Published in final edited form as:

J Med Genet. 2012 August ; 49(8): 545–546. doi:10.1136/jmedgenet-2012-100966.

Translational Genomic Medicine: Common Metabolic Traits and Ancestral Components of Mexican Americans

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Obesity, type 2 diabetes, hyperlipidemia, hypertension, and liver disease, are common metabolic disorders in Mexican Americans, the largest minority population in the US. Mexican Americans are an admixed population with European, Amerindian, and African ancestries. Association of ancestral components and these common metabolic disorders is a compelling issue because it may provide significant insight into personalized medicine based on quantitative ethnic information.

It has not been possible to get precise ancestral information for Mexican Americans using questionnaires. Indeed, siblings in the same family may give different ethnic information. Thanks to the impressive progress of human genomics research, genetic ancestral analysis using DNA polymorphism markers offers the opportunity to acquire accurate ancestry/ethnicity data in admixed human populations(1-2). Quantitative ancestral information can be readily acquired by genotyping a set of ancestry informative markers (AIMs) across the human genome. The AIMs are comprised of a number of autosomal single nucleotide polymorphisms (SNP) with substantially different allele frequencies in different ancestral populations. We used this approach to investigate the ancestral components of our community based Cameron County Hispanic Cohort (CCHC) consisting of Mexican Americans with high rates of obesity, type 2 diabetes, hyperlipidemia, hypertension, and liver disease (3). With these data we then sought correlations between ancestral components and common metabolic traits.

The CCHC is a random sample from a Mexican American population recruited in a small US city, Brownsville, Cameron County in South Texas. This study investigated 1551 CCHC individuals, and sampling bias was corrected based on Census 2000 data to account for age, gender, tract/block and household clustering (Table 1). By genotyping a set of AIMs (including 103 SNPs) specifically designed for Mexican Americans by Kosoy et al.(1), ancestral components of each CCHC participant were quantified using a maximum likelihood algorithm implemented in the Admixture software(4). Distribution of genotype frequencies of the 103 AIMs is shown in Supplementary Figure 1. Ancestral analysis showed the CCHC participants had predominantly one-dimensional admixture of European

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Conflict of Interest statement: None declared.

Contributors Hui-Qi Qu conceived the study, researched the data, and wrote the manuscript. Quan Li researched data, reviewed/edited the manuscript. Yang Lu performed the experiments. Susan P Fisher-Hoch and Joseph B McCormick developed the CCHC, and wrote the manuscript.

and Amerindian ancestries. Correlation analysis between percentages (%) of ancestry components and common metabolic traits, including body mass index (BMI), serum lipids, blood pressure, liver transaminases, and type 2 diabetes diagnosis, was examined using the IBM SPSS Statistics Version 19 software (SPSS Inc, Chicago, IL). Type 2 diabetes was defined using the 2010 Clinical Practice Recommendations of the American Diabetes Association (ADA)(5).

Correlation tests showed that Amerindian ancestry was associated with higher serum triglyceride and non-HDL cholesterol in males, lower systolic blood pressure in females, lower serum HDL-cholesterol and higher serum ALT levels in both genders. In contrast, no association between ancestral component and BMI or type 2 diabetes diagnosis was found (Table 2).

The associations of Amerindian ancestry and higher serum triglyceride levels/ higher serum ALT levels explain previous observations that Mexican Americans have higher triglycerides(6) and greater risk of developing liver disease(7). That the ancestral effect on triglycerides is seen in males, suggests that gender related factors, including both biology and life style may be important and warrant further study. Despite the association of Amerindian ancestry with lower serum cholesterol levels, the overall pattern is not optimal, since the beneficial serum HDL cholesterol (HDL-c) is also lower in people with a larger contribution of Amerindian ancestry. The association of Amerindian ancestry and lower systolic BP may explain the lower prevalence of hypertension in female Mexican Americans(8-9), suggesting greater focus should be placed on male Mexican Americans for control of hypertension. Interestingly, this study shows that Amerindian ancestral effect on BMI and diabetes risk is less obvious than its effect on metabolic traits as serum lipids, ALT, and blood pressure. The strength of this study on ancestral effects was that it was performed within a population with homogenous Hispanic culture and life-styles, thus largely removing these confounding effects. A critical mechanism underlying the Amerindian ancestral effects may be related to lower insulin sensitivity, which has been demonstrated in our study(10).

