

Southern African Genomes Sequenced: Benefits for Human Health Expected

Human genomes from Southern African Bushmen and Bantu individuals have been sequenced by a team of scientists seeking a greater understanding of human genetic variation and its effect on human health. The study's findings will be published in the journal *Nature* on 18 February 2010. The research was completed by scientists from American, African, and Australian research institutions, with support from Penn State University in the United States and from several U.S. companies that market DNA-sequencing instruments.

"We sequenced the personal genomes of four Bushmen participants who are tribal leaders from their communities and are at least 80 years of age, and from one Bantu participant who is in his late 70s," said Stephan Schuster, a professor at Penn State and a co-leader of the project. The *Nature* paper reveals the identities of each of these five participants. The other co-leader, Vanessa Hayes of the University of New South Wales, who also is a group leader at Children's Cancer Institute Australia, added, "The Bantu participant is Archbishop Desmond Tutu, who, through his Tswana and Nguni ancestry, is an ideal representative for most Southern Africans."

The study identified 1.3-million genetic variants that scientists previously had not observed. These genetic variations reveal that Southern Africans are quite distinct genetically from Europeans, Asians, and West Africans. The study also reveals striking levels of genetic differences among the individual study participants. Webb Miller, professor of biology and computer science at Penn State, who performed the comparative analysis of the genomes, underscores the genetic uniqueness of the Bushmen by saying, "On average, there are more genetic differences between any two Bushmen in our study than between a European and an Asian. To know how genes affect health, we need to see the full range of human genetic variation, and Southern Africa is the place to look."

This study used three new sequencing technologies, which deliver DNA sequences

with unprecedented economy and speed. Tim Harkins, who led the study's industry partners, said, "This project provides a unique opportunity to compare the strengths of current sequencing technologies, and it demonstrates that their combination results in data that is more accurate than from projects using only one of these methods." As sequencing technologies evolve, the number of genomic studies is growing exponentially. "Human genomics is becoming a realistic and powerful medical resource that will gain momentum in 2010," Schuster said.

A nearly life-long medical history accompanies each of the study's five personal genomes, facilitating the identification of genetic differences that may have contributed to particular health conditions. The researchers expect that these genomes will enable more accurate identification of diseases caused by rare genetic variants in Southern Africans and also in the global human population. To date, a genome-wide approach to identifying genetic disease susceptibility has disproportionately benefited the Western World in comparison to the African continent but "As a result of this project," Hayes said, "Southern Africans will immediately be included in genome-wide disease association studies, increasing our ability to examine regionally significant diseases."

Because the research team has made the five genomes sequenced in its study freely available, the scientists expect that Southern Africans will be better represented in future studies of how genetic variation influences the effectiveness of drugs -- a research field known as pharmacogenomics, which relies on human genome sequences and is considered by many to be the future of drug design. "To make our results easier to use than earlier genome sequences, we have established freely available Internet servers at Penn State," Miller said. Inclusion in pharmacogenomic studies is expected to benefit Southern Africans, who often have been poorly represented in pharmaceutical trials and who suffer from population-based differences in the effectiveness of drugs, such as anti-viral treatments for HIV/AIDS. The new data also is expected to help Southern African scientist and Southern African entrepreneurs to develop appropriate treatments when world-wide approaches fail locally.

The Bushmen that participated in this study are the first people whose genomes have been sequenced that still practice a hunter/gatherer lifestyle, enabling scientists to correlate the unique physiology of Bushmen with the genetic variants detected in this study. "The availability of Bushman and Southern African Bantu genomes permits researchers to examine one of the few remaining instances in the world of coexisting foraging and farming groups," said Schuster. The study identified several genetic adaptations in the Bushmen that make them ill-suited to certain perils of an agricultural lifestyle, including high-fat diets and exposure to malaria.

The research, which involved 50 investigators, was led by Penn State University. Other institutions participating in the study include the Children's Cancer Institute Australia, the University of New South Wales, the University of Washington, the Human Genome Sequencing Center at Baylor College of Medicine, Harvard Medical School, the University of Limpopo in the Republic of South Africa, Cornell University, the Genome Center of Washington University in St. Louis, the Broad Institute, the Sperling Foundation, and the National Human Genome Research Institute, along with supporters in Namibia. Industrial partners of the study include Roche Diagnostics Corporation and Applied Biosystems, with several additional U.S. companies having opted to join the ongoing project in the future.

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