GENOMICS

Initiative Aims to Minister To Mexico's Unique Genetic Heritage

MEXICO CITY—When Hernán Cortés landed on Mexico's eastern coast in 1519, he brought more than a conquering army that would soon topple the Aztec empire. He and his men also brought their genomes. In the 50,000 years or so since the European and Amerindian populations had last been in contact, their genomes had diverged in small but significant ways. A mutation here, a difference in selection pressure there, and inexorably some genetic variations became prevalent in one population and all but absent in the other. When Cortés married his indigenous translator La Malinche, their union—and many others like it—set the divergent genomes on a collision course.

Five hundred years later, the average Mexican genome contains a mixture of European, Amerindian, and African ancestry. The quest to understand the consequences of that heritage got a boost last month, when telecommunications billionaire Carlos Slim Helú announced a plan to plow $74 million into the Slim Initiative for Genomic Medicine in the Americas (SIGMA), which aims to develop diagnostic tools and medicines for diseases, including breast cancer and type 2 diabetes, that are especially prevalent in the Mexican population.

Until recently, large-scale human genome sequencing initiatives focused almost exclusively on populations of European ancestry, says Eric Lander, a geneticist and director of the Broad Institute in Cambridge, Massachusetts, which is teaming up on SIGMA with the Carlos Slim Health Institute here. That European bias makes genomic findings less relevant for people of other backgrounds. Most gene variations, or alleles, are present in all human populations, Lander explains, but their frequencies "differ a lot." What scientists learn from studying the genome of one population "may or may not apply [to] individuals of other ancestries," says Bogdan Pasaniuc, a population geneticist at the University of California, Los Angeles.

As a case in point, a study published online this week in *Nature Medicine* found that the platelets of African Americans form blood clots faster than those of white Americans when exposed to a particular clotting agent. This difference may mean that blood-thinning medications designed with the European genome in mind are not as effective for African Americans. Similar issues could be plaguing Latin Americans, leaving them underserved by the technologies that are supposed to be revolutionizing health care, says epidemiologist Miguel Betancourt, global solutions director at the Slim institute. In medicine, he says, "genomics is the language of the future." Without a comprehensive understanding of the Latin American genome and its specific risk factors, he says, Mexicans will be left behind.

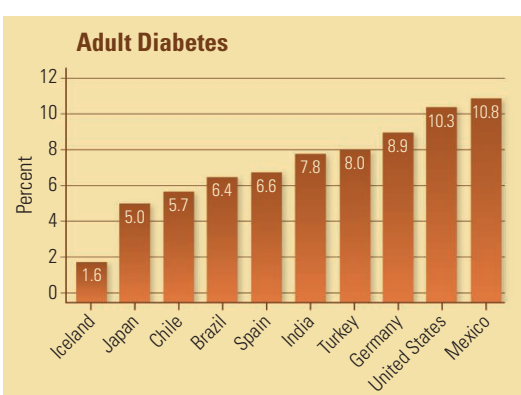
That didn't sit right with Slim, whose 2013 net worth of $67.1 billion ranked him as the second richest person in the world. In 2010, his foundation provided $65 million for SIGMA's first stage, during which scientists from Mexican universities and government institutes like the National Institute of Genomic Medicine (INMEGEN) here worked with Broad to comb through the Mexican genome for disease-related alleles. The search paid off: By sequencing tumors from Mexican patients, SIGMA-funded researchers found several new genes implicated in breast cancer. They also identified new mutations associated with head and neck cancer, and brought a decadelong struggle to a satisfying conclusion by pinpointing the genetic risk factor for the devastating kidney disease MCKD1. And perhaps most significant for Mexico, the country with the world's highest rate of adult diabetes (see graph), SIGMA researchers recently uncovered the first genetic risk factor for type 2 diabetes that appears to be specific to Latin American populations. The paper detailing the variant, called SLC 16 A11, is in press at *Nature*.

The Slim institute hopes to move fast to translate these basic discoveries into clinical tools, Betancourt says: "We are very impatient here." During SIGMA's second phase, which will last until 2016, Broad will take the lead on developing drugs that target the newly identified disease pathways, while Mexican partners work on new diagnostic tools for Latin American populations. "Everyone that shares the Amerindian genome will benefit" from SIGMA, Betancourt predicts.

Genomics experts hail the effort. "I have no question the goals [of SIGMA] will be achieved," says former INMEGEN director Gerardo Jiménez, a professor of public health at Harvard University. But translating genomics insights into useful tools and practices will take much longer than the program's 3-year second phase, Jiménez says, "especially in an economy like Mexico's," in which more than half the population lives in poverty.

Socioeconomic realities also mean that Mexican scientists must "aim for the lowest possible cost" by simplifying diagnostics and treatments or by focusing on technologies that don't require refrigeration or electricity, INMEGEN director-general Xavier Soberón says. "We cannot just copy" techniques that work in other countries. Only by taking into account Mexico's present reality will scientists be able to develop tools to help the descendents of Cortés and La Malinche reckon with the history written in their genomes. **–LIZZIE WADE**

Family tree. The typical Mexican genome contains a mixture of European and Amerindian ancestry, represented by the family in this 1770 painting.



At risk. An allele discovered by SIGMA researchers may help explain why Mexico has the world's highest prevalence of adult diabetes (2010 data).

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