Interestingly, in spite of the high prevalence (~32%) of type 2 diabetes in this Mexican American population, our study didn't identify any association between ancestral component and type 2 diabetes. This finding suggests genetic or racial factors may not explain the high risk of type 2 diabetes in this population, which may overthrow the traditional pessimistic idea about genetic susceptibility of type 2 diabetes in Mexican Americans, thus encourage active diabetes control.

The observations in this report may serve as a paradigm of translational human genomics research to serve prevention/intervention of common diseases in Mexican Americans. This approach will be getting more practical with the progress of genotyping technology and the price of SNP genotyping going down. Clinical practice of chronic diseases and public health in admixed populations may be tremendously improved by quantitative ethnic information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank our cohort recruitment team, particularly Rocio Uribe, Elizabeth Braunstein and Julie Ramirez and Dr. Anne Rentfro; our laboratory staff, particularly Marcela Montemayor; and Christina Villarreal for administrative support. We thank Valley Baptist Medical Center, Brownsville for providing us space for our Center for Clinical

and Translational Science Clinical Research Unit. H.Q.Q. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

This work was supported by MD000170 P20 funded from the National Center on Minority Health and Health Disparities (NCMHD), and the Centers for Translational Science Award 1U54RR023417-01 from the National Center for Research Resources (NCRR). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. H.Q.Q is supported by intramural funding from the University of Texas School of Public Health.

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Table 1
Description of the study participants (Weighted on Census data)

Characteristics	Males(n=723)	Females (n=828)
Age (yr)	46.2±18.9	47.7±18.6
BMI	30.5±6.5	30.9±7.4
Serum triglyceride (mg/dL)	190.8±221.9	160.3±122.4
High-density lipoprotein (HDL) cholesterol (mg/dL)	43.6±10.1	49.7±11.9
Non-HDL cholesterol (mg/dL)	145.9±40.2	138.4±39.0
Systolic blood pressure (mmHg)	119.8±15.0	116.5±18.5
Diastolic blood pressure (mmHg)	73.6±10.5	69.4±9.8
ALT (U/L)	48.5±27.2	38.0±15.3
AST (U/L)	37.6±18.1	32.9±14.3
Diabetes diagnosis (ADA 2010 ^a , non-diabetes/pre-diabetes/diabetes)	248/244/231	353/204/271

^aThe 2010 Clinical Practice Recommendations of the American Diabetes Association (ADA)(4).

Table 2
Correlation of Amerindian ancestral component and metabolic disorders in both genders

Symptoms	Males	Females
	Pearson's r (<i>P</i> values)	Pearson's r (<i>P</i> values)
BMI	0.061 (<i>P</i> =0.106)	0.015 (<i>P</i> =0.673)
Serum triglyceride (mg/dL)	0.080 (<i>P</i> =0.033) *	0.047 (<i>P</i> =0.177)
High-density lipoprotein (HDL) cholesterol (mg/dL)	-0.108 (<i>P</i> =0.004) **	-0.099 (<i>P</i> =0.004) **
Non-HDL cholesterol (mg/dL)	-0.081 (<i>P</i> =0.029) *	-0.033 (<i>P</i> =0.347)
Systolic blood pressure (mmHg)	-0.041 (<i>P</i> =0.269)	-0.119 (<i>P</i> =5.81×10 ⁴) **
Diastolic blood pressure (mmHg)	0.021 (<i>P</i> =0.576)	-0.020 (<i>P</i> =0.564)
ALT (U/L)	0.100 (<i>P</i> =0.007) **	0.110 (<i>P</i> =0.002) **
AST (U/L)	0.092 (<i>P</i> =0.013) *	0.039 (<i>P</i> =0.259)
Diabetes diagnosis (ADA 2010)	-0.005 (<i>P</i> =0.900)	0.004 (<i>P</i> =0.908)

* *P*<0.05;

** *P*<0.01.