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Genetic ancestry in relation to the metabolic response to a U.S. versus traditional Mexican diet: a randomized crossover feeding trial among women of Mexican descent

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Abstract

Background—Certain populations with a large proportion of Indigenous American (IA) genetic ancestry may be evolutionarily adapted to traditional diets high in legumes and complex carbohydrates, and may have a detrimental metabolic response to U.S. diets high in refined carbohydrates and added sugars. We tested whether IA ancestry modified the metabolic response to a U.S. versus traditional Mexican diet in a controlled dietary intervention.

Methods—First and second generation Mexican immigrant women (n=53) completed a randomized crossover feeding trial testing the effects of a U.S. versus traditional Mexican diet. The metabolic response to the diets was measured by fasting serum concentrations of glucose, insulin, IGF-1, IGFBP-3, adiponectin, CRP, IL-6, and computed $HOMA_{IR}$. Blood collected at baseline was used for genotyping and estimation of African, European, and IA ancestries with the use of 214 Ancestry Informative Markers.

Results—The genetic ancestral background was 56% IA, 38% European, and 6% African. Women in the highest IA ancestry tertile (>62%) were shorter in height, less educated and less acculturated to the U.S. lifestyle, and tended to have higher waist-to-hip ratio compared to women

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Author contributions: C.S.C., M.L.N., and J.W.L.; K.L.B., L.L., and A.V. designed the experimental diets; K.L.B., L.L., X.S. implemented the study protocol; C.S.C., M.S.T., J.D.T., and C.Y.W analyzed data; M.S.T. wrote the paper; M.S.T., C.S.C., and M.L.N. had primary responsibility for final content; and all co-authors critically reviewed and revised the manuscript.

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The trial was registered at clinicaltrials.gov (identifier: NCT01369173)

in the middle and lowest IA ancestry tertiles, respectively. Compared to the U.S. diet, the traditional Mexican diet tended to reduce glucose, insulin, IGF-1, IGFBP-3, and $HOMA_{IR}$ among women in the middle IA ancestry group (IA ancestry ≤45–62%); while having no effect on biomarkers related to inflammation.

Conclusions—We observed modest interactions between IA ancestry and the metabolic response to a U.S. versus traditional Mexican diet among Mexican immigrant women.

Keywords

Ancestry Informative Markers; Controlled Feeding Trial; Genetic Ancestry; Mexican immigrants; Traditional Mexican diet; U.S. diet

INTRODUCTION

As Mexican immigrants acculturate to the U.S. lifestyle, they tend to transition from consuming traditional Mexican foods to adopting U.S. dietary patterns (1, 2). U.S. diets commonly consumed by the majority of the population are usually high in processed foods, refined carbohydrates, added sugars, and low in plant foods; while traditional Mexican diets are usually high in fruits and vegetables and complex carbohydrates and legumes rich in dietary fiber (2–5). According to the thrifty gene hypothesis (6), populations with a large proportion of Indigenous American (IA) genetic ancestry, may be evolutionarily adapted to diets high in legumes and complex carbohydrates. Consuming an inexpensive and readily available U.S. diet high in processed foods, refined carbohydrates, and added sugars may lead to a detrimental metabolic and/or inflammatory response placing these groups at a disproportionately higher risk of metabolic disease (7–9).

The distribution of genetic ancestry among Mexican immigrants is widely variable, ranging from individuals who are indistinguishable from European ancestry populations to individuals who are indistinguishable from IA populations (e.g., Mayan or Pima) (9–13). In this regard, one of the key questions is the degree to which genetics and environment (e.g., socioeconomic status (SES), diet, and physical activity) contribute to the risk of metabolic disease. Among Mexican immigrants, greater adherence to a U.S. diet has been associated with increased risk of metabolic disease, including, obesity, insulin resistance (IR), systemic inflammation, and breast cancer (3, 5). Whether a greater proportion of IA ancestry in this population modifies the metabolic response to specific dietary patterns kept or adopted by Mexican immigrants has not been previously investigated.

In a randomized controlled feeding trial we found that compared to a U.S. diet, a traditional Mexican diet reduced IR and circulating concentrations of insulin-like growth factors (IGFs) among Mexican immigrant women (14). Building on this research, we aimed to evaluate the interplay between genetic ancestral background and diet-related risk of metabolic disease. We hypothesized that IA genetic ancestral background would modify the metabolic response to a U.S. versus traditional Mexican diet among first and second generation, healthy Mexican immigrant women.

