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EDITORIAL

VALUE OF GENETIC STUDIES TO IDENTIFY TYPE 2 DIABETES SUSCEPTIBILITY GENES

Type 2 diabetes, in conjunction with obesity and other components of the metabolic syndrome is an important cause of morbidity and mortality worldwide.[1] The recent concept of chronic inflammation in a patient with diabetes has brought potential implications for the pathophysiology of this disease. Initially, it was demonstrated that the expression of TNFα, a proinflammatory cytokine, was increased in the adipocytes of obese animals and TNFα neutralization induced a decrease in insulin resistance in these animals,[2] thus establishing the first connection between preinflammatory cytokines and insulin resistance. Various studies have confirmed a relationship between obesity, DT2, insulin resistance and inflammatory markers.[3,4] Subsequently, it was possible to confirm the presence of inflammation as a predictor of DT2 development.[5] Nevertheless, it is still unclear how we should use inflammatory markers in the follow-up of diabetic patients. It is not well established whether they would serve to indicate which patients are at risk for cardiovascular disease and which new preventive measures should be adopted in the presence of these markers.

On the other hand, DT2 is known as a genetic disease and a positive family history for DT2 is indicative of early biochemical detection. The association between family history and obesity doubles the risk of developing DT2 in a patient. Individual susceptibility for the development of DT2 is strongly influenced by genetic factors and this fact justifies the efforts to identify and characterize susceptibility genes for this disturbance.

In addition to the polygenic character present in most cases of DT2 and obesity, environmental factors such as lifestyle, social issues and fetal surroundings may significantly influence the development of this disorder.[6] The search for DT2 susceptibility genes began with cloning the gene for human insulin in 1980. At first, genes that were the most probable candidates for the action and secretion of insulin[7] were studied and later several genetic markers were investigated through various analytical strategies, culminating with recent genome-wide association studies.[8] Until the present moment, DT2 appears to be due to more susceptibility genes than was originally predicted, and each gene has a very discrete impact on the risk of disease. However, there are infrequent DT2 subtypes that have specific genetic alterations, and MODY3 is the most common of these subgroups.[9] Variants of the hepatocyte nuclear

factor 1α gene induce progressive failure of the beta cells and therefore the investigation of mutations in this gene may be performed with the objective of early detection and adequate intervention.

There will continue to be difficulties in the search for contributing genes for complex genetic disorders such as DT2 and only the perseverance and discernment of investigators can overcome these difficulties.

To this end, Bid, *et al.*[10] have evaluated the presence of polymorphisms in IL-4 and IL-1RN genes in diabetic patients and in normal controls, verifying that these polymorphisms serve as markers of susceptibility to DT2 in the studied population, stimulating the performance of new studies to search for a better understanding of the mechanisms involved in this relationship.

In conclusion, it is worth highlighting that identifying genes that influence metabolic processes that induce diabetes allows further advances in the elucidation of the pathophysiology of this endocrine disturbance, even if these genes are not direct determinants for diabetes susceptibility. These studies are expected to provide new avenues for obtaining the optimal methods of prevention and treatment of DT2 and its complications.

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