Extended Abstract

# Genetics and epigenetics of cardio-metabolic complex diseases

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**Abstract**

The metabolic syndrome (MS) constitutes a combination of underlying risk factors for an adverse outcome, cardiovascular disease. Thus, the clinical behavior of the MS can be regarded as a whole. Nevertheless, from a pathogenic point of view, understanding of the underlying mechanisms of each MS intermediate phenotype, obesity, hypertension, type 2 diabetes and particularly insulin resistance is a difficult task. Systems biology introduces a new concept for revealing the pathogenesis of human disorders and suggests the presence of common physiologic processes and molecular networks influencing the risk of a disease. It will be showed a model of this concept to explain the genetic determinants of MS-associated phenotypes.

Based on the hypothesis that common physiologic processes and molecular networks may influence the risk of MS disease components, we propose systems-biology approaches i.e. a gene enrichment analysis and the use of a protein-protein interaction network. Our results show that a network driven by many members of the nuclear receptor super family of proteins, including retinoid X receptor and farnesoid X receptor (FXR), in addition to Clock, SLC6A4, PGC1A, etc, may be implicated in the pathogenesis of the MS by their interactions at multiple levels of complexity with genes involved in metabolism, cell differentiation and oxidative stress. In addition, it will be discussed alternative genetic mechanisms that are gaining acceptance in the physiopathology of the MS components, in particular fatty liver disease: the regulation of transcriptional and post-transcriptional gene expression by micro-RNAs and epigenetic modifications such as DNA methylation of not only nuclear but mitochondrial genes.