Name: José-Jaime Martínez-Magaña Email: jose.martinez-magana@yale.edu
PI Name: Janitza Montalvo-Ortiz PI Email: janitza.montalvo-ortiz@yale.edu

Local Ancestry-Aware Meta-Analysis of Genome-Wide Association Studies for Substance Use Traits in Latin American Populations

José Jaime Martínez-Magaña[1], Elizabeth Atkinson[2], Paola Giusti-Rodríguez[3], Marcos Leite Santoro[4], Sylvia Wassertheil-Smoller[5], Martha Daviglus[6], Krista M Perreira[7], Humberto Nicolini[8], Alexandre C Pereira[9], Sintia Iole Belangero[10], Mariana Moysés-Oliveira[11], Katherine L Tucker[12], Jose Ordovas[13], Jorge Ameth Villatoro-Velazquez[14], Maria Elena Medina-Mora[15], Luis Augusto Rohde[16], Rodrigo Affonseca Bressan[17], Euripedes Constantino Miguel[18], Pedro Mario Pan[19], Giovanni Abrahao Salum[20], Priscila F. Tempaku[11], Monica L. Andersen[11], Sergio Tufik[11], Latin American Genomics Consortium, Janitza L. Montalvo-Ortiz[2]

[1]Department of Psychiatry, Yale School of Medicine, New Haven, CT
[2]Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX
[3]Department of Psychiatry, University of Florida College of Medicine, Gainesville, FL
[4]Laboratório de Neurociências Integrativas (LiNC - UNIFESP), São Paulo, Brazil
[5]Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY
[6]Institute for Minority Health Research, College of Medicine University of Illinois at Chicago, IL
[7]Department of Social Medicine, University of North Carolina School of Medicine, Chapel Hill, NC
[8]Laboratorio de Enfermedades Psiquiátricas, Neurodegenerativas y Adicciones, Instituto Nacional de Medicina Genómica, Secretaría de Salud, Ciudad de Mexico, México
[9]Laboratory of Genetics and Molecular Cardiology, Heart Institute (Incor), University of São Paulo Medical School, São Paulo, Brazil
[10]Genetics Division of Department of Morphology and Genetics of Universidade Federal de São Paulo (UNIFESP), Brazil
[11]Sleep Institute, Associação Fundo de Incentivo à Pesquisa, São Paulo, Brazil.
[12]Biomedical and Nutritional Sciences, Zuckerberg College of Health Sciences, University of Massachusetts Lowell
[13]Nutrition and Genetics, Gerald J. and Dorothy R. Friedman School of Nutrition Sciences and Policy, Tufts University
[14]Dirección de Investigaciones Epidemiológicas y Psicosociales, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz (INPRFM), Ciudad de México, México
[15]Faculty of Psychology, Universidad Nacional Autónoma de México, Circuito Ciudad Universitaria 04510, Coyoacan, Mexico City, Mexico
[16]National Institute of Developmental Psychiatry, CNPq, São Paulo, Brazil
[17]Interdisciplinary Laboratory of Clinical Neurosciences (LiNC), Department of Psychiatry, Escola Paulista de Medicina, Universidade Federal de São Paulo, Rua Major Maragliano, 241, São Paulo, SP, Brazil
[18]Institute of Psychiatry (IPQ), Universidade de Sao Paulo, Rua Dr. Ovidio Pires de Campos, 785, Sao Paulo, SP CEP 05403-903, Brazil
[19]Laboratory of Integrative Neuroscience (LINC)Universidade Federal de São Paulo, Brazil
[20]National Institute of Developmental Psychiatry for Children and Adolescents (INPD), São Paulo, Brazil

Genome-wide association studies (GWAS) have made substantial progress in understanding the genetic liability of alcohol consumption. However, efforts modeling ancestry-specific effects in GWAS studies in admixed populations, like the Latin American (LA) population, has been minimal. LAs are highly admixed with a mosaic of different proportions of European, Amerindigenous (AMR), and African (AFR) descent, which could be difficult to model in GWAS analysis. However, innovative approaches have been recently developed using local ancestry information. Here, we analyzed local ancestry-specific effects for alcohol consumption in admixed LA populations. We conducted a meta-analysis of local ancestry-aware GWAS of alcohol consumption in 11,655 individuals of LA descent. We identified associations with rs1874323 (p-value = 2.5760e-08) in the MAGI1 gene, rs6833926 (p-value = 3.0010e-08) in the ARAP2 gene, two in the SLIT3 gene (rs73805262, p-value = 9.9540e-09; rs115143510; z = p-value = 1.2250e-08), and one intergenic variant (rs3929849, p-value = 2.3930e-09) in those individuals where the section of the genome comes from AFR descent. We also identified intergenic variants in those where the region is of AMR descent (rs4130378, p-value = 9.673e-09; rs536315876 p-value = 4.3640e-09; rs115675116, p-value = 4.3190e-09). Our study significantly contributes to the ongoing efforts to understand the ancestry-specific genetic architecture of alcohol consumption in Latin American populations. The novel genetic associations identified in highly admixed Latin American individuals highlight the importance of conducting ancestry-aware GWAS to identify potential ancestry-specific loci.