Scientists identify gene that is consistently altered in obese individuals

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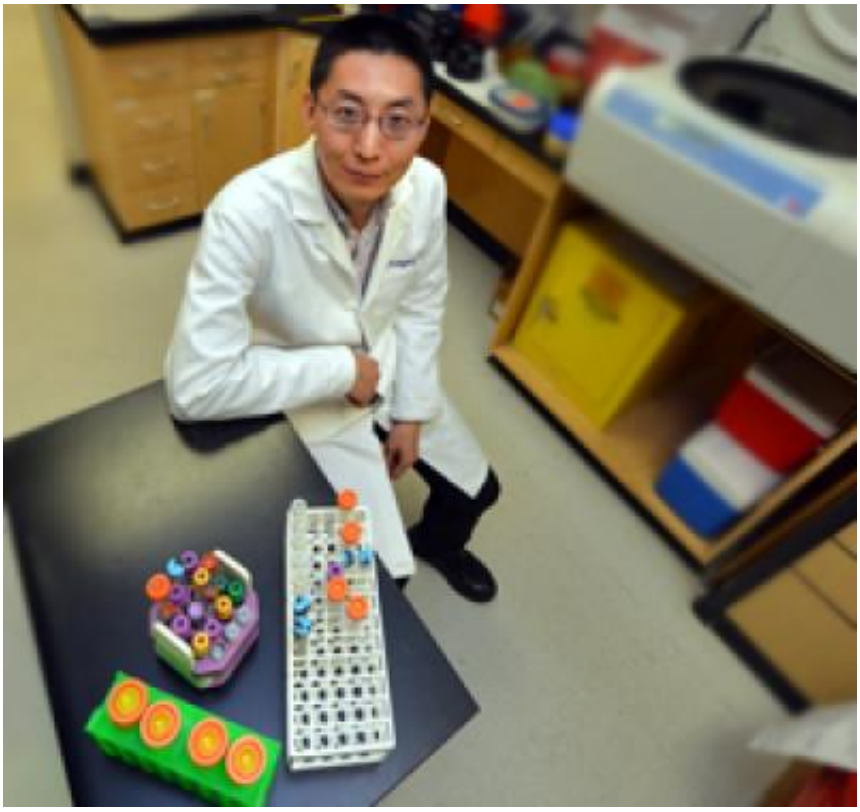

Food and environment can chemically alter your gene function and scientists have identified a gene that is consistently altered in obesity. Credit: Phil Jones, GRU campus photographer

Food and environment can chemically alter your gene function and scientists have identified a gene that is consistently altered in obesity.

The gene LY86 was among a group of 100 genes identified as likely contributors to obesity through genome-wide association studies comparing the DNA of thousands of obese and lean individuals, said Dr. Shaoyong Su, genetic epidemiologist at the Medical College of Georgia at Georgia Regents University.

Su looked at progressively larger groups of obese versus lean individuals and found LY86 consistently and highly chemically altered, or methylated, in the obese individuals. "The association is solid; the methylation of this gene is important in obesity," Su said.

It's known that obesity is highly inheritable; that if parents are obese, children are at higher risk. However environment, including high-fat foods and chemical exposure, can put you at risk as well, said Su. Methylation is one way the body adjusts to its environment.

He received the 2013 Scott Grundy Fellowship Award for Excellence in Metabolism Research for his studies and is presenting the work this week during the Epidemiology and Prevention/Nutrition, Physical Activity and Metabolism Scientific Session of the American Heart Association in New Orleans.

Previously LY86 had been known as an inflammation gene and Su's studies show, in fact, it may be contributing to more than just obesity. He found high methylation of LY86 also was associated with increased inflammation – a risk factor for a variety of maladies such as heart disease and cancer – as well as insulin resistance, a cause of diabetes. This association also held up among a group of about 703 subjects that, like the general public, included obese, lean and average-weight individuals.

Now he wants to go back to the animal model to see whether methylation changes gene expression up or down in fat mice as well as

fat, pregnant mice and their offspring. He believes that a lot of methylation starts in the womb and there are unfortunate real-life circumstances that support that theory.

For example, in the Dutch famine of 1944 near the end of World War II, babies born to starving mothers experienced DNA methylation that made them better able to survive such depravation, but in the more plentiful environment in which they grew up, put them at increased risk for cardiovascular disease as well as diabetes, obesity and other health problems.

He's already moving forward with more human studies as well, looking at a new group of lean and obese individuals, analyzing their DNA expression to see if increased methylation of LY86 means the gene is expressed more or less. Generally, higher methylation is thought to translate to lower gene expression.

He also wants to pin down whether methylation results from things like a high-fat diet, unfortunate genetics or both. These types of details may help explain why some individuals grow obese with a bad diet and little physical activity while others don't, Su said. It also may mean that positive environmental change, such as a better diet or more physical activity, can reverse at least some of the methylation. People may not get thin, for example, but they may reduce their risk for obesity-related disease, Su said.

LY86's clear importance in obesity emerged by first merging the gene list from the genome wide association studies with a genome wide methylation database on a small cohort of seven obese and seven lean individuals. The finding of increased methylation held up in subsequent groups of 46 obese/46 leans, 230 obese/413 leans as well as the general population panel of 703 at the GRU Institute of Public and Preventive Health. The research was supported by the National Institutes of Health.

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