MATERIALS AND METHODS

Subjects and study design

The study participants and study design have been previously described (14). Briefly, 58 healthy, Mexican or Mexican American women (first and second generation), ages 18–45 years, enrolled in the trial. Out of 58 study participants, 53 completed the trial that consisted two 24-day intervention periods, separated by a washout period of 28 days. In one period they consumed a traditional Mexican diet and in the other a typical U.S. diet. The order of the diets was randomized. Exclusion criteria included elevated fasting glucose (≥100 mg/dl), pregnancy, lactation or cessation of menses, BMI <18.5 or >40 kg/m^2, smoking, physician-diagnosed disease requiring dietary restrictions or certain medications, or intake of ≥2 alcoholic drinks per day. The Institutional Review Board and Clinical Trials Office of the Fred Hutchinson Cancer Research Center (FHCRC) approved the study and all participants signed written informed consent. The trial was registered at clinicaltrials.gov (identifier: NCT01369173). Participants provided demographic, acculturation, habitual diet and physical activity through self-administered questionnaires and research staff measured height, weight, waist circumference and hip circumference at baseline using standardized protocols (15).

All food and beverages were prepared by the FHCRC Human Nutrition Laboratory. Participants came to the study center three times per week for food pick-ups and body weight measures. Participants were instructed to consume only the foods provided and to return any unconsumed food to study staff. Diets were eucaloric (e.g., diets that provided energy content for weight maintenance) and did not differ in macronutrient composition as a percent of total energy (50% from carbohydrates, 35% from fat, and 15% from protein). Experimental diets differed in foods and beverages such that the traditional Mexican diet included corn tortillas, beans, traditional soups, Mexican-mixed dishes, citrus fruits, vegetables, full-fat milk and Mexican cheeses. The U.S. diet, on the other hand, included processed foods, mixed dishes such as mac and cheese and pizza, refined carbohydrates and added sugars and it was based on the proportion of foods and beverages that contributes the most to Americans daily intake as reported in the National Health and Examination Nutrition Survey (NHANES, 2007–2010) (15). Adherence to controlled diets was carefully monitored and participants' energy intakes were controlled and adjusted as needed to maintain their weight within 3% of baseline measures.

Sample collection and analyses

Blood was collected on the first day and last day of each intervention period after a 12–hour fast by trained research staff. Specimens were locally processed and stored at −80°C until analyses. Glucose was measured on a Roche Module P chemistry autoanalyzer (Roche Diagnostic Inc., Indianapolis, IN) at the Northwest Lipid Research Laboratories (University of Washington, WA). Insulin was measured using a Tosoh 2000 autoanalyzer (Tosoh Biosciences Inc., South San Francisco, CA) at the Diabetes Endocrinology Research Center Immunoassay Laboratory (University of Washington, WA). The rest of the biomarkers assessments and the genotyping were conducted at the FHCRC Biomarker Core Laboratory and the Molecular Epidemiology Laboratories. Immunoassays were used to measured total

adiponectin (Total Adiponectin EIA, Aplco), IGF-1 (Human IGF-I Quantikine ELISA, R&D Systems), IGFBP-3 (Human IGFBP-3 Quantikine ELISA, R&D Systems), and IL-6 (Human IL-6 Quantikine HS ELISA, R&D Systems). CRP was measured using CRP (3)-Wide Range reagent (Kamiya Biomedical Company) on Roche Cobas Mira chemistry analyzer with a high sensitivity protocol. The intra-assay CVs were 0.7%, 7.8%, 1.3%, 1.5%, 1.8%, 2.3%, and 3.3% for glucose, insulin, adiponectin, IGF-1, IGFBP-3, IL-6, and CRP, respectively. The details of specimen collection and analysis have been previously described (14).

