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Shortcut in search for genes

Map of variations tracks the 0.1% setting us apart

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The search for the causes of complex genetic diseases received a major boost today with the publication of the first map of human genetic variations, the subtle genetic changes that make each of us different from our neighbors.

Humans worldwide share 99.9 percent of their genetic blueprint. It is that 0.1 percent difference, however, that makes each person unique, and that is the root of the genetic mischief that causes diseases like diabetes, asthma, hypertension, cancer and a host of others.

In the past, researchers had to sift through the entire 3 billion individual chemical letters, called "nucleotides," that comprise the human blueprint in their search for disease-causing genes. But now it has become clear that each of those individual changes, called "single nucleotide polymorphisms" or SNPs, is linked to a large block of DNA, called a "haplotype," that is generally inherited intact.

By focusing on haplotypes, researchers are able to reduce the number of sites that must be searched to a much more manageable 1 million, sharply speeding up the search for genetic change.

An international consortium of more than 200 researchers from six countries reported Wednesday at an American Society of Human Genetics meeting in Salt Lake City that they had completed a haplotype blueprint, called a "HapMap," using genetic information from individuals around the world. The map was to be published today in the journal Nature.

The map should help scientists "pinpoint the genetic basis of many human diseases more quickly and more efficiently than ever before," said Dr. Pui-Yan Kwok of UCSF, a team leader in the project.

Ferreting out the subtle differences between individuals in many different cultures and ethnic groups around the world, Kwok said, should lead to a deeper understanding of just how a wide variety of environments, lifestyles, diets and cultural pressures may have played a role in the processes of natural selection that have made some population groups susceptible to some diseases and resistant to others. "The HapMap is a phenomenal tool that is making possible research that was impractical, if not unimaginable, only a few years ago," said Dr. Yusuke Nakamura of the University of Tokyo's Human Genome Center. Identifying the genes that produce susceptibility to diseases such as diabetes will lead to new techniques for diagnosis, treatment and, eventually, even prevention, scientists said.

Already, researchers using preliminary data from the three-year $138 million project have identified a gene that plays a key role in age-related macular degeneration, the leading cause of blindness among

elderly people.

Teams in Japan, Canada and the United Kingdom have begun screening the haplotypes of thousands of individuals with a variety of diseases, comparing them with healthy control groups to identify genetic susceptibility not only to chronic diseases like hypertension and bipolar disorder, but also to infectious diseases like tuberculosis and malaria.

"We will see an outpouring of discovery in the next two to three years," said Dr. Francis Collins, director of the National Human Genome Research Institute of the National Institutes of Health, U.S. Department of Health and Human Services, Bethesda, Md.

The team used DNA from blood samples collected from 269 individuals around the world, including Japanese from Tokyo, Yoruba from Nigeria, Han Chinese from Beijing and Utah residents with ancestry from northern and western Europe.

Researchers will soon expand that database, using DNA samples from two other groups in Africa and five from the rest of the world, said Dr. Charles N. Rotimi of Howard University.

Chronicle Science Editor David Perlman contributed to this report.

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