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Incorporación de marcadores genéticos poblacionales en paneles de detección temprana de EHGNA: un complemento a los enfoques basados en biomarcadores

Sergio Flores-Carrasco[1], Ángel Roco-Videla[2], Román Montaña[3]

[1]Universidad Arturo Prat. Santiago, Chile. [2]Facultad de Ingeniería. Universidad Católica de la Santísima Concepción. Concepción, Chile. [3]Escuela de Enfermería. Facultad de Ciencias de la Salud. Universidad Católica Silva Henríquez. Santiago, Chile

Correspondence: Sergio V. Flores
e-mail: seflores_@unap.cl

Dear Editor,

The study by Santos et al. on oxidative biomarkers associated with non-alcoholic fatty liver disease (NAFLD) in children makes a relevant contribution to the clinical and metabolic understanding of this condition (1). However, the genetic dimension of the studied phenotype was not explored in depth. We propose complementing that approach with five extensively replicated SNPs that show promise for inclusion in early genetic detection panels for NAFLD, all genotyped in 3009 samples

according to Ensembl data. For each variant, we examine population variability using data from the 1000 Genomes Project (2) and Ensembl (3), with emphasis on Latin American and European populations, which we consider relevant for regional applicability.

The SNP rs738409 (PNPLA3), a missense variant (I148M), is the most robustly associated marker for NAFLD (4). This variant disrupts lipid remodeling in hepatocytes by impairing triglyceride hydrolysis, leading to hepatic fat accumulation. It affects 2 transcripts, is associated with 140 phenotypes, and has been cited in 1562 studies. The risk allele G shows high global variability (8.6-71.8 %), with moderate heterogeneity in Europe (17.2 % in Finland (FIN) to 25.7 % in Spain (IBS)) and high in Latin America (31.7 % in Puerto Rico (PUR) to 71.8 % in Lima, Peru (PEL)).

The SNP rs58542926 (TM6SF2), also missense (E167K), impairs secretion of triglyceride-rich lipoproteins from the liver, thereby promoting hepatic fat retention and contributing to NAFLD susceptibility (5). It affects 2 transcripts, is associated with 436 phenotypes, and has been cited in 647 studies. The risk allele T ranges globally from 2.3 % to 9.1 %. In Europe, it shows moderate heterogeneity (4.7 % in Italy (TSI) to 9.1 % in Utah residents with Northern and Western European ancestry (CEU)); similarly, in Latin America (4.7 % in PEL to 9.1 % in PUR).

The SNP rs1260326 (GCKR), a missense variant (P446L), affects 1 transcript, is associated with 1376 phenotypes, and has been cited in 956 studies. Functionally, it modulates glucose and lipid metabolism by reducing inhibition of glucokinase, thereby promoting de novo lipogenesis in the liver. The risk allele T reaches frequencies of up to 59.2 % in Han Chinese in Beijing (CHB) and shows moderate heterogeneity in Europe (30.3 % in FIN to 50.9 % in TSI) and high in Latin America (32.4 % in PEL to 43.6 % in Colombia (CLM)).

The SNP rs641738 (MBOAT7), also missense, affects 2 transcripts, is associated with 37 phenotypes, and has been cited in 317 studies. It

likely alters phospholipid remodeling in cell membranes, which may contribute to hepatic inflammation and fibrosis. The T allele shows global frequencies ranging from 12 % to 62.6 %. In Europe, heterogeneity is moderate (41.6 % in IBS to 46.3 % in TSI), while in Latin America it is high (24.7 % in PEL to 43.3 % in PUR).

Finally, rs72613567 (HSD17B13), an insertion with protective effect, affects 2 transcripts, is associated with 12 phenotypes, and has been cited in 232 studies. This loss-of-function variant truncates an enzyme involved in retinol metabolism and has been associated with reduced liver injury and inflammation. The AA allele shows high global variability (1.4 % in Yoruba in Ibadan, Nigeria (YRI) to 39.8 % in Chinese Dai in Xishuangbanna (CDX)), low heterogeneity in Europe (22.2 % in FIN to 26.4 % in Great Britain (GBR)), and high in Latin America (5.3 % in PEL to 24.0 % in PUR).

We consider that incorporating these polymorphisms into risk panels could enhance early detection and stratification of NAFLD patients. However, their application should be calibrated according to local frequencies and the genetic structure of each population.

Conflict of interest: The authors declare no conflict of interest.

Artificial intelligence: The authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

REFERENCES

1. Santos PQD, Rocha R, Daltro CHDC, Andrade SCS, Cotrim HP. Serum glutathione peroxidase is associated with nonalcoholic fatty liver disease in children and adolescents. Nutr Hosp 2024;41(6):1165-71. DOI: 10.20960/nh.05105
2. 1000 Genomes Project Consortium; Auton A, Brooks LD, Durbin RM, Garrison EP, Kang HM, et al. A global reference for human genetic variation. Nature 2015;526(7571):68-74. DOI: 10.1038/nature15393
3. Martin FJ, Amode MR, Aneja A, Austine-Orimoloye O, Azov AG, Barnes I, et al. Ensembl 2023. Nucleic Acids Res 2023;51(D1):D933-41. DOI: 10.1093/nar/gkac958
4. Romeo S, Kozlitina J, Xing C, Pertsemlidis A, Cox D, Pennacchio LA, et al. Genetic variation in PNPLA3 confers susceptibility to nonalcoholic fatty liver disease. Nat Genet 2008;40(12):1461-5. DOI: 10.1038/ng.257
5. Kozlitina J, Smagris E, Stender S, Nordestgaard BG, Zhou H, Tybjærg-Hansen A, et al. Exome-wide association study identifies TM6SF2 variant that confers susceptibility to nonalcoholic fatty liver disease. Nat Genet 2014;46(4):352-6. DOI: 10.1038/ng.2901