms linking the effects of cytokines (TNF-α) and adipokines (leptin and resistin) on de novo lipogenesis and PCSK9 expression.

Method

Human hepatocellular liver carcinoma cell line (HepG2) and HepG2 overexpressing PCSK9 ($HepG2^{PCSK9}$) were used as in vitro tools. qPCR, Western blot, ELISA and luciferase reporter assays, together with siRNA directed to STAT3 and SOCS3, were used.

Results

HepG2 expresses leptin (ObRl), resistin (Adenylyl cyclase-associated protein 1, CAP1), and adiponectin (AdipoR2) receptors. Notably, HepG2PCSK9 expresses higher levels of ObRl and AdipoR2. Twenty-four h treatment of HepG2 with TNF-α (10 ng/mL), leptin (200 ng/mL) and resistin (50 ng/mL) induced the expression of both PCSK9 (2.3-, 2.0- and 3.5-fold, respectively) and the suppressor of JAK/STAT pathway, SOCS3 (3-, 1.8- and 1.9-fold, respectively). TNF-α and leptin increased the secreting PCSK9 (+15% and +20%, respectively) but only leptin stimulated (+46%) PCSK9 promoter activity (+20%). TNF-α, leptin and resistin induced the gene expression of apolipoprotein (apo) B, sterol regulatory element-binding protein 1 (SREBP1), stearoyl-CoA desaturase-1 (SCD-1), fatty acid synthase (FAS) and microsomal triglyceride transfer protein (MTP). The TNF-α mediated effects were inhibited by transfection with siRNA anti-STAT3, suggesting the involvement of the JAK/STAT pathway.

Conclusions

Pro-inflammatory cytokines and adipokines up-regulate PCSK9 expression and the key genes involved in the de novo lipogenesis. Future analyses will investigate the potential role of JAK/STAT/SOCS3 pathways in mediating these effects.

Approval from all authors Confirm

Affiliations (1) Università degli Studi di Milano - La Statale, Milan, Italy
(2) Università degli Studi di Padova, Padua, Italy

Authors Margherita Botta (1)

Cristina Songia (1)
Chiara Macchi (1)
Alberto Corsini (1)
Nicola Ferri (2)
Paolo Magni (1)
Massimiliano Ruscica (1) Presenting

Presenting author Male

Registration Confirm

Categories 1 – Cellular and systemic lipid metabolism

Presentation Either

Atherosclerosis publication Yes

Contact us if you have a problem or wish to withdraw a submission: info@eas-elc.org