LETTER TO THE EDITOR

High frequency of the ancestral allele from SNV rs11212617 polymorphism of the *ATM* gene in a Mexican Norwest population

Alta frecuencia del alelo ancestral del polimorfismo rs11212617 de SNV del gen ATM en una población del noroeste de México

*Claudia B. Montaño-Montejano[1], Diana García-Cruz[1,2], José Sánchez-Corona[3], Héctor V. Ortega[4], and Sergio A. Ramírez-García[5]**

[1]Department of Molecular Biology and Genomics, University Center for Health Sciences, University of Guadalajara, Guadalajara, Jalisco, Mexico; [2]Department of Molecular Biology and Genomics, Institute of Human Genetics Dr. Enrique Corona Rivera, University Center of Health Sciences, University of Guadalajara, Guadalajara, Jalisco, Mexico; [3]Molecular Medicine Division, Western Biomedical Research Center, Western National Medical Center, Mexican Social Security Institute, Guadalajara, Jalisco, Mexico; [4]Department or Service, Thomas Jefferson University, Philadelphia, Pennsylvania, United States; [5]Institute of Nutrition of the University of the Sierra Sur, Miahuatlán de Porfirio Díaz, Oaxaca, Mexico

Sr. Editor:

ATM gene with locus at 11q22.3 codes for ataxia telangiectasia nuclear protein kinase (ATM), which regulates the cell cycle through the P53, BCRA1 and RB proteins[1]. It is made up of 66 exons and 65 introns (Fig. 1A)[1]. Some of its genetic variants are related to diseases such as ataxia telangiectasia and other immunometabolic pathologies (Fig. 1)[1,2]. In the Mexican population, variants of this gene have only been reported in breast cancer[3]. He SNV rs11212617, which consists of an A > C transversion in an open reading frame (C11orf65), has also been associated with diabetes and cardiovascular disease[4], but it has not been studied in Mexico. With these considerations, the SNV rs11212617 was analyzed in mestizo Mexicans according to the Chakraborty selection criteria for the proportion of the SNV minor allele, for which 269 DNA samples from healthy individuals were included[4]. Detection of SNV has been made through PCR-RFLP *(Polymerase Chain Reaction-Restriction Fragment Length Polymorphism)* and isoelectric focusing electrophoresis by SSCP *(Single-Strand Chain Polymorphism)*, as previously reported (Fig. 1B)[5], and it was corroborated by automated sequencing. Thus, the distribution of alleles in the analyzed population shows the following relative frequencies: ancestral allele A 0.7918 (n = 426) and 0.2081 (n = 112) for allele C. Genotypes: homozygous A 0.639 (n = 172), heterozygous 0.304 (n = 82) and homozygous C 0.055 (n = 15). The distribution does not present significant differences with the expected frequencies (χ^2 = 1,528; p = 0.216), so the variant is in Hardy Weinberg equilibrium (Table 1). The observed heterozygosity was 0.82, the expected 0.88 and the maximum 0.5 (p = 0.71).

In conclusion, this report is the first regional and national study of the SNV rs11212617 *ATM* gene in mixed-race Mexicans, and creates a benchmark for future association studies in metabolic, vascular, oncological, and infectious diseases in the Mexican population.

Acknowledgments

In memory of Dr. José Sánchez Corona, pioneer and leader of medical and molecular genetics in Mexico, our thanks for the support in carrying out the work. The authors thank CONACYT for the CONACYT 827836 scholarship to carry out Postgraduate studies in favor of Claudia B. Montaño-Montejano.

***Correspondence:**
Sergio A. Ramírez-García
E-mail: sergioNABMSP@gmail.com

Date of reception: 02-07-2021
Date of acceptance: 29-09-2021
DOI: 10.24875/CIRUE.M21000316

Cir Cir (Eng). 2022;90(2):273-275
Contents available at PubMed
www.cirugiaycirujanos.com

