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Contacts:
Terry Collins, +1-416-538-8712 (o), +1-416-878-8712 (m), tc@tca.tc;
Gerardo Jimenez-Sanchez, MD, PhD, National Institute of Genomic Medicine,
+52-55-5350-1901 o +52-55-5350-1902 (o); gjimenez@inmegen.gob.mx

The full article will be published on Monday, May 11, 2009 at 5pm US Eastern Daylight Time/9 pm GMT, it is available on request at the New Agency of Proceedings of the National Academy of Science (PNAS), +1-202-334-1310; PNASnews@nas.edu

Landmark Mexican Study Reveals Significant Genetic Variation Between Nation's Population And World's Other Known Genetic Subgroups

Study moves scientists closer to identifying individuals at risk or resistant to flu and other diseases, and to the potential of creating genome-customized drugs

Mexico City - Could genetic differences explain why some people and not others have died of H1N1 Influenza A?

That is among the questions raised by a landmark Mexican study showing significant genetic variation between Mestizos (Latin Americans of mixed European and Amerindian ancestry) and the world's other known genetic subgroups.

The study, by Mexico's National Institute of Genomic Medicine (INMEGEN), will be published at 5 pm EDT Monday May 11 by the Washington DC-based Proceedings of the National Academy of Sciences, USA (PNAS).

Led by Dr. Gerardo Jimenez-Sanchez of INMEGEN, a team of 16 Mexican researchers (listed below), analyzed the genetic composition of 300 Mestizos from six geographically distant states in Mexico and one Amerindian population (30 members of the indigenous Zapotecas group in the state of Oaxaca).

They discovered that genetically the Mexican Mestizo and Indigenous populations are substantially different from the three other known human genetic subgroups (Yoruba from Africa, Caucasians of European descent, and the Chinese and Japanese of Asia), whose DNA make-ups were documented through the historic International HapMap Project, 2002 to 2006.

The Mexican research was undertaken to establish the comparability of Latino genomes to others in the global search for health-related genes throughout humanity.

A recent study in Asia identified a genetic characteristic in Asians that indicates a susceptibility to Hepatitis B; other studies have identified people with genetic predispositions to HIV1 or Kawasaki Disease.

While the latest work is at far too early a stage to enlighten authorities on the current outbreak of H1N1 Influenza A, it may one day help explain why, for example, with cases of that virus appearing worldwide, fatalities to date have occurred almost exclusively in Mexico.

Says Dr. Jimenez-Sanchez: "It is not possible today to say genetic variation is responsible for the unique H1N1 Influenza A mortality rate in Mexico. However, knowledge of genomic variability in the Mexican population can allow the identification of genetic variations that confer susceptibility to common diseases, including infections such as the flu."

"It will also help develop pharmacogenomics to help produce medicines tailored to people of a specific genetic group, to the creation of drugs that are both safer and more effective."

The young National Institute of Genomic Medicine in Mexico City was established in 2004 under then-Health Minister Julio Frenk, now Dean of the School of Public Health, Harvard University.

"This study makes clear that Latin Americans with mixed ancestry are different enough from other people worldwide that a full-scale genomic mapping project would be wise both scientifically and economically. It would allow doctors to analyze fewer genetic markers when diagnosing the risk that a patient will develop a disease that depends on complex factors," says Dr. Frenk.

"Mexico has created a state-of-the-art genomic medicine institution, unique in Latin America, where world-class scientific research can be developed to understand the molecular relationships between humans and germs. This valuable facility will enable Mexico to prepare for the health challenges that await us all in the future."

Dr. Edison T. Liu, President of the Human Genome Organization (HUGO) said: "This work by the INMEGEN group is important both for the scientific content which can be used to direct personalized medicine in Mexico, but also for its sociologic impact in defining the uniqueness of Mexico's genetic heritage."

"Studies such as this are helping us define the future of the genome era," says Dr. Jeffrey Trent, President of the Translational Genomics Research Institute, Phoenix, Arizona. "Gaining a clearer understanding of how genetic variation plays a role in disease, including the risk to some infections, will help tip the scales in our favour in terms of understanding and treating disease at the individual level."

