The Molecular Pathogenesis of Obesity: An Unfinished Jigsaw Puzzle

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Abstract

***Introduction**: Obesity is a common but highly complex disease, which evolved from interactions of multiple genes and the environment. In the past decade, there have been major advances in our understanding of the molecular genetics and pathogenesis of obesity, especially with regards to the genetics and functions of chemical mediators and their receptors, such as leptin, the leptin receptor, neuropeptide Y, the melanocortin-4 receptor, agouti-related protein and the peroxisome-proliferator-activated receptor γ2. **Methodology**: Recent studies and reports on the obesity genes and chemical mediators were reviewed. **Results**: Despite exciting discoveries of single gene mutations with haplo-insufficiency in human subjects, and single-gene disorders resulting in obesity, most cases of obesity are likely the result of subtle interactions of several related genes with environmental factors, which favour the net deposition of calories as fat, culminating in the obese phenotype. Obesity is unlikely to be caused by a single gene defect unless it is extreme (body mass index >60), or present in an isolated population group. However, research has established that genes at multiple loci may interact centrally to determine satiety, and peripherally to influence the metabolic rate of obese individuals. **Conclusion**: The mechanisms of action of these genes in the development of obesity are now being examined, with the aim of eventually discovering a therapeutic intervention for obesity.*

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Key words: Agouti-related protein, Leptin, Melanocortin-4 receptor, Neuropeptide Y, Uncoupling protein

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