

Editorial

GENES INVOLVED IN THE METABOLIC SYNDROME

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The metabolic syndrome (MS) was defined in an effort of the most important medical organizations to assess the risk for both cardiovascular disease and diabetes mellitus. The prevalence of the MS has reached, in 2004, 20-25% of the entire population; it varies depending which definition we use ¹. The most commons are those of the World Health Organization (WHO), International Diabetes Association (IDF), National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP III), American Heart Association and The National Heart, Lung and Blood Institute (AHA/NHLBI). Several synonyms were suggested: *Syndrome X*, *The Deadly Quartet*, *Insulin Resistance Syndrome*, *Cardio-metabolic Syndrome*. It is defined by multiple metabolic abnormalities, including abdominal obesity, hypertension, dyslipidemia, insulin resistance, and impaired glucose tolerance. The central pathogenic factor seems to be the visceral obesity that can lead to insulin resistance with the development of impaired glucose tolerance, hyperglycemia, and type 2 diabetes. Visceral obesity is also associated with many pathophysiologic changes, including sodium retention and volume expansion, increased sympathetic nervous activity, and stimulation of the renin-angiotensin system. Adipose tissue is also an active endocrine organ that secretes a variety

of molecules known as adipocytokines into the circulation; these have profound effects on the

vasculature and metabolism. The etiology of the MS is complex, determined by both genetic and environmental factors ².

Taking into consideration that more than 50% of the variance of arterial blood pressure, lipid levels and body mass index are attributable to genetic influences, there are some important directions of genetic research to be presented.

1. **Animal Models:** helped to identify a large number of candidate genes based on biologic and pathologic relevance. Currently, the rodent models for metabolic syndrome include Dahl salt-sensitive/resistant rat, spontaneously hypertensive rat, Zucker diabetic fatty rat, KKAy mouse, and ob, db, tubby, agouti, fatty acid translocase (FAT) mice and the Wistar Ottawa Karlsburg W rat ³.
2. **Genome Wide Scan:** method consists of searching the entire human genome to detect chromosomal regions linked to MS phenotypes by using genetic markers and linkage analyses. Several GWS performed recently have shown a strong link between MS components (weight, waist circumference, leptin, leptin/insulin ratio) and chromosomes 1,2,3,6,7,9,10,19. One promising approach is to narrow the list of genes by using freely available bioinformatics tools for prioritization ^{4,5}.

3. **Candidate Genes Approach:** consists of searching for the association of candidate genes based on the presumed functional changes that accompany a particular syndrome. Several potential candidate genes have been suggested by their biologic relevance to associated to the MS: genes affecting insulin sensitivity (PPAR γ , insulin receptor substrates, CAPN10 a.o.); genes affecting lipid metabolism (CD36, 11 β -HSD I, upstream constriction factor 1 a.o.); genes regulating free fatty acid metabolism (adiponectin, β -adrenergic receptor, fatty acid binding protein 2 a.o.); genes regulating glucose uptake in skeletal muscle (glycogen synthase 1 a.o.), genes

producing monogenic obesity (leptin a.o.); genes related to inflammation (TNF α , CRP a.o.)^{3,6,7}.

MS is a spectrum of diseases ranging from rare monogenic forms caused by highly penetrant and infrequent mutations in a few genes to more-prevalent polygenic and multifactorial forms, where environmental factors, personal habits and genetic factors conferring resistance or susceptibility to the disease can play an important role. All this genetic research aims to be able to give us the tools in order to predict and to treat adequately all the people that are genetically susceptible to this disease.

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