

**Office of Genetics and Disease Prevention
Public Health Perspectives**

**Obesity and Genetics: What We Know, What We Don't Know and
What It Means**

Introduction: Rising rates of obesity seem to be a consequence of modern life, with access to large amounts of palatable, high calorie food and limited need for physical activity. However, this environment of plenty affects different people in different ways. Some are able to maintain a reasonable balance between energy input and energy expenditure. Others have a chronic imbalance that favors energy input, which expresses itself as overweight and obesity. What accounts for these differences between individuals?

What We Know:	What We Don't Know:
Biological relatives tend to resemble each other in many ways, including body weight. Individuals with a family history of obesity may be predisposed to gain weight and interventions that prevent obesity are especially important.	Why are biological relatives more similar in body weight? What genes are associated with this observation? Are the same genetic associations seen in every family? How do these genes affect energy metabolism and regulation?
In an environment made constant for food intake and physical activity, individuals respond differently. Some people store more energy as fat in an environment of excess; others lose less fat in an environment of scarcity. The different responses are largely due to genetic variation between individuals.	Why are interventions based on diet and exercise more effective for some people than others? What are the biological differences between these high and low responders? How do we use these insights to tailor interventions to specific needs?
Fat stores are regulated over long periods of time by complex systems that involve input and feedback from fatty tissues, the brain and endocrine glands like the pancreas and the thyroid. Overweight and obesity can result from only a very small positive energy input imbalance over a long period of time.	What elements of energy regulation feedback systems are different in individuals? How do these differences affect energy metabolism and regulation?
Rarely, people have mutations in single genes that result in severe obesity that starts in infancy. Studying these individuals is providing insight into the complex biological pathways that regulate the balance between energy input and energy expenditure.	Do additional obesity syndromes exist that are caused by mutations in single genes? If so, what are they? What are the natural history, management strategy and outcome for affected individuals?

<p>Obese individuals have genetic similarities that may shed light on the biological differences that predispose to gain weight. This knowledge may be useful in preventing or treating obesity in predisposed people.</p>	<p>How do genetic variations that are shared by obese people affect gene expression and function? How do genetic variation and environmental factors interact to produce obesity? What are the biological features associated with the tendency to gain weight? What environmental factors are helpful in countering these tendencies?</p>
<p>Pharmaceutical companies are using genetic approaches (pharmacogenomics) to develop new drug strategies to treat obesity</p>	<p>Will pharmacologic approaches benefit most people affected with obesity? Will these drugs be accessible to most people?</p>
<p>The tendency to store energy in the form of fat is believed to result from thousands of years of evolution in an environment characterized by tenuous food supplies. In other words, those who could store energy in times of plenty, were more likely to survive periods of famine and to pass this tendency to their offspring.</p>	<p>How can thousands of years of evolutionary pressure be countered? Can specific factors in the modern environment (other than the obvious) be identified and controlled to more effectively counter these tendencies?</p>

What It Means

1. For people who are genetically predisposed to gain weight, preventing obesity is the best course. Predisposed persons may require individualized interventions and greater support to be successful in maintaining a healthy weight.
2. Obesity is a chronic lifelong condition that is the result of an environment of caloric abundance and relative physical inactivity modulated by a susceptible genotype. For those who are predisposed, preventing weight gain is the best course of action.
3. Genes are not destiny. Obesity can be prevented or can be managed in many cases with a combination of diet, physical activity, and medication.
4. Drugs that will aid in losing weight or maintaining a healthy weight are being developed and are expected to be available in the next few years.
5. People who are affected with overweight and obesity are often victims of stigmatization and discrimination. It is time to stop blaming the victim. Many obesity researchers believe that people who struggle with their weight are pushing against thousands of years of evolution that has selected for storing energy as fat in times of plenty for use in times of scarcity. It is time to recognize their struggle, understand their challenges and support their need for lifelong efforts to achieve better health.