Genetic ancestry estimation

DNA was extracted from baseline blood using the Qiagen whole blood kit. Genotypes were collected on the Illumina BeadExpress platform using standard protocols. We used a modified version of the AIMs selection algorithm developed by Galanter et al (16, 17), that allows for a 4-way population admixture model, to select a set of 220 AIMs (Supplemental Table 1). African, European, and Indigenous American (IA) ancestry estimates obtained with the AIMs panel were strongly correlated with genome-wide genotype-based estimates in reference samples (Correlation coefficients of 0.88, 0.95, and 0.96 respectively). It is well known that AIMs panels tend to overestimate the influence of minor ancestral components (16, 18). When evaluating the correlation between estimates for individuals who had more than 10% ancestry from a minor component (as estimated by the genome-wide panel), then the correlation between genome-wide estimates and panel estimates increased greatly (>0.90 correlation for African ancestry proportion).

A panel of 214 of the 220 selected AIMs passed QC on the BeadExpress genotyping platform. In DNA samples passing QC, the call rate for the 214 AIMs analyzed averaged 99.7% +/− 0.3%, with a minimum of 97.5% of genotypes called. After Bonferroni correction for 214 tests, none of the AIMs showed significant departure from Hardy Weinberg Equilibrium in either reference ancestral population (669 reference European samples or 131 reference Native American samples). Ancestry was estimated using the ADMIXTURE software package v1.23 (19). The ADMIXTURE algorithm was primed with five EM steps at K=3 populations, and converged rapidly. Bootstrap replication using the default 200 bootstrap replicates yielded a standard error of less than 4% for each ancestry component within an individual. Reference populations were included in the analysis to anchor the inferred ancestries on nominally un-admixed individuals (K=3 ancestral populations). These reference populations included HapMap reference panels (YRI, ASW, HCB, JPT and MXC populations), and indigenous populations from the Americas (Nahua, Quechua, Aymara, Zapoteca, Tepehuano, and Maya) (16).

Statistical Analyses

The power analysis for the detection of the interaction of diet and ancestry was conducted using Quanto (version 1.2.4; 2009; University of Southern California, CA), and the coefficient of the interaction was on the scale of standard deviations of the biomarker measurements per unit increase in the ancestry measurement. Based on the calculation, we would have 80% power to detect changes of 2 standard deviations in the biomarkers. Indigenous American (IA) ancestry tertiles were created as: ≤45% IA ancestry (lowest), >45 to ≤62% IA ancestry (middle), and >62% IA ancestry (highest), respectively. Natural

logarithmic transformation was applied to insulin, $HOMA_{IR}$, adiponectin, hs-CR and IL-6 biomarker concentrations to achieve approximate normality. General linear models (unadjusted) were used to compare means of demographic and baseline characteristics across IA ancestry tertiles for continuous variables and chi-squared tests for categorical variables. General linear models adjusted for age, acculturation and BMI were used to compare baseline biomarker concentrations across IA ancestry tertiles, with the Duncan multiple range tests *post hoc* whenever the overall test indicated a statistically significant difference between IA ancestry tertiles. Linear mixed models were used to test the effect modification of ancestry on the metabolic response to the U.S. versus traditional Mexican diet, including participant as a random effect while treating diet sequence, feeding period, baseline and washout biomarker concentrations, age, acculturation, and BMI, ancestry (as continuous variable) and the interaction between ancestry and diet variables as fixed effects. Also, linear mixed effects models including participants as random effect and diet sequence, feeding period, baseline and washout biomarker concentrations, age, acculturation, and BMI as fixed effects were used to investigate the biomarkers responses to the diet intervention within each category of IA ancestry tertiles. We examined the presence of potential carry-over effects with the inclusion of the diet sequence variable (in addition to other variables including diet and feeding period) as a fixed effect in the mixed effects models. This variable (sequence) was not found to be significantly associated with the biomarkers responses to the diet intervention and hence, no carry-over effect was detected in our analysis. This might be related to the wash-out period of 28 days between each diet period being probably appropriate enough to minimize the carry-over effects. All analyses were performed using SAS (version 9.3; SAS Institute Inc., Cary, NC), all tests were two-sided and P values <0.05 were considered statistically significant.

