

Study reveals remarkable genetic diversity across Mexico

By Staton Wade

In the largest genetic study of Native Americans to date, researchers have discovered a level of genetic diversity across Mexico that is as extensive as that observed between Europeans and Chinese. This unexpected diversity may have important implications for diagnosis and treatment of diseases, such as lung disease, that rely on clinical thresholds for disease diagnosis that differ depending on ethnicity.

Carlos Bustamante, Ph.D., of Stanford University, and Esteban Burchard, M.D., of the University of California, San Francisco, led the [study](http://www.ncbi.nlm.nih.gov/pubmed/24926019), published in the June 13 issue of the journal *Science*. Bustamante and Burchard collaborated with an international team of researchers from New York, the UK, Mexico, Puerto Rico, France, and NIEHS.

Linked Audio

[Listen to a podcast from the journal *Science* in which Bustamante discusses the study's findings. \(18:18\)](#)

Modern mestizos reflect Native American genetic substructure

The researchers analyzed one million genetic loci in 511 Native Mexican individuals, from 20 indigenous populations, as well as 500 admixed mestizos, or Mexicans with mixed ancestry, from 10 Mexican states. While previous Native American studies have been limited to one gene or a small population size, this study provided the kind of large-scale data that until now has been available only for populations of European descent.

What the researchers found was a surprising amount of genetic diversity, reflecting the high degree of isolation between indigenous groups in Mexico. Interestingly, the same genetic substructure was observed in metropolitan populations of mestizos, despite generations of mixing with Europeans and Africans.

Implications for lung disease diagnosis

To understand the possible health implications of Mexican genetic diversity, the researchers turned to data from genome-wide association studies of asthma, performed in Mexican and Mexican-American populations.

NIEHS researcher Stephanie London, M.D., Dr.P.H., led one of those [studies](http://www.ncbi.nlm.nih.gov/pubmed/?term=PLOS+Genet.+5%2C+e1000623+(2009)), which aimed to identify genetic loci associated with the response to ozone in asthmatic children in Mexico City. "We have been collaborating with co-first author Chris Gignoux, Ph.D., and Burchard for many years, to examine admixture in our Mexico City study, and how it can contribute to knowledge of both population genetics and the identification of disease genes," said London.

This latest collaboration allowed the researchers to predict clinical measures of lung function across the diverse populations of Mexico, based on ancestry. The results of the new study revealed that individuals from Yucatan in the east and Sonora in the west vary greatly in measurements of normal lung function. This variation is relevant when diagnosing lung diseases such as asthma and chronic obstructive pulmonary disease.

The authors also pointed out that the availability of rich genetic data sets in previously understudied populations, such as Native Americans, will greatly improve large-scale genetic mapping efforts, such as the HapMap and 1000 Genomes projects.

Citation: Moreno-Estrada A, Gignoux CR, Fernandez-Lopez JC, Zakharia F, Sikora M, Contreras AV, Acuna-Alonzo V, Sandoval K, Eng C, Romero-Hidalgo S, Ortiz-Tello P, Robles V, Kenny EE, Nuno-Arana I, Barquera-Lozano R, Macin-Perez G, Granados-Arriola J, Huntsman S, Galanter JM, Via M, Ford JG, Chapela R, Rodriguez-Cintrón W, Rodriguez-Santana JR, Romieu I, Sienra-Monge JJ, del Rio Navarro B, London SJ, Ruiz-Linares A, Garcia-Herrera R, Estrada K, Hidalgo-Miranda A, Jimenez-Sanchez G, Carnevale A, Soberon X, Canizales-Quinteros S, Rangel-Villalobos H, Silva-Zolezzi I, Burchard EG, Bustamante CD. (2014). Human genetics. The genetics of Mexico recapitulates Native American substructure and affects biomedical traits. *Science* 344(6189):1280-1285.

(Staton Wade, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Chromatin and Gene Expression Group.)



"As we deploy genomics technology in previously understudied populations like those of Latin America, we discover remarkable richness in the genetic diversity of these important groups and why it matters for health and disease," Bustamante said. (Photo courtesy of Deneb Semprum)



"Our genetic and lung function data from Mexico were combined with data from Dr. Burchard's U.S.-based study of Mexican-Americans, to examine the contribution of ancestry to the lung function parameters commonly used in clinical medicine, for diagnosing and monitoring diseases," London said. (Photo courtesy of Steve McCaw)