Hormonal regulation of gene expression related to acylation stimulating protein production and function in ex vivo adipose tissue explant culture

Bashair Al Riyaami1, Prof. Simon Langley-Evans1, Prof. Andy Salter4 and Prof. Jumana Saleh2

1 Biosciences, Division of Nutritional sciences - The University of Nottingham (UK)
2 Biochemistry department, faculty of Medicine and Health science-Sulatn Qaboos University (Oman)

Background

Adipose metabolism is mediated through a complex network of hormonal signals including reproductive hormones. Acylation stimulating protein (ASP) synthesis occurs through the interaction between complement C3, factor B and adipins in adipose tissue. ASP demonstrates potent lipogenic effects that are modulated by sex hormones in vivo and in vitro. Human studies suggest a particular role for ASP in female lipid metabolism. ASP was found to strongly associate with fluctuating progesterone levels in females across the menstrual cycle [1]. In addition, elevations in ASP levels were seen in women with metabolic diseases such as polycystic ovary syndrome (PCOS) [2], suggesting that ASP metabolism may be altered in association with sex hormones disturbances. The connection of ASP to female fat metabolism and hormonal changes is collated in a recent review [3]. In this study, an ex vivo investigation was carried out to analyse expression of genes related to ASP production and function.

Methods

Adipose tissue was harvested from ovariectomized rats (n=6), and treated with sex steroids at physiological concentrations; progesterone (10⁻⁴ M), estrogen (10⁻⁴ M), P&E (10⁻⁸ &10⁻⁹ M) and testosterone (10⁻⁴ M) and chylomicrons (100 mg TG/ml media). The addition of chylomicrons to the media of cultured adipocytes has been shown to stimulate ASP production. Tissue explants were cultured for 24 hours at 37 °C and 5% CO2. media were collected for ASP and TG measurement. Tissue were harvested in RNA Later solution for RNA extraction and gene expression. Statistical analysis was performed by SPSS statistical program.

Results

**ASP tissue explant production in visceral and subcutaneous adipose tissue:**

The results showed that ASP production was only influenced by co-treatment with P&E hormones in both visceral and subcutaneous adipose tissues (p=0.011 and p=0.007, respectively) when compared to the control group (Figure 1).

**Relation of ASP with related precursors and lipogenic gene expression:**

Interestingly, in P&E treated subcutaneous adipose tissue, along with a reduction in ASP concentration, factor B gene expression decreased significantly (p=0.032) and CSL2 receptor expression increased significantly (p=0.05) when compared to the control group. Factor B correlated positively with ASP concentration (p=0.012, r=0.6). Figure 2 (A). In addition, Factor D were positively correlated with ASP concentration (p=0.013, r= 0.61). DGAT gene expression correlated positively with CSL2 receptor (p=0.04, r=0.51).

In visceral adipose tissue, ASP correlated negatively with TG level in the media (p=0.007, r= -0.75) and DGAT gene expression correlated positively with CSL2 receptor (p<0.001, r=0.97) as shown in Figure 2 (B) and (C).

Discussion and conclusion

The findings showed that ASP concentration and expression of precursors and related lipogenic factors maybe regulated under the combined effect of (P&E) treatment compared to individual hormone effects. The unexpected decrease in ASP production in subcutaneous tissue maybe explained by the negative correlation with CSL2 receptor and this suggests increased uptake of ASP by adipocytes. The positive correlation between CSL2 and DGAT suggests a regulatory effect of P&E hormones on the ASP-C5L2 signaling pathway and triglyceride uptake. Further analysis of the mechanism involved may clarify the influence of female hormones on fat storage and distribution.

References