RESULTS

We first examined the overall distribution of African, European, and IA ancestry. In this sample of 58 healthy, first and second generation Mexican immigrant women, the overall distribution of ancestry was 56% IA, 38% European, and 6% African (Figure 1). We then examined the distribution of demographic characteristics and baseline measures for the women who completed the trial (n=53) across IA ancestry tertiles: 45% IA ancestry (lowest), >45 to 62% IA ancestry (middle), and >62% IA ancestry (highest), respectively (Table 1). Women in the highest IA ancestry tertile (>62%) were shorter in height (P<0.05), less educated (P<0.05), and less acculturated to the U.S. lifestyle (P<0.05), and tended to have higher waist-to-hip ratio (P=0.07) compared to women in the middle and lowest IA ancestry tertiles, respectively.

Table 2 shows the baseline (pre-intervention) serum fasting concentrations of biomarkers of metabolic disease risk across IA ancestry tertiles. Women in the highest IA ancestry tertile (>62%) tended to have lower circulating concentrations of IGF-1 (P=0.09), and significantly lower circulating concentrations of IGFBP-3 compared to women in the middle and lowest IA ancestry tertiles, respectively (P<0.05). There was no association of ancestry with the IGF-1/IGFBP-3 ratio and baseline serum concentrations of adiponectin, CRP and IL-6.

Results testing whether IA ancestry modified of the exploratory analysis on the metabolic response to the controlled intervention diets (U.S. versus traditional Mexican diet) stratified by IA ancestry tertile are shown in Table 3. Overall, the effect modification associations observed were modest. Compared to the U.S. diet, the traditional Mexican diet tended to reduce glucose (P=0.08), and insulin concentrations (P<0.05) among women in the middle IA ancestry tertile, and tended to reduce insulin concentrations among women in the lowest IA ancestry tertile (P=0.06). Similarly, compared to the U.S. diet, the traditional Mexican diet significantly reduced HOMAIR (P<0.05) and circulating concentrations of IGFBP-3 (P<0.01) and, while tended to reduce IGF-1 (P=0.06) among women in the middle IA ancestry tertile. We found no significant effect of effect modification of ancestry in the response to the diet intervention diets for IGF-1/IGFBP-3 ratio, and serum concentrations of CRP and IL-6 in any of the IA ancestry strata. Lastly, compared to the U.S. diet, the traditional Mexican diet tended to increase adiponectin concentrations among women in the middle IA ancestry tertile (P=0.07). There was no statistically significant difference in the biomarkers response to the diet intervention among the IA strata. In additional analyses, a cross-product interaction term of IA ancestry (as continuous variable) and diet treatment (U.S. vs. Mexican) were tested in adjusted linear mixed models that also included the main effect variables but we found no statistically significant interaction for any of the biomarkers examined (data not shown).

DISCUSSION

In this randomized, crossover feeding trial among first and second generation, healthy Mexican immigrant women, we found a modest effect modification by IA ancestry in the metabolic response to the U.S. versus traditional Mexican diet among women in the middle IA ancestry tertile (>45 to ≤62%). Further, IA ancestry was associated with several baseline demographic and anthropometric characteristics, as well as baseline circulating concentrations of IGF-1 and IGFBP-3, independent of age, BMI, and acculturation status.

In cross-sectional analyses of baseline measures (pre-intervention), we found that women with greater IA ancestry tended to have higher adiposity (waist-to-hip ratio), were more likely to be less educated and less acculturated to the U.S. lifestyle compared to women with greater European ancestry, consistent with previous findings (12, 13, 20). Greater IA ancestry tended to be associated with baseline waist-to-hip ratio, but not with BMI, as previously reported among Hispanic women (12, 13, 21) suggesting a greater contribution of visceral fat to the risk of metabolic disease in this ethnic group. Of particular interest is our finding of an inverse association between IA ancestry and baseline circulating concentrations of IGF-1 and IGFBP-3. Insulin-like growth factors (IGFs) are peptides known to promote cellular proliferation of normal breast cells, and therefore, high circulating concentrations of IGF-1 and IGFBP-3 are associated with increased risk of breast cancer (22–24). This is in agreement with studies by Fejerman et al, in which greater European versus IA ancestry among women of Mexican descent was associated with increased risk of breast cancer (25, 26).

We previously showed that compared to the U.S. diet, the traditional Mexican diet improved insulin sensitivity and reduced circulating concentrations of IGF-1 and IGFBP-3 (14).