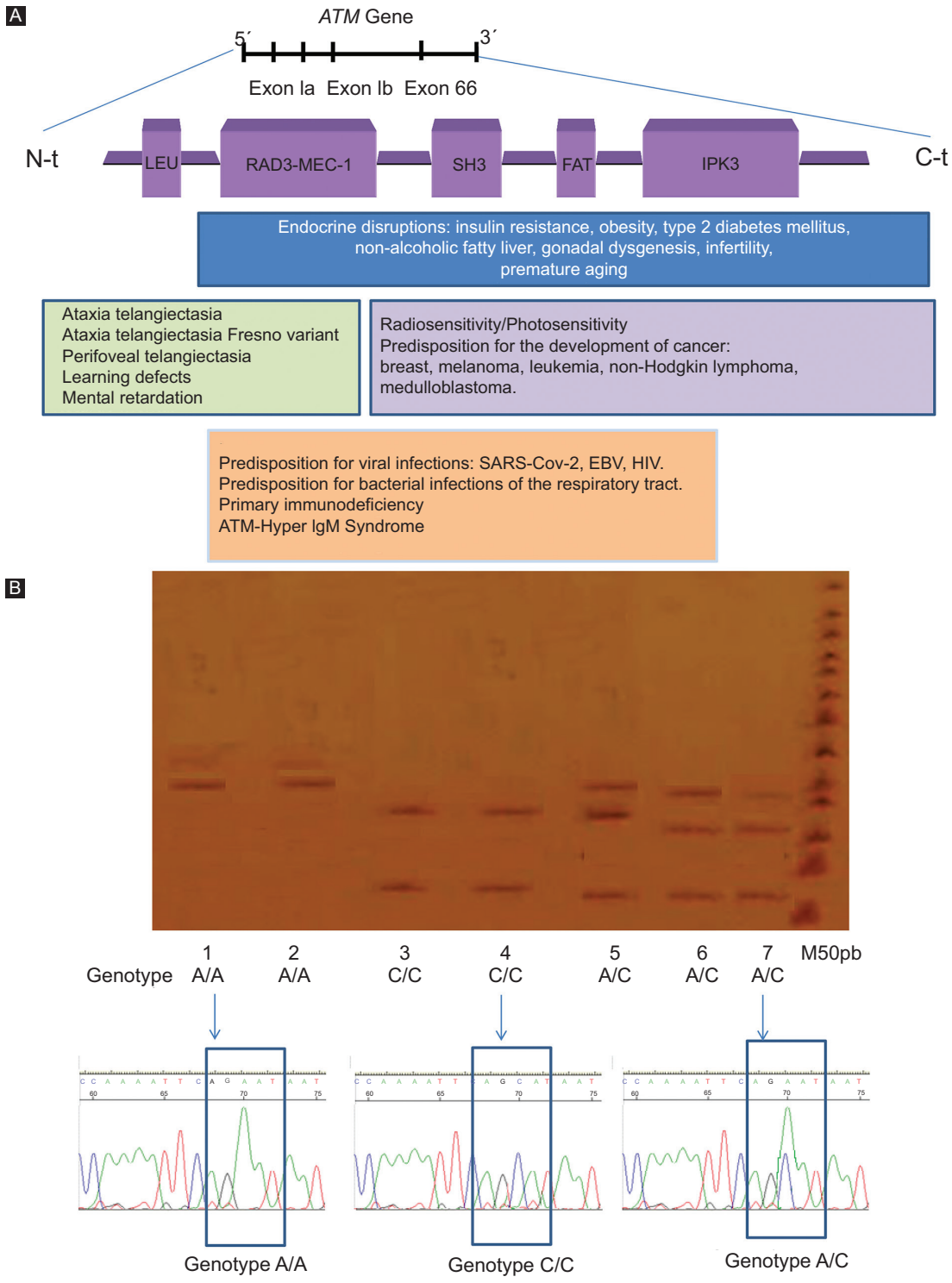

Figure 1. A: *clinical spectrum of the variome and proteome of the ataxia telangiectasia gene (ATM).* **B:** *homogeneous PAGE20% electrophoresis and electropherogram of Sanger sequencing of the PCR-FRLP products of SNV rs11212617. The conditions for PCR amplification and enzymatic digestion with HpyCH4III were as previously described[5]. The electrophoresis of the PCR digestion products was run using the PhastSystem™ equipment (Amersham Biosciences) for 1.5 hours. Phase 1.1 10 Vh, 10 mA, 2.0 W, 5 °C, 55 Vh. Phase 1.2 150 V, 1 mA, 2.5 W, 5 °C, 10 Vh, and differed by sizes and cutouts. The 209 bp fragment generates two products, one of 153 bp and the other of 56 bp. The 209 bp band corresponds to the homozygous genotype (A/A) (lanes 1 and 2 of the gel). When three bands are present, 209, 153 and 56 bp, respectively, it corresponds to the heterozygous genotype (A/C) (lanes 5, 6 and 7 of the gel). Finally, if there are two bands, 153 and 56 bp, it corresponds to the homozygous genotype (C/C) (lanes 3 and 4 of the gel), which is confirmed by Sanger sequencing.*

