Arthritis & Rheumatism
AMERICAN COLLEGE OF RHEUMATOLOGY
EDUCATION · TREATMENT · RESEARCH
WILEY-BLACKWELL

Arthritis & Rheumatism, Volume 65, October 2013 Abstract Supplement

Abstracts of the 2013 American College of Rheumatology/Association of Rheumatology Health Professionals Annual Meeting
San Diego, CA October 25-30, 2013.

GWAS In Hispanic And Latin American Individuals Enriched For Amerindian Ancestry Identifies A New Locus Associated With Systemic Lupus Erythematosus.

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Background/Purpose:

Systemic lupus erythematosus (SLE), a chronic autoimmune disease with a strong genetic component, exhibits a 9:1 female to male ratio and disproportionate impact on individuals of admixed ancestries in the Americas. We performed a genome-wide association scan on individuals from Latin America and the United States enriched for Amerindian while admixed with European ancestry.

Methods:

A total of 4516 individuals were genotyped, 2906 for the Illumina Human

Quadv1 (OMNI1) and data from1610 out-of-study controls for the OMNI2.5 Bead array was obtained yielding, 996,672 SNPs for final analysis (580,483 SNP were on both BeadArrays). After quality control filters were applied, a total of 3710 individuals were kept for genetic association analysis. The final inflation factor was 1.00 using the 2 first principal components (PC). Principal component analysis revealed 2 differentiated populations that corresponded to a South American (individuals from Argentina, Chile and Peru; N = 875), and a North American group composed of individuals from Mexico, and Hispanics and Native Americans from the United States (N = 2835). SNP-SLE association was tested using logistic regression model adjusting for PC. Results for the additive model are reported.

Results:

One novel genetic association was identified in chromosome 10, between INA, USMG5 and PDCD11 (rs4917385, Pvalue = 7.48 × 10–8, min FDR p-value=0.00099, OR=0.75, CI=0.67–0.84). Several known lupus susceptibility loci were replicated. Overall, the strongest effect was that of TNPO3-IRF5 locus, followed by the HLA class II region. Regions previously associated in Europeans that were associated for the first time in individuals with enriched Amerindian ancestry were TNFSF4, NCF2, NMNAT2, JAZF1, FAM167A-BLK, and PTTG1-MiR146a. Regions previously associated in Asians and associated for the first time in individuals with enriched Amerindian ancestry were SLC15A4 and WDFY4.

Conclusion:

We identify a new locus for SLE in chromosome 10. Our data show the major importance of genes outside the HLA in the susceptibility for lupus in this population and provide support for loci previously found in Asians and Europeans.

Disclosure: M. E. Alarcon Riquelme, None; J. T. Ziegler, None; M. E. Comeau, None; E. Sanchez, None; B. Pons-Estel, Abbott Laboratories, 2; E. Acevedo, None; J. M. Cucho, None; I. Garcia de la Torre, None; M. H. Cardiel, None; P. Miranda, Janssen, HGS, Medimmune, Celltrion, Sanofi, Roche, Pfizer, and MSD, 9, Pfizer Inc, 9; L. Cattogio, None; M. Maradiaga, None; J. Esquivel-Valerio, None; J. F. Moctezuma, None; M. Garcia, None; G. Berbotto, None; A. Babini, None; H. Scherbarth, None; S. Toloza, None; J. A. James, None; T. Tusie-Luna, None; J. B. Harley, None; R. Zidovetski, None; C. Langefeldt, None; C. O. Jacob, None.

To cite this abstract, please use the following information:
Riquelme, Marta Eugenia Alarcon, Ziegler, Julie T., Comeau, Mary E., Sanchez, Elena, Pons-Estel, Bernado, Acevedo, Eduardo, et al; GWAS In Hispanic and Latin American Individuals Enriched For Amerindian Ancestry Identifies a New Locus Associated With Systemic Lupus Erythematosus. [abstract]. Arthritis Rheum 2013;65 Suppl 10 :1639
DOI: 10.1002/art.2013.65.issue-s10