

Scientists decode human chromosome 16

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The U.S. Department of Energy Joint Genome Institute (JGI), culminating a 16-year effort, has completed its share of the Human Genome Project with the publication of the DNA sequence and analysis of [chromosome](#) 16 in the Dec. 23 issue of [Nature](#).

"The Department of Energy is very proud of its historic role in the sequencing of the human genome--and very excited by the advances our pioneering discovery-class science now is making possible in the fields of both medicine and energy," said Secretary of Energy Spencer Abraham. "DOE launched the human genome program and developed the DNA sequencing and computational technologies that made possible the unraveling of the human genetic code. Now we are using these skills and resources as a powerful tool for clean energy and a cleaner environment."

U.S. Sen. Pete Domenici (R-NM), a leading congressional proponent of efforts to sequence the human genome, was the catalyst for freeing up the first significant federal genomics investment. "DOE has risen to the challenge and fulfilled the promise made to the public. Their work has led to the identification of signatures embedded in the DNA sequence that control the intricate functions conducted by the trillions of cells in our bodies.

"The considerable resources that DOE has assembled to tackle the human genome are now being dedicated to illuminating the genomes of organisms that may figure into biological solutions to such challenges as economical hydrogen production, carbon sequestration, and environmental clean-up," Domenici said.

Three Chromosomes Completed

JGI is the first of the five primary Human Genome Project sequencing sites, known as the "G5," to publish scientific articles describing each of the human chromosomes that they originally committed to sequence. DOE's commitment entailed chromosomes 5, 16, and 19, all sequenced by JGI, representing 11 percent of the human genome.

The Nature paper delves into the 78.8 million bases, or letters of DNA code, on Chromosome 16, home to 880 genes including those implicated in the development of breast and prostate cancer, Crohn's disease and adult polycystic kidney disease. With the advancements accrued over the last five years at the JGI Production Genomics Facility, sequence is now being produced at a rate of 2.5 billion bases per month--or the equivalent of a human genome in just five weeks.

JGI researchers characterized the many regions on chromosome 16 that have been copied to other places within the chromosome, and even to the other chromosomes, a phenomenon known as segmental duplication. They compared these human sequences to regions conserved over time in other vertebrate genomes, including chimpanzee, dog, mouse, rat, chicken and pufferfish to shed light on changes that have occurred since the last common ancestor, ranging from five million to 400 million years ago.

The effort to complete the sequence of chromosome 16 was led by JGI researchers Joel Martin and Len Pennacchio and included over 100 researchers from the partnership of Los Alamos, Lawrence Berkeley and Lawrence Livermore national laboratories, as well as the Stanford Human Genome Center, the Department of Genome Science of the University of Washington, and Children's Hospital in Oakland, CA. In addition to the research article in Nature, a large color poster highlighting biologically important elements of all three chromosomes

sequenced by JGI along with DOE's other contributions to genomics is featured in the publication.

"The success of the Human Genome Project was enabled by the selfless dedication and creativity of thousands of scientists around the world," said Aristides Patrinos, Associate Director of Science for Biological and Environmental Research, who has led the DOE genomics effort since 1995. "It has been an honor and a thrill to the DOE team to have played such a pivotal role in the launching and successful completion of this most noble of human undertakings."

Chromosome 16 was the original focus of DNA repair gene studies initiated at DOE's Los Alamos National Laboratory in 1988. Additional interest stemmed from the discovery of genes on chromosome 16 implicated in the detoxification and transport of heavy metals.

Genome Effort Began in 1987

The Department of Energy and its predecessor agencies for decades have sponsored genomics research, including basic studies of DNA replication, damage, and repair, and the consequences of radiation-induced heritable mutations. In 1987, recognizing its pioneering contributions to discovery class science, a federal report recommended DOE assume a leadership role in an expansive multidisciplinary undertaking to map and sequence the human genome. Thus, between 1988 and 1989, three genome research centers were established at Lawrence Berkeley, Lawrence Livermore, and Los Alamos national laboratories. These were combined in 1997 into the DOE Joint Genome Institute (JGI).

With this genomics powerhouse now recognized, JGI continues to advance the frontiers of genome sciences through the advent of the Community Sequencing Program (CSP). The CSP will provide a world-

class sequencing resource for the expanding diversity of disciplines--geology, oceanography, and ecology, among others--that can benefit from the application of genomics. Priority is given to sequencing organisms that are relevant to DOE missions.

"The Human Genome Project stands as the crown jewel and capstone of 20th century biology," said Charles DeLisi, Arthur G. B. Metcalf Professor of Science and Engineering at Boston University. "The Department of Energy's role as the project's prime mover, and its continued leadership throughout the course of the project, reminds us of the enormous wealth of talent in the DOE national laboratory system--talent that, in the case of the HGP, has served not just the nation, but all the peoples of the world."

From 1985 to 1987, DeLisi led the effort to launch the Human Genome Project, galvanizing an international team of researchers to collect the necessary resources, develop groundbreaking technologies, and propel the nation in an epic quest to map and sequence the human genome.

Source: DOE/Joint Genome Institute

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