Building upon these findings, in the present study we found a modest effect modification of IA ancestry in relation to the metabolic response to the intervention diets. This interaction seemed strongest for insulin sensitivity biomarkers and IGFs and only among women in the middle IA ancestry tertile. These findings suggest that genetic ancestral background may play a role in the metabolic response to specific dietary patterns kept or adopted by Mexican immigrants that can lead to future risk of diabetes. Consistent with our results, in a large observational study evaluating the association between genetic ancestry and risk of diabetes in a multi-ethnic cohort of postmenopausal women (n=16,476) who participated in the Women's Health Initiative, it was found that among Hispanic women, greater IA ancestry was associated with increased risk of diabetes (13). However, since our diet-ancestry findings in this report are limited to women in the middle IA ancestry tertile, it is possible that other factors underlie the observed associations. For example, women in the middle IA ancestry tertile had lower waist-to-hip ratio (non-statistically significant), and were more likely to have more education (P=0.02) and to be more acculturated to the U.S. lifestyle (P=0.04) compared to women in the lowest (≤45%) or highest IA ancestry tertiles (>62%), respectively. It is possible that these differences in SES (higher education status) influence the ancestry-metabolic response association in a manner that could not be captured using these standard methods. Similar results for differences in SES have been shown to be strongly associated with admixture proportions and disease risk in Hispanic populations. For example, in several studies among Hispanics evaluating the association between ancestry and disease risk, adjustments for SES significantly attenuated these associations (13, 27, 28), and in some cases the association become non-significant after adjustments for SES (29).

We found no effect modification of IA ancestry in response to the intervention diets for the inflammatory biomarkers examined, including CRP and IL-6. Although, there was a non-statistically significant increase in adiponectin levels (P=0.07) in the Mexican vs US diet but only among women in the middle IA ancestry group. It is possible that the conditions of weight stability in our study played an important role in the null results. Similar to our results and under conditions of weight stability, others have found no diet-induced effect on inflammatory biomarkers, including CRP and adiponectin (30, 31). On the other hand, others have being able to demonstrate a diet-induced inflammatory response in dietary interventions that were coupled with weight loss. These findings suggests that diet-related changes in inflammatory profiles are greater when coupled with weight loss, in part, due to the strong association between adiposity and inflammation (32, 33).

Our study is not without limitations. The modest sample size may have precluded us from finding a more robust effect modification of genetic ancestry in relation to the metabolic response to the intervention diets. Despite this limitation, a novel contribution of the present study is the use of AIMs to better understand the interplay between genetic ancestral background and diet-related risk of metabolic disease in a population that displays a great degree of genetic admixture.

In conclusion, we observed a modest interaction between IA ancestry and the metabolic response to a U.S. versus traditional Mexican diet among women in the middle IA ancestry tertile, who were also more educated and acculturated to the U.S. when compared to their counterparts. Future experimental and longitudinal studies evaluating the extent by which IA

ancestry plays a role in diet-related risk of metabolic disease will be necessary to confirm these results.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AIMs	Ancestry Informative Markers
CRP	C-reactive protein
$HOMA_{IR}$	homeostasis model assessment of insulin resistance
IA	Indigenous American
IGF-1	insulin-like growth factor-1
IGFBP-3	insulin-like growth factor binding protein-3
IL-6	interleukin-6
NHW	non-Hispanic white
SES	socio-economic status
T2D	type 2 diabetes
WC	waist circumference

