Pennington Nutrition Series
Healthier lives through education in nutrition and preventive medicine
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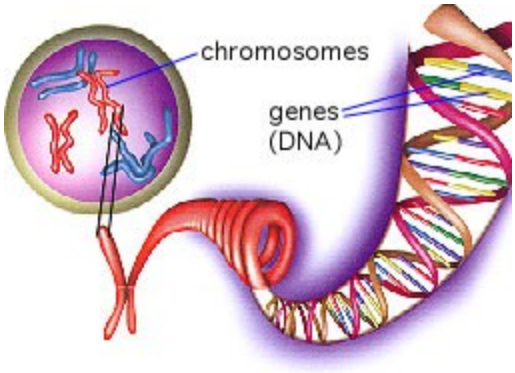
Genetic Considerations

Much of the information provided comes from The Human Obesity Gene Map: The 2004 Update. The 2004 edition is the eleventh update of the human obesity gene map. To date, over 600 genes, markers, and chromosomal regions have been associated or linked with human obesity.



Single Gene Mutations

A total of 173 obesity cases due to single-gene mutations in 10 different genes have been identified. When a gene is mutated, the protein it produces is partially or completely ineffective. This can disrupt the cells activity.

Mendelian disorders

Mendelian simply means of, relating to, or designating Gregor Mendel or his theories of genetics and inheritance of traits. There are six different Mendelian disorders discussed in the 2004 update.

1.) Cushing's Syndrome

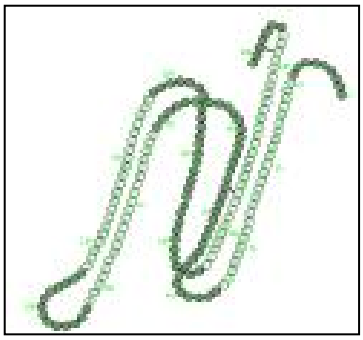
This is a condition that occurs when the body's tissues are exposed to excessive levels of cortisol for long periods of time.

Normal levels of cortisol are essential to:

- The maintenance of blood pressure and cardiovascular function
- The regulation of the immune system's inflammatory response
- The balance of the effects of insulin in breaking down sugar for energy
- The regulation of the metabolism of proteins, carbohydrates, and fats
- In helping the body respond to stress appropriately.

2.) Cortisone Reductase Deficiency

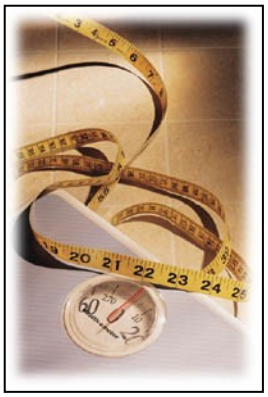
In this condition, the synthesis of cortisol from cortisone is reduced. This leads to an androgen excess and a polycystic ovary syndrome-like disorder with obesity and insulin resistance.



Human Growth Hormone

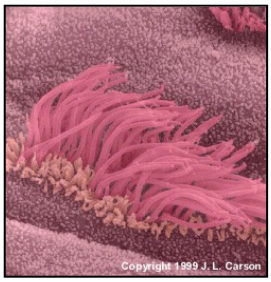
3.) Isolated Growth Hormone Deficiency

This is a condition caused by mutations in the growth hormone gene. Adult patients with this condition are described as having central obesity.



4.) X-Linked Syndromic Mental Retardation 16

Obesity in these affected individuals is very common. With this condition, there is a protein that controls protein production in other cells making them partially or completely ineffective once produced.



5.) Bardet-Biedl Syndrome

Of the previously reported disorders, the greatest advance has been in the understanding of this syndrome. There have been recent new gene discoveries related to this condition. Most genes involved appear to play a role in proteins that help move body fluids. It is clear that these genes are related to the syndrome, however how these genes relate to obesity and insulin resistance is uncertain.

6.) Albright Hereditary Osteodystrophy-Like Syndrome and others

Information on new mutations in casual genes have been added for many conditions this year.

Murine Gene-deficient and Transgenic Models of Obesity

When referring to the term murine, we mean of or relating to a rodent of the family Muridae or subfamily Murinae, including rats and mice. By transgenic, we mean of, relating to, or being an organism whose genome has been altered by the transfer of a gene or genes from another species or breed: *transgenic mice; transgenic plants.*

The murine obesity gene map identifies 166 genes that, when mutated or expressed as transgenes in the mouse, result in phenotypes that affect body weight and obesity. The map has been completely revised in 2004 and contains all genes that affect obesity in either a positive manner (promoting leanness) or a negative manner (promoting body weight gain and adipose tissue increases).

The mouse is clearly established as a valuable model system in which to study the biological roles of obesity genes. The development of gene-deficient and transgenic mutations are vastly important in that they not only allow for the identification of these genes related to obesity but also lead to a more detailed phenotype.

- Models of obesity can help scientists address the role that the genes may play in the regulation of food intake and absorption, fat and carbohydrate use, thermogenesis, and physical activity and basal metabolic rate.

Association Studies

Associations between candidate genes and obesity-related phenotypes have been found. A total of 358 studies covering 113 candidate genes have reported significant associations. This year's update includes 21 new candidate gene entries.

Associations discovered include:

- Associations with body weight, BMI, overweight, and obesity
- Associations with body composition, fat distribution, and energy expenditure
- Associations with changes in body weight and body composition
- Negative associations with obesity-related phenotypes

Linkage Studies

There is evidence for genetic linkages with obesity-related phenotypes. More than 20 positive linkages have been recently published. Most of the genome-wide studies were based primarily on BMI measurements. Studies of BMI measures were performed on participants from the Framingham Heart Study linking BMI and obesity to particular chromosomes in these subjects. Similar studies were conducted on individuals with type 2 diabetes, sleep apnea, and childhood obesity linking their BMI with markers on certain chromosomes.

In conclusion, the large number of genes and their location indexed in the obesity gene map is a good indication of the complexity and challenge in the task of identifying genes associated with susceptibility to obesity. The goal still remains to identify the right combination of genes and mutations that are associated with this increased risk of common diseases and to determine how environmental factors interact with these genes and mutations to determine the risk.

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To promote healthier lives through research and education in nutrition and preventive medicine.

The Pennington Center has several research areas, including:

- Clinical Obesity Research
- Experimental Obesity
- Functional Foods
- Health and Performance Enhancement
- Nutrition and Chronic Diseases
- Nutrition and the Brain
- Dementia, Alzheimer's and healthy aging
- Diet, exercise, weight loss and weight loss maintenance

The research fostered in these areas can have a profound impact on healthy living and on the prevention of common chronic diseases, such as heart disease, cancer, diabetes, hypertension and osteoporosis.

The Division of Education provides education and information to the scientific community and the public about research findings, training programs and research areas, and coordinates educational events for the public on various health issues.

We invite people of all ages and backgrounds to participate in the exciting research studies being conducted at the Pennington Center in Baton Rouge, Louisiana. If you would like to take part, visit the clinical trials web page at www.pbrc.edu or call (225) 763-3000.