Fat Genes

Can we blame extra pounds on our genes? Several researchers at UNC Gillings School of Global Public Health are identifying which genes may have an impact on body weight and investigating precisely how that impact occurs.

- **Kari North, PhD**, epidemiology associate professor, studies risk factors for cardiovascular disease – and obesity is a big one. She and colleague Keri Monda, PhD, proposed a potential location for a gene that controls waist circumference. "Then we realized we needed a lot more samples to discover more loci," North says. Through a project called GIANT, which has 125,000 participants, they have identified 18 new genetic markers associated with obesity-related traits. "It helps us understand on a molecular level how individuals become obese," North says. Now her team is working on how these genes interact with environmental factors including gender and physical activity.
- **Rosalind Coleman, MD**, nutrition professor, uses "knockout mice," each of which lacks a specific enzyme and so a specific genetic function, to identify precise roles of enzymes that metabolize fatty acids. People who are obese or insulin resistant frequently have fatty livers, but the team found that mice lacking one particular enzyme had *less* fat in their livers, even when the mice were obese. Another group of mice that lacked a different enzyme – the one that activates most of the fatty acids in fat tissue – got fatter, not thinner. The surprising discoveries will lead to more nuanced understanding of the role these enzymes play in human obesity, insulin resistance, diabetes and heart disease.
- The more weight a person gains, the more insulin resistant he or she will be. As insulin resistance rises, so does glucose level, which increases the likelihood of diabetes. Insulin normally controls the liver's glucose production, but the liver of someone with high insulin resistance keeps producing glucose even when it shouldn't. "We're asking why the liver is not turning off when glucose is coming in from the gastro-intestinal tract," says **Terry Combs, PhD**, nutrition assistant professor, whose team recently identified in mice a gene they believe plays a critical role in the process. "What insulin does is turn on the expression of this gene," he says, explaining that when the gene is on, the liver turns off glucose production. Now Combs' lab is working to discover whether the same genetic mechanism occurs in people.
- **Daniel Pomp, PhD**, professor of genetics, nutrition, and cell and molecular physiology at Carolina Center for Genome Sciences, wondered why some people run marathons while others lie around on the couch. Using specially bred mice, he and his team are looking for the genes associated with a predisposition to exercise, a trait that can prevent or control obesity. "There is not one single exercise gene or one obesity gene," he says. "There are maybe 50, each with a relatively small impact." His lab's findings may help humans maintain a healthy weight, but it won't be a magic bullet. "We know how much a person exercises is 30 to 40 percent influenced by genes," Pomp says. "But we don't want people to use [their genetic makeup] as an excuse. The information is meant to make you work harder if you're predisposed not to exercise much."

–Kathleen Kearns

TIP

Eat five servings of fruits and vegetables daily.

Dr. Kari North

Dr. Rosalind Coleman

Dr. Terry Combs

Dr. Daniel Pomp

PHOTOS BY LINDA KASTLEMAN