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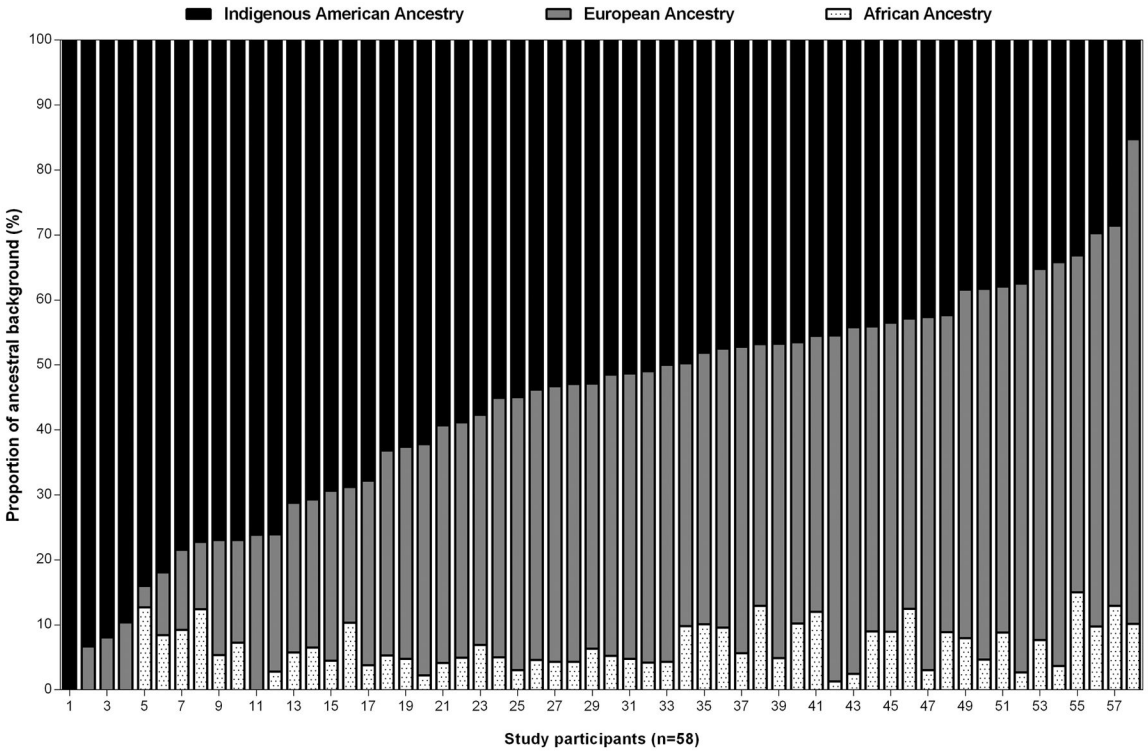

FIGURE 1.

Genetic ancestral background composition for 58 healthy, first and second generation Mexican immigrant women from three populations – Indigenous American (IA), European, and African – with the use of 214 Informative Ancestry Markers (AIMs)

TABLE 1

Demographic characteristics of 53 healthy, first and second generation Mexican immigrant women across Indigenous American (IA) ancestry tertiles

	IA ancestry tertiles			
	Lowest IA ≤ 45% (*n* = 18)	**Middle IA > 45 to ≤62% (*n* = 17)**	**Highest IA > 62% (*n* = 18)**	***P* value[1]**
Baseline characteristics	**N (%) or Mean ± SD**			
Age, *years*	27 ± 8	27 ± 10	28 ± 7	0.8
Weight, *kg*	67.6 ± 11.5	65.7 ± 14.0	66.2 ± 10.8	0.8
Height, *cm*	163 ± 5[a]	159 ± 6[b]	157 ± 6[b]	0.005
Body mass index, *kg/m²*	25.4 ± 4.8	25.9 ± 5.7	26.8 ± 3.9	0.6
BMI categories				0.2
Normal weight: ≥18.2–24.9	11 (61)	10 (59)	6 (33)	
Overweight: ≥25–29.9	4 (22)	3 (18)	9 (50)	
Obese: ≥30.0	3 (17)	4 (23)	3 (17)	
Waist circumference, *cm*	83.8 ± 11.2	81.3 ± 13.8	86.8 ± 11.2	0.4
Hip circumference, *cm*	102 ± 8	100 ± 12	102 ± 9	0.7
Waist to hip ratio (WHR)	0.82 ± 0.06[a]	0.81 ± 0.07[a]	0.85 ± 0.06[b]	0.07
Education				0.02
High school diploma	1 (6)	3 (19)	7 (47)	
Some college or ≥ college	16 (94)	13 (81)	8 (53)	
Marital Status				0.2
Married	4 (22)	5 (29)	8 (47)	
Single	14 (78)	12 (71)	8 (24)	
Employment Status				0.05
Employed	11 (61)	7 (41)	8 (50)	
Full time student	6 (33)	10 (59)	4 (25)	
Unemployed	1 (6)	0 (0)	4 (25)	
Place of birth				0.2
Mexico	12 (67)	8 (47)	13 (72)	
United States	6 (33)	9 (53)	5 (28)	
Language spoken				0.06
Spanish	9 (53)	4 (24)	11 (61)	
English	8 (47)	13 (76)	7 (39)	
Language Thought				0.3
Spanish	1 (6)	2 (12)	4 (22)	
English	17 (94)	15 (88)	14 (78)	
Ethnic identity				0.2
Mexican	11 (61)	9 (53)	14 (78)	
Mexican American	7 (39)	8 (47)	4 (22)	
Acculturation score	1.6 ± 1.7[a]	2.4 ± 1.5[b]	1.1 ± 1.4[a]	0.04

