

The Expression of Genes involved in Lipid Metabolism in Obesity

T Lappalainen¹, M Kolehmainen¹, U Schwab^{1,2}, L Pulkkinen¹, R Rauramaa³, M Uusitupa¹, H Gylling^{1,2}.

¹Department of Public Health and Clinical Nutrition/Food and Health Research Centre, University of Kuopio, ²Kuopio University Hospital, ³Kuopio Research Institute of Exercise Medicine, Kuopio, Finland

In general, obesity is characterized by an expanded mass of adipose tissue. When caloric intake exceeds nutritional requirements, need for an additional fat mass store is increased through adipogenesis. There are few studies suggesting that a failure of adipogenesis triggers insulin resistance in obesity finally leading to type 2 diabetes.

We have conducted studies to identify lipid metabolism related genes which are differentially expressed in adipose tissue of lean and obese subjects. Seventy-five overweight to obese subjects (BMI 32.9 ± 2.8 kg/m², mean \pm SD) with impaired glucose tolerance and other features of metabolic syndrome, aged 60 ± 7 years participated in the lifestyle modification intervention for 33.3 ± 1.1 weeks. In addition, healthy normal weight controls (n=11) were recruited. Abdominal subcutaneous adipose tissue biopsies were taken at baseline and after the intervention. The gene expressions of the enzymes involved in lipid metabolism were studied using real-time QPCR. In addition to adipogenic transcription factors PPAR γ 2 and SREBP-1c, stearoyl-CoA desaturase 1 (SCD1) and palmitoyl-CoA oxidase 1 (ACOX1) were also studied.

Our preliminary data show that obese subjects, especially women, have significantly impaired mRNA expression of SREBP-1c and SCD1, although they have larger adipocyte cell size. Concerning the gene encoding ACOX1, this is the first study to demonstrate that it is down-regulated in adipose tissue in response to weight reduction. Although the oxidative capacity of white adipose tissue in general is relatively low, this phenomenon may have a role in weight regain.

Our data support the hypothesis that impaired expression of adipogenic genes may result in the development of larger adipocytes, and thus, metabolic disturbances of adipose tissue metabolism. Furthermore, these findings will provide information on obesity-induced changes in lipid metabolism-related factors in adipose tissue. The changes characterized in gene expression in adipose tissue may play an important role in the development and maintenance of obesity-related co-morbidities.