Is there a 'healthy' obesity gene?

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Why is it that some obese people are healthier than others? This was one of the main questions Dr. Chaodong Wu of the College of Agriculture and Life Sciences — Texas A&M University System — and a group of researchers tried to answer in a recent study.

The study, which will appear in a July issue of the *Journal of Biological Chemistry,* used genetically modified mice to investigate the genetic aspects of why some obese people do not develop certain medical problems typically associated with obesity, especially Type 2 diabetes.

Wu noted that Xin Guo, a Ph.D. candidate in the college's department of nutrition and food sciences, contributed significantly to the study.

"Previous research had indicated that a regulatory enzyme which is encoded by the gene PFKFB3 protects against diet-induced fat tissue inflammation and systemic insulin resistance," said Wu, who also has a Texas AgriLife Research appointment. "Increasing evidence shows that fat deposition, or amount, is not directly associated with the inflammation or insulin resistance in the development of obesity-related metabolic diseases."

Wu said the inducible 6-phosphorofructo-2-kinase (iPFK2) enzyme links metabolic and inflammatory responses and may underlie what he refers to as "healthy" obesity.

"While many obese people develop Type 2 diabetes, heart conditions and other chronic health problems associated with being significantly

overweight, other obese people do not," he said. "And while obesity in general is not healthy, some obese people do not develop the diseases more commonly associated with a less-than-healthy diet. Furthermore, a number of thinner people may have the sort of health problems more typically associated with obesity."

Wu said he and the other researchers theorized that these diseases are associated with the cellular inflammatory response brought on by obesity.

"We also thought this gene could conceivably be targeted for use in the treatment of diabetes, especially Type 2, commonly associated with obesity," he said. "We wanted to find out what might happen to a subject if that particular gene was activated."

Wu and his fellow researchers used laboratory mice to explore the effect of a targeted adipocyte overexpression of the gene/enzyme combination on diet-induced inflammatory responses and insulin sensitivity.

"We were trying to find out what it is in adipose, or fat, tissue that may trigger a negative response that leads to disease — and how to modulate that response," he said. "In our study, we learned overexpression of the iPFK2 enzyme increases fat deposition, suppresses inflammatory responses and improves insulin sensitivity in both adipose and live tissues."

As an extension of this research, Wu said, it may be possible to identify a pharmacological agent or bioactive agent which may have the desired effect on this gene toward reducing obesity-related cellular inflammatory response.

"We're hoping that, as one of its outcomes, this research will help lead to finding bioactive compounds or some type of supplement that might be

taken to help activate this gene toward the promotion of health," he said. "It would also be a good idea to compare and contrast this research with studies done on what constitutes a healthy diet and the effect of such a diet at a cellular level. "

Wu said that would allow for screening bioactive compounds in a healthy diet to determine to what degree these might be applicable for the treatment of disease brought on by unhealthy obesity in an animal model.

"As a further extension, one might study different types of obese people and try to isolate additional specific genes that determine a healthy versus an unhealthy obesity and find a way to modulate the expression of those genes toward disease prevention and health promotion," he said. "Once you find the link between the gene and the obese status of the individual, then you could work with experts in chemical research to produce or replicate whatever pharmacological or bioactive compound is needed to treat unhealthy obesity."

Wu said it is important to determine positively to what degree obesity as a health problem is due to a person's genetic makeup as it relates to their ability to store fat, as well as what type of fat – saturated or non-saturated – the individual may store.

"Fat composition is more important than fat deposition, or content," he said. "We know fat cells secrete some of their own bioactive compounds that we may be able to isolate and identify for use in promoting health."

Wu said it will be necessary to discover the role of certain genes in the composition and deposition of fats beyond what has already been identified as being stored in the adipose tissue of mice.

"Then we may be able to produce a dietary supplement or other

bioactive compound that would have a positive health effect," he said. "This could be used as a targeted treatment for obesity-related diseases such as Type 2 diabetes in a way that would have limited or minimal side effects."

Provided by Texas A&M University

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