

Genetic study shows that low body fat may not lower risk for heart disease and diabetes

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Having a lower percentage of body fat may not always lower your risk for heart disease and diabetes, according to a study by an international consortium of investigators, including two scientists from the Institute for Aging Research of Hebrew SeniorLife, an affiliate of Harvard Medical School (HMS).

The Institute researchers, Douglas P. Kiel, M.D., M.P.H., and David Karasik, Ph.D., who are working with the Framingham Heart Study, identified a gene that is linked with having less body fat, but also with an increased risk of type 2 diabetes and heart disease, examples of so-called "metabolic diseases."

"We've uncovered a truly fascinating genetic story and, when we found the effect of this gene, we were very intrigued by the unexpected finding," says Dr. Kiel, a senior scientist at the Institute for Aging Research and a professor of medicine at HMS. "People, particularly men, with a specific form of the gene are both more likely to have lower percent body fat, but also to develop heart disease and type 2 diabetes. In simple terms, it is not only overweight individuals who can be predisposed for these <u>metabolic diseases</u>."

Reported online in the journal <u>Nature Genetics</u> on June 26, 2011, the investigators examined the genomes of more than 75,000 people to look for the genes that determine <u>body fat percentage</u>. They found strong evidence for a gene, called IRS1, to be linked with having less body fat. On further study, they found that this gene also leads to having unhealthy



levels of cholesterol and <u>blood glucose</u>.

To understand why a gene that lowers body fat can be harmful, the scientists in the international consortium found that the gene lowers only the "subcutaneous" fat under the skin, but not the more harmful "visceral" fat that surrounds organs. The study authors speculate that people with this gene variant are less able to store fat safely under the skin and may, therefore, store fat elsewhere in the body, where it may interfere with normal organ function. All observations were more pronounced in men than in women and, indeed, many apparently lean men still carry too much abdominal fat.

"Genetic variants may not only determine the amount of total fat in your body," says Dr. Kiel, "but also what kind of fat you have. Some collections of fat, such as the kind located just under the skin, may actually be less harmful than the type located in the abdominal cavity, which may increase the risk of developing metabolic disease."

The effect, the researchers add, may be more pronounced in men due to the different body fat distributions between the sexes. Men store less fat than women, so they are more sensitive to changes in its distribution.

Provided by Hebrew SeniorLife Institute for Aging Research

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