ISSN (electrónico): 1699-5198 - ISSN (papel): 0212-1611 - CODEN NUHOEQ S.V.R. 318

Nutrición Hospitalaria

DOI: http://dx.doi.org/10.20960/nh.03865

Carta al Director

DISCORDANCE BETWEEN ALLELIC AND GENOTYPE FREQUENCIES FOR CD36 rs3211938 BETWEEN MEXICAN MESTIZO SAMPLES: SAMPLE BIAS, GENOTYPING ERROR, OR MICROEVOLUTION?

Dear Editor,

The article published by Martín-Márquez et al. (1) shows evidence on the association between the GT CD36 rs3211938 genotype and high levels of glucose, ox-LDL, HDL-cholesterol, and IR, and increased BMI in Mexican mestizo T2DM (type-2 diabetes *mellitus)* patients from western Mexico. The criteria used to define "mestizo" (2) allow further research to survey those statistical associations in other Latin American mestizo populations.

The cited work did not address the Hardy-Weinberg (H-W) equilibrium to contrast the concordance between allelic and genotype frequencies under the null hypothesis of absence of evolutionary factors operating on populations. The H-W test has been used to detect sampling bias (3) and genotyping errors (4). In addition, the allelic and genotype frequencies were not contrasted with data reported by other studies.

We collected information on the variation of CD36 rs3211938 from the public database 1000 Genomes (1 kg) (5; www.internationalgenome.org) and the allelic frequencies are different from those reported by Martín-Marquez et al. In the four Latin American population samples contained in 1 kg (n = 692 individuals), including Mexico, Colombia, Peru, and Puerto Rico, only one allele G, from a Peruvian individual, was found. Thus, the frequency of the allele G is 0 % in Mexico and 0.0007 % in the pooled Latin American samples from 1 kg. In Europe, East Asia, and South Asia that frequency is 0 % both in 1 kg and the ALFRED database (6; https://alfred.med.yale.edu/alfred). In the article here discussed, the frequencies of G were 10.34 % and 25.44 % in the NT2DM (non-type-2 diabetes *mellitus)* and T2DM samples, respectively.

We analyzed genic differentiation using the exact G test implemented in Popgene (7). Significant differentiation was found between the three pairwise comparisons: NT2DM *vs.* TD2M, p = 0.02204; NT2DM *vs.* Mexico from 1 kg (MXL), p = 0.00013; NT2DM *vs.* MXL, p = 0. Genotypic differentiation showed the same pattern: NT2DM *vs.* TD2M, p = 0.01100; NT2DM *vs.* MXL, p = 0.00010; NT2DM *vs.* MXL, p = 0.

Finally, the H-W equilibrium is rejected in the T2DM sample, showing heterozygote excess (Table I). In summary, our find-

Table I. Hardy-Weinberg analysis for CD36 rs3211938 in Mexican mestizo populations

Sample	Observed genotype frequencies (%)			Allele frequencies (%)		Expected genotype frequencies (%)			P_{chi}	P_{exact}
	T/T	T/G	G/G	T	G	T/T	T/G	G/G		
NT2DM	46 (79.30)	12 (20.70)	0 (0)	104 (89.66)	12 (10.34)	46.62 (80.38)	10.76 (18.55)	0.62 (1.07)	0.680	1
T2DM	28 (49.10)	29 (50.90)	(0 (0)	85 (74.56)	29 (25.44)	31.69 (55.59)	21.62 (37.93)	3.69 (6.47)	0.036*	0.0497*
MXL	64 (100)	0 (0)	0 (0)	128 (100)	0 (0)	64 (100)	0 (0)	0 (0)	-	-

NT2DM: non-type-2 diabetes mellitus *sample; T2DM: type-2 diabetes* mellitus *sample; *p value < 0.05; Pchi = p value for the Chi2 test; Pexact = p value for the Fischer exact test implemented in Genpop.*

Conflicts of interest: the authors have no conflicts of interest to declare.

ings suggest a sample bias or genotyping error. An alternative, less plausible hypothesis is the occurrence of micro-evolutionary processes on CD36 rs3211938 in western Mexico, increasing the frequency of allele G and heterozygosity. Further research is needed in order to understand the discordance between allelic and genotype frequencies observed in the article by Martín-Márquez et al., the differences among datasets, and their implications on the role of CD36 rs3211938 on the metabolic profile of Mexican mestizo populations.

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