



# NIH NEWS RELEASE

National Human Genome Research Institute

## **FOR IMMEDIATE RELEASE**

For more information, contact:  
Geoff Spencer  
NHGRI  
(301) 402-0911  
[spencerg@mail.nih.gov](mailto:spencerg@mail.nih.gov)

## **NHGRI Expands Effort to Revolutionize Sequencing Technologies**

### *Grants Awarded to Develop Faster, Cheaper DNA Sequencing*

**BETHESDA, Md.**, Mon., Aug. 8, 2005 – The National Human Genome Research Institute (NHGRI), part of the National Institutes of Health (NIH), today announced it has awarded grants totaling more than \$32 million to advance the development of innovative sequencing technologies intended to reduce the cost of DNA sequencing and expand the use of genomics in biomedical research and health care.

“The efforts are aimed at speeding the rate at which the next generation of sequencing technologies become available in the scientific lab and the medical clinic,” said NHGRI Director Francis S. Collins, M.D., Ