MicroRNA mediates gene-diet interaction related to obesity

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Eating more n-3 polyunsaturated fatty acids, commonly known as omega-3 fatty acids, may help carriers of a genetic variant on the perilipin 4 (PLIN4) gene locus lose weight more efficiently. Based on this observation, researchers at the Jean Mayer Human Nutrition Research Center on Aging (USDA HNRCA) at Tufts University identified a microRNA (miRNA) which may elucidate the underlying biological mechanism.

Led by Jose M. Ordovas, PhD, director of the Nutrition and Genomics Laboratory at the USDA HNRCA, researchers genotyped seven single nucleotide polymorphisms (SNPs), also known as gene variants, from men and women of mostly white European ancestry enrolled in the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study and the Framingham Offspring Study. Carriers of the gene variant tended to weigh more and exhibit higher body mass index (BMI), which would increase their risk of becoming obese. Yet carriers with higher omega-3 fatty acid intakes tended to weigh less than carriers who consumed little or no omega-3 fatty acids.

Ordovas believes this to be the first example of a genetic variant that creates a miRNA binding site that influences obesity-related traits through a gene-diet interaction. Although further research is necessary, the findings suggest that miRNA activity is a possible target for dietary-based weight-loss therapies for obesity. The results were published online April 20 by the journal PLoS ONE.

"We tested for miRNA activity after seeing significant interactions between the gene variant, characteristics of obesity, and omega-3 fatty acid intake in our meta-analysis in two large populations," says Ordovas, who is also a professor at the Friedman School of Nutrition and Science Policy at Tufts. "When a gene variant is that informative, you get a strong sense that it may be functional."

The family of perilipin genes controls the release of perilipin proteins which dictate how fat is stored and broken down in the body. The current study adds to a body of research of the perilipin gene family and its role in obesity risk, yet most of the work focuses on perilipin 1 (PLIN1). "In the past, studies have shown gene variants in the PLIN1 gene locus are associated with obesity risk and appear to be regulated by polyunsaturated fat. It is encouraging that we saw both loci expressed in similar ways," Ordovas adds.

Ordovas and colleagues say future studies could explore the role of miRNA in both the PLIN1 and PLIN4 genes. "Variants that may create or destroy miRNA binding sites have tremendous potential for functional consequence, and we would want to investigate if this is occurring in the other perilipin genes," says Kris Richardson, MS, corresponding author and a doctoral student at the Sackler School of Graduate Biomedical Sciences at Tufts. "Also, replication of our results in larger populations which record the dietary information of its participants would help clarify the role of perilipin genes interacting with dietary fats such as omega-3 fatty acids and impacting weight."

Omega-3 fatty acids are polyunsaturated fats mostly found in fatty fish such as tuna, salmon and sardines. The recently-issued 2010 Dietary Guidelines for Americans say that "(f)at intake should emphasize monounsaturated and polyunsaturated fats."

More information: Richardson K, Louie-Gao Q, Arnett DK, Parnell

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