[1] General linear models for continuous variables and chi-squared tests for categorical variables

[ab] Labeled means in a row with differing superscripts letters are significantly different from one another, using general linear models with the Duncan multiple range test ($P<0.05$).

TABLE 2

Baseline serum concentrations of biomarkers of disease risk across Indigenous American (IA) ancestry tertiles

	All study participants (*n* = 53)	IA ancestry tertiles			
		Lowest IA ≤ 45% (*n* = 18)	Middle IA > 45 to ≤62% (*n* = 17)	Highest IA > 62% (*n* = 18)	
Biomarkers	**Mean ± SEM or Geometric Mean (95% CI)**				***P* value[1]**
Glucose,[2] *mg/dL*	91.9 ± 7.1	91.3 ± 7.2	89.6 ± 7.9	94.6 ± 5.3	0.1
Insulin,[3] *μU/mL*	9.9 (8.6, 11.3)	9.5 (7.7, 12)	9.6 (7.7, 12)	10.5 (8.4, 13)	0.8
$HOMA_{IR}$[3]	2.2 (1.9, 2.6)	2.2 (1.7, 2.7)	2.1 (1.7, 2.7)	2.4 (1.9, 3.1)	0.6
IGF-1,[2] *ng/mL*	149 ± 45	162 ± 53^{a}	149 ± 55^{a}	136 ± 41^{b}	0.09
IGFBP-3,[2] *ng/mL*	2430 ± 440	2600 ± 426^{a}	2423 ± 451^{b}	2265 ± 402^{b}	0.02
IGF-1/ IGFBP-3	6.1 ± 1.4	6.3 ± 1.3	6.1 ± 1.7	5.9 ± 1.1	0.7
Adiponectin,[3] *μg/mL*	6.9 (6.3, 7.6)	7.5 (6.4, 8.9)	6.6 (5.5, 7.8)	6.6 (5.6, 7.8)	0.4
hs-CRP,[3] *mg/L*	0.9 (0.6, 1.2)	0.6 (0.4, 0.9)	1.2 (0.7, 2.0)	0.9 (0.6, 1.4)	0.1
IL-6,[3] *pg/mL*	1.4 (1.2, 1.6)	1.2 (0.9, 1.5)	1.5 (1.2, 2.0)	1.5 (1.1, 1.9)	0.3

Abbreviations: $HOMA_{IR}$, homeostasis model assessment for insulin resistance; hs-CRP, high-sensitivity C-reactive protein; IA, Indigenous American Ancestry IGF-1, insulin-like growth factor-1; IGFBP-3, IGF-binding protein-3; IL-6, interleukin-6.

[1] General linear regression models were adjusted for age, acculturation, and BMI

[2] Mean ± SEM

[3] Geometric means (95% CI)

[ab] Labeled means in a row with differing superscripts letters are significantly different from one another, using general linear models with the Duncan multiple range test (P<0.05).

TABLE 3

Metabolic response to controlled U.S. versus traditional Mexican diet on serum biomarkers of disease risk stratified by Indigenous American (IA) ancestry tertiles as determined by Ancestry Informative Markers (AIMs)[1]