"We have studied a number of genomics initiatives in the developing world and emerging economies, recently published in Nature Reviews Genetics. There is no doubt that INMEGEN is a unique institution and one of the most advanced in the world in terms of its infrastructure but, more importantly, in its linkage to the national health system. It is a model for the rest of the world," said Prof. Abdallah Daar of the McLaughlin-Rotman Centre for Global Health at the University Health Network and University of Toronto.

The INMEGEN study was financially supported by the Federal Government of Mexico, with in-kind support of the Mexican Health Foundation (FUNSALUD) and the Gonzalo Río Arronte Foundation.

The papers authors:

Irma Silva-Zolezzi, Alfredo Hidalgo-Miranda, Jesus Estrada-Gil, Juan Carlos Fernandez-Lopez, Laura Uribe-Figueroa, Alejandra Contreras, Eros Balam-Ortiz, Laura del Bosque-Plata, David Velazquez-Fernandez, Cesar Lara, Rodrigo Goya, Enrique Hernandez-Lemus, Carlos Davila, Eduardo Barrientos, Santiago March, and Gerardo Jimenez-Sanchez.

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Background:

The human genome project (1990-2004) identified common genetic variation, mostly Single Nucleotide Polymorphisms (SNPs), which provide the basis for genetic individuality. Genetic variants associated to susceptibility to common disease and the ability to predict disease-associated risks and response to treatments are the basis of genomic medicine.

The International HapMap Project (2002-2006) systematically analyzed genetic variation in three ancestral populations: Yoruba from Africa, Caucasian of European descent, Han Chinese and Japanese from Asia. This project created a haplotype map of these populations as a tool to identify disease-related genes in a more efficient way. This project did not include the Latin American populations, which are of recent admixture from ancestral populations that include native Indians of the region. This represented a potential risk of segregating Mexican population from genomic medicine in the future.

Mexico is developing a national platform in genomic medicine. In 2004, the Mexican government founded the National Institute of Genomic Medicine (INMEGEN) to conduct world-class scientific research, implement technological platforms and develop educational programs in genomic medicine (www.inmegen.gob.mx).

In addition to generating important scientific information, INMEGEN's Mexican Genome Diversity Project has produced unprecedented human and technological infrastructure in Mexico in less than 5 years. INMEGEN is the most advanced institution in Latin America with the ability to study interactions between humans and the environment, including microorganisms, enabling Mexico to prepare for future challenges. It's research aims to identify genetic variation that predisposes to common diseases in Mexicans.

A haplotype map provides a resource of significant impact to enable faster identification of disease-related genes. However, the question was whether the HapMap from ancestral populations would fit the Mexican population. This study indicates that the genetic structure in the Mexican population would identify tagSNPs that better fit this population and speed genome-wide association studies and

admixture mapping at a much lower cost. This would be a corner stone to develop genomic medicine in Mexico.

Goal of the Mexican Genome Diversity Project: To determine common genomic variation in the Mexican Mestizo population and compare different regions in Mexico, as well as to compare such variability with results from the HapMap. In addition, the project produced a simple visual map of the genetics of different population groups throughout the country (http://diversity.inmegen.gob.mx).

In general, the Mestizo genomes occupy points on a linear spectrum that ranges from Amerindian to European. There are major differences between Mexican Mestizos and subgroups of the HapMap such as Africans or Chinese, although Mexican Mestizos share 96 percent of their haplotypes with the complete HapMap population.

Haplotype sharing analysis showed that all Mexican subpopulations share, on average, 86% (84-87%) of the common haplotypes when one subpopulation is used as a reference and that the proportion of shared haplotypes increases to an average of 96% (95-97%) when each subpopulation is compared to any pair of the studied subpopulations. These results support the idea that a haplotype map of the Mexican Mestizo population may help reduce the number of tagSNPs required to characterize common genetic variation in this population.

Relevant publications:

(1) Jimenez-Sanchez, G (2003) Developing a platform for genomic medicine in Mexico. Science 300:295-296.
(2) Seguin B, Hardy BJ, Singer PA, Daar AS (2008) Genomics, public health and developing countries: The case of the Mexican National Institute of Genomic Medicine (INMEGEN). Nat Rev Genet 9(Suppl 1):S5-S9.
(3) Jimenez-Sanchez G, Silva-Zolezzi I, Hidalgo A, March S (2008) Genomic medicine in Mexico: Initial steps and the road ahead. Genome Res 18:1191-1198.