MedicalXpress

Obesity and weight loss change splicing pattern of obesity and type 2 diabetes genes

May 21 2015

Alternative splicing of obesity and type 2 diabetes related genes may contribute to the pathophysiology of obesity, according to research from the University of Eastern Finland. Obesity leads to changes in the splicing pattern of metabolically relevant genes such as TCF7L2 and INSR, resulting in impaired insulin action. However, weight loss, induced by either obesity surgery or a very low-calorie diet, reverses these changes. The findings, presented by Dorota Kaminska, MSc, in her doctoral dissertation, increase our understanding of splicing dysregulations in obesity and can result in a new, more targeted treatment and more accurate diagnostics of metabolic disorders.

Both obesity and type 2 diabetes are complex diseases that are caused by a combination of genetic, environmental and lifestyle factors. Obesity is strongly associated with other metabolic complications including insulin resistance and type 2 diabetes, however the mechanisms linking the two conditions remain unclear.

Alternative splicing is the process by which a single gene produces more than one protein. Almost all human genes undergo some form of alternative splicing, which compensates for the relatively low number of genes present in the human genome. The study focused on determining the effects of obesity and weight loss on alternative splicing of metabolically active genes (TCF7L2 and INSR). Furthermore, the study identified alternatively spliced genes in the genomic regions associated with obesity risk, demonstrating that splicing of the TCF7L2, INSR and MSH5 genes in subcutaneous fat is regulated by weight loss. The study

also found that body mass index is a main determinant of TRA2B, BAG6 and MSH5 splicing in subcutaneous fat; however, the functional consequences of this finding require further investigation.

The study carried out at the Department of Clinical Nutrition of the University of Eastern Finland was based on data from the Kuopio Obesity Surgery (KOBS), very low calorie diet (VLCD), Metabolic Syndrome in Men (METSIM) and European Network on Functional Genomics of Type 2 Diabetes (EUGENE2) studies.

The researchers suggest that modulating alternative splicing may result in a new therapeutic approach against obesity-associated phenotypes.

The original articles were published in *Diabetes*, *Diabetologia* and *Adipocyte* journals.

Provided by University of Eastern Finland