Table 1. Global allele and genotypic frequencies of the SNV rs11212617 *ATM gene*

Population	Allele frequency			Genotype frequency				
	No. subjects	A	C.	AA	AC	CC	$\chi 2$	p
Current study	269	**0.7918**	0.2081	0.639	0.304	0.055	1.5280	0.2164
South Indian*	112	0.65	0.35	0.39	0.52	0.09	2.2219	0.1361
Caucasians*	113	0.54	0.47	0.27	0.54	0.19	0.8784	0.3486
China*	43	0.31	0.69	0.09	0.44	0.47	0.0284	0.8662
Japan*	86	0.38	0.67	0.19	0.39	0.42	2.3156	0.1281
Africa*	113	0.19	0.81	0.02	0.34	0.65	1.3993	2.2368
Africa								
GnomAD	8682	0.2752	0.7248	NR	NR	NR	NR	NR
Asia								
1000 genomes/South Asia	978	0.627	0.373	NR	NR	NR	NR	NR
gnomAD/East Asia	1552	0.3595	0.6405	NR	NR	NR	NR	NR
Europe								
ALPHA	82410	0.5793	0.4206	NR	NR	NR	NR	NR
GnomAD	18866	0.5760	0.4239	NR	NR	NR	NR	NR
America								
PAGE/Native American	1260	0.523	0.477	NR	NR	NR	NR	NR
PAGE/Native Hawaiian	4534	0.400	0.599	NR	NR	NR	NR	NR
PAGE/Africa-American	32516	0.277	0.722	NR	NR	NR	NR	NR
PAGE/Mexican ancestry	10808	**0.621**	0.378	NR	NR	NR	NR	NR
PAGE/Puerto Rico	7918	0.520	0.479	NR	NR	NR	NR	NR
PAGE/Cuba	4230	0.557	0.442	NR	NR	NR	NR	NR
PAGE/Dominican Republic	3828	0.448	0.551	NR	NR	NR	NR	NR

Note: dbSNP 2021.
*Data taken from Vilvanathan S et al.[6]
ALPHA: aggregate frequencies of alleles and genotypes; gnomAD: genome aggregation database; NR: data not reported; PAGE: Population Architecture Study using Genomics and Epidemiology; SGDP_PRJ: Simons Genome Diversity Project.

Funding

COECYTJAL Fund 2013 and POA-2020 Doctoral Program in Human Genetics, University of Guadalajara, in favor of Diana García-Cruz. PRODEP-SEP-Ca Strengthening Program-2014, in favor of Sergio A. Ramirez-Garcia.

Conflicts of interest

There are no conflicts of interest on the part of the authors.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were carried out on humans or animals for this research.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

References

1. Saviozzi S, Saluto A, Taylor A, Last F, Rebini F, Paradisio MC et al. A late onset variant of ataxia telangiectasia with a compound heterozygous genotype, A8030G/7481insA. J Med Genet. 2002;39:57-61.
2. Ahmadi A, Behmanesh M, Boroumand MA, Boroumand MA, Tavallaei M. Up-regulation of MSH2, XRCC1 and ATM genes in patients with type 2 diabetes and coronary artery disease. Diabetes Res Clin Pract. 2015;109:500-6.
3. Calderón ZF, Ocampo GG, López-Márquez FC, Recio-Vega R, Serrano-Gallardo LB, Ruiz-Flores P. ATM polymorphisms IVS24-9delT, IVS38-8T>C, and 5557G>A in Mexican women with familial and/or early-onset breast cancer. Mexican Public Health 2014;56:206-12.
4. Chakraborty R, Zhong Y. Statistical power of an exact test of Hardy-Weinberg proportions of genotipic data at a multiallelic locus. Hum Heredity. 1994;44:1-9.
5. Shokri F, Ghaedi H, Ghafouri FS, Movofagh A, Abediankenari S, Mahrooz A et al. Impact of ATM and SLC22A1 polymorphisms on therapeutic response to metformin in Iranian diabetic patients. Int J Mol Cell Med. 2016;5:1-7.
6. Vilvanathan S, Gurusamy U, Mukta V. Allele and genotype frequency of a genetic variant in ataxia telangiectasia mutated gene affecting glycemic response to metformin in South Indian population. Indian J Endocrinol Metab. 2014;18:850-4.