Genome-wide association study identifying novel variant for fasting insulin and allelic heterogeneity in known glycemic loci in Chilean adolescents: The Santiago Longitudinal Study

Por: Buchanan, VL (Buchanan, Victoria L.)[1]; Wang, YJ (Wang, Yujie)[1]; Blanco, E (Blanco, Estela)[2]; Graff, M (Graff, Mariaelisa)[1]; Albala, C (Albala, Cecilia)[3]; Burrows, R (Burrows, Raquel)[3]; Santos, JL (Santos, Jose L.)[4]; Angel, B (Angel, Barbara)[3]; Lozoff, B (Lozoff, Betsy)[5]; Voruganti, VS (Voruganti, Venkata Saroja)[6,7]; Guo, XQ (Guo, Xiuqing)[8]; Taylor, KD (Taylor, Kent D.)[8]; Chen, YDI (Chen, Yii-Der Ida)[8]; Yao, J (Yao, Jie)[8]; Tan, JY (Tan, Jingyi)[8]; Downie, C (Downie, Carolina)[1]; Highland, HM (Highland, Heather M.)[1]; Justice, AE (Justice, Anne E.)[1,9]; Gahagan, S (Gahagan, Sheila)[2]; North, KE (North, Kari E.)[1] ...Menos

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Abstract

Background The genetic underpinnings of glycemic traits have been understudied in adolescent and Hispanic/Latino (H/L) populations in comparison to adults and populations of European ancestry.

Objective To identify genetic factors underlying glycemic traits in an adolescent H/L population.

Methods We conducted a genome-wide association study (GWAS) of fasting glucose (FG) and fasting insulin (FI) in H/L adolescents from the Santiago Longitudinal Study.

Results We identified one novel variant positioned in the CSMD1 gene on chromosome 8 (rs77465890, effect allele frequency = 0.10) that was associated with FI (beta = -0.299, SE = 0.054, p = 2.72x10(-8)) and was only slightly attenuated after adjusting for body mass index z-scores (beta = -0.252, SE = 0.047, p = 1.03x10(-7)). We demonstrated directionally consistent, but not statistically significant results in African and Hispanic adults of the Population Architecture Using Genomics and Epidemiology Consortium. We also identified secondary signals for two FG loci after conditioning on known variants, which demonstrate allelic heterogeneity in well-known glucose loci.

Conclusion Our results exemplify the importance of including populations with diverse ancestral origin and adolescent participants in GWAS of glycemic traits to uncover novel risk loci and expand our understanding of disease aetiology.

Palabras clave

Palabras clave de autor:adolescent; glucose; GWAS; insulin
KeyWords Plus:IRON-DEFICIENCY; GENETIC-LOCI; TRAITS; METAANALYSIS; ARCHITECTURE; IMPUTATION; INSIGHT; REGIONS; HEAD; BIAS

Información del autor

Dirección para petición de copias:
University of North Carolina University of North Carolina Chapel Hill Univ N Carolina, Dept Epidemiol, 123 W Franklin St,Bldg C,Suite 4217, Chapel Hill, NC 27599 USA.
Dirección correspondiente: Buchanan, VL (autor correspondiente)

Univ N Carolina, Dept Epidemiol, 123 W Franklin St,Bldg C,Suite 4217, Chapel Hill, NC 27599 USA.

Direcciones:

[1] Univ N Carolina, Dept Epidemiol, 123 W Franklin St,Bldg C,Suite 4217, Chapel Hill, NC 27599 USA
[2] Univ Calif San Diego, Div Acad Gen Pediat Child Dev & Community Hlth, La Jolla, CA 92093 USA
[3] Univ Chile, Inst Nutr & Food Technol, Dept Publ Hlth Nutr, Santiago, Chile
[4] Pontificia Univ Catolica Chile, Sch Med, Dept Nutr Diabet & Metab, Santiago, Chile
[5] Univ Michigan, Dept Pediat, Ann Arbor, MI 48109 USA
[6] Univ N Carolina, Dept Nutr, Kannapolis, NC USA
[7] Univ N Carolina, UNC Nutr Res Inst, Kannapolis, NC USA
[8] Harbor UCLA Med Ctr, Lundquist Inst, Dept Pediat, Inst Translat Genom & Populat Sci, Torrance, CA USA
[9] Geisinger, Dept Populat Hlth Sci, Danville, PA USA

Direcciones de correo electrónico:vicbucha@live.unc.edu

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