Biomarkers	*n*	U.S. diet	*n*	Traditional Mexican diet	Mean Diff.	*P* for diet effect within tertiles[2]
Glucose,[3] *mg/dL*						
Lowest IA ancestry ≤45%	16	87 ± 1.3	16	88 ± 1.4	−1.6	0.30
Middle IA ancestry >45 to ≤62%	18	90 ± 1.9	18	85 ± 2.0	4.0	0.08
Highest IA ancestry >62%	17	93 ± 1.8	18	91 ± 1.8	1.6	0.13
Insulin,[4] *μU/mL*						
Lowest IA ancestry ≤45%	16	8.8 (7.1, 11)	16	7.7 (6.2, 9.6)	1.1	0.06
Middle IA ancestry >45 to ≤62%	18	10.5 (8.8, 12.6)	18	7.4 (6.2, 8.9)	3.1	0.01
Highest IA ancestry >62%	17	8.8 (7.3, 10.7)	18	8.6 (7.2, 10.3)	0.2	0.82
HOMAIR[4]						
Lowest IA ancestry ≤45%	16	1.9 (1.5, 2.3)	16	1.7 (1.4, 2.1)	0.2	0.12
Middle IA ancestry >45 to ≤62%	18	2.3 (1.9, 2.9)	18	1.5 (1.3, 1.9)	0.8	0.01
Highest IA ancestry >62%	17	2.0 (1.6, 2.5)	18	1.9 (1.6, 2.3)	0.08	0.74
IGF-1,[3] *ng/mL*						
Lowest IA ancestry ≤45%	16	160 ± 6.0	16	160 ± 5.5	-0.07	0.98
Middle IA ancestry >45 to ≤62%	18	152 ± 4.0	18	142 ± 4.2	10.3	0.06
Highest IA ancestry >62%	17	135 ± 4.6	18	130 ± 4.2	5.2	0.40
IGFBP-3,[3] *ng/mL*						
Lowest IA ancestry ≤45%	16	2577 ± 65	16	2468 ± 67	109	0.25
Middle IA ancestry >45 to ≤62%	18	2455 ± 52	18	2327 ± 54	128	0.004
Highest IA ancestry >62%	17	2255 ± 54	18	2166 ± 50	85	0.26
IGF-1/ IGFBP-3						
Lowest IA ancestry ≤45%	16	6.3 ± 0.2	16	6.6 ± 0.2	−0.3	0.21
Middle IA ancestry >45 to ≤62%	18	6.1 ± 0.5	18	6.1 ± 0.2	0.05	0.76
Highest IA ancestry >62%	17	5.8 ± 0.2	18	5.9 ± 0.2	−0.1	0.61
Adiponectin,[4] *μg/mL*						
Lowest IA ancestry ≤45%	16	7.2 (6.7, 7.7)	16	7.0 (6.5, 7.6)	14.7	0.58

Biomarkers	*n*	U.S. diet	*n*	Traditional Mexican diet	Mean Diff.	*P* for diet effect within tertiles[2]
Middle IA ancestry >45 to ≤62%	18	6.4 (5.8, 7.0)	18	7.2 (6.6, 7.9)	−8.2	0.07
Highest IA ancestry >62%	17	6.3 (5.8, 6.8)	18	6.1 (5.6, 6.5)	2.1	0.34
hs-CRP,[4] *mg/L*						
Lowest IA ancestry ≤45%	16	0.5 (0.4, 0.8)	16	0.5 (0.4, 0.8)	−0.002	0.98
Middle IA ancestry >45 to ≤62%	18	1.2 (0.6, 2.4)	18	1.0 (0.5, 2.1)	0.2	0.71
Highest IA ancestry >62%	17	1.2 (0.8, 1.9)	18	1.4 (0.9, 2.1)	−0.2	0.61
IL-6,[4] *pg/mL*						
Lowest IA ancestry ≤45%	16	1.1 (0.9, 1.4)	16	1.2 (0.9, 1.5)	−0.1	0.51
Middle IA ancestry >45 to ≤62%	18	1.5 (1.1, 2.2)	18	1.4 (1.0, 1.9)	0.2	0.64
Highest IA ancestry >62%	17	1.6 (1.3, 1.9)	18	1.4 (1.1, 1.7)	0.2	0.36

Abbreviations: $HOMA_{IR}$, homeostasis model assessment for insulin resistance; hs-CRP, high-sensitivity C-reactive protein; IA, Indigenous American Ancestry IGF-1, insulin-like growth factor-1; IGFBP-3, IGF-binding protein-3; IL-6, interleukin-6.

[1] All regression models were adjusted for baseline and washout biomarker concentrations, diet sequence, feeding period, age, acculturation and BMI.

[2] *P* values are from linear mixed models testing the intervention effect of the U.S. versus Traditional Mexican diet within IA ancestry tertiles.

[3] Mean ± SEM

[4] Geometric means (95% CI)