

## Can We Pop a Pill to Cure Obesity?

Genetic Studies of a Complex Trait

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**Characteristics like obesity and many other behavioural traits are the result of the interaction of various environmental factors and lifestyle with multiple genes. This article describes recent research on the molecular biology of some forms of obesity that suggests possible ways to control the condition.**

Is obesity merely the result of eating too much or is it possible that there is a genetic basis for the condition? Scientists have been asking this question for many years and the answer that emerges from recent work is: probably both. Over the years at least five independent single-gene mutations leading to the obese phenotype have been isolated. Obesity<sup>1</sup> is therefore a condition that involves the expression of multiple genes. In addition to being *polygenic*, it is a complex characteristic that requires the interaction of the environment with the products of these genes. Some other traits that fall into this category

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include intelligence, schizophrenia and congenital heart disease.

### Cloning of the *ob* Gene

A *recessive* mouse mutation called *obese* (*ob*) was first identified in the 1950s. When both copies of the normal *obese* gene are mutated as in the (*ob/ob*) mouse it causes profound obesity and a form of diabetes, often seen in humans. Some scientists recently reported the cloning of the mouse *obese* gene (*ob*) and its human homologue in the journal *Nature*. This gene appears to play an important role in the maintenance of body weight and appetite. The *ob* gene codes for a 4.5 kb<sup>2</sup> mRNA (messenger, ribonucleic acid) capable of making a protein with 167 amino acids (See *Box 1*). Its coding sequence is *highly conserved* or, in other words, largely unchanged among various vertebrate species. When the amino acids of the Ob<sup>3</sup> protein in mice and humans are compared, 84% of them

<sup>1</sup> Obesity implies body weight in excess or equal to 20% above ideal body weight. Generally obesity is determined by comparing standard tables for height and weight or by calculation of body mass index (body weight in kg/height in meters). More precise indications can be obtained by skin-fold measurements.

<sup>2</sup> 1kb = 1000 nucleotide bases

<sup>3</sup> *ob* refers to the gene while *Ob* refers to the protein

<sup>4</sup> 1kD = 1000 dalton, 1 dalton =  $1.66024 \times 10^{-24}$  g.

