

ATM is a Gene Target in the Clinical Following of Diabetic Retinopathy

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INTRODUCTION

In the current era of translational medicine, it is important to search for genetic markers that may be useful in the clinical management of patients with diabetic retinopathy, as well as for their prognosis and evolution, one of the genes worth exploring in this regard, is the ataxia telangiectasia gene known as ATM. This gene may be the connection between genomic instability and metabolic stress that occurs in diabetic patients.

The ATM gene has its locus on chromosome 11q23, has 66 exons and codes for the ATM protein, which is a regulator of the cell cycle through the phosphorylation of TP53, BCRA-1, BLM, NBS-1, CHK2, CDK2, CD25, FANCD, RAD 17. The ATM protein, has five domains, one of the most important is the N-terminal region encoded by the 3' portion of the gene because it shows homology with the mammalian and mouse IPK3. This is relevant since it regulates AMPK, which regulates and amplifies metabolism, participating in the regulation of insulin signaling, hence it is also a hepatic genomic marker of metformin, since it is used in the treatment of diabetes and as adjuvant in cancer and is related to dysglycemia and insulin resistance [1-13].

The genetic variants of ATM at the level of polymorphisms have been associated with the risk of diabetes in the Asian population, as in the case of the SNP rs189037C>T with locus

in the promoter region, while the SNP rs11212617 has been associated with the response to metformin in Iranian population and population in the United Kingdom, as well as the development of coronary syndromes. Effectively functional SNP rs189037 participates in coronary stenosis. Increased expression of the ATM gene in diabetics and in patients with coronary syndromes has been reported at the expression level [1-13].

With these considerations we can comment insights of the ATM gene, which is a regulator of the metabolism of glucose control, its alteration leads to dysglycemia and insulin resistance, at the level of ophthalmology this is very important because the alteration of the homeostasis of the glucose leads to the development of retinopathy in the diabetic patient or to the progression of retinopathy, this is a frontier of research that has to be explored both by association studies with polymorphisms such as SNP rs189037 and rs11212617 as well as expression level genetics. There is evidence that can explain why we make this application; since ATM acts as a defense against a variety of stressors, at least demonstrated at the level of hematopoietic stem cells (HSC) of the bone marrow (BM). The loss or dysfunction of ATM is detrimental both to the function of HSC and to microvascular repair, whose chronicity in diabetics represents a condition associated with HSC

depletion and inadequate vascular repair, in rodent and microarray models in individuals diabetics, show an increase of ATM mRNA. Second, some ATM null alleles have been found in idiopathic perifoveal telangiectasia [1-13].

Undoubtedly, these evidences suggest that the ATM gene is the connection between genomic instability, as well as the cell cycle and metabolic stress that occurs in diabetic patients, which can lead to the development of chronic microangiopathic complications such as diabetic retinopathy, which will have to be demonstrated in the coming years.

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