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Body weight influenced by thousands of genes

Obesity quick fix unlikely; problem even more complex than previously thought

PHILADELPHIA (January 14, 2008) – Reporting in the online journal *BMC Genetics*, researchers from the Monell Center have for the first time attempted to count the number of genes that contribute to obesity and body weight.

The findings suggest that over 6,000 genes – about 25 percent of the genome – help determine an individual's body weight.

“Reports describing the discovery of a new ‘obesity gene’ have become common in the scientific literature and also the popular press,” notes Monell behavioral geneticist Michael G. Tordoff, PhD, an author on the study.

“Our results suggest that each newly discovered gene is just one of the many thousands that influence body weight, so a quick fix to the obesity problem is unlikely.”

To obtain an estimate of how many genes contribute to body weight, the Monell researchers surveyed the Jackson Laboratory Mouse Genome Database for information on body weights of knockout mouse strains.

Knockout mice have had a specific gene inactivated, or “knocked out.” By studying how the knockout mice differ from normal mice, researchers obtain information about that gene’s function and how it might contribute to disease. Mice can provide valuable information on human disease because they share many genes with humans.

The knockout approach is so useful that the inventors of the technology were awarded the 2007 Nobel Prize in Medicine. Knockout mice are now standard tools in all mouse models of behavior and disease.

In 60% of strains, knocking out a gene produces mice that are nonviable; that is, the mouse cannot survive without the knocked out gene.

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The Monell survey revealed that body weight was altered in over a third of the viable knockout stains; 31 percent weighed less than controls (indicating that the missing genes contribute to heavier body weight), while another 3 percent weighed more (contributing to lighter weight).

Extrapolating from the total number of genes in the mouse genome, this implies that over 6,000 genes could potentially contribute to the body weight of a mouse.

Tordoff comments, "It is interesting that there are 10 times more genes that increase body weight than decrease it, which might help explain why it is easier to gain weight than lose it."

Because body weight plays a role in many diseases, including hypertension, diabetes, and heart disease, the implications of the findings extend beyond studies of obesity and body weight. Gene knockouts reported to affect these diseases and others could potentially be due to a general effect to lower body weight.

The findings also hold clinical relevance, according to lead author Danielle R. Reed, PhD, a Monell geneticist. "Clinicians and other professionals concerned with the development of personalized medicine need to expand their ideas of genetics to recognize that many genes act together to determine disease susceptibility."

Maureen P. Lawler also contributed to the study, which was funded by the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute on Alcohol Abuse and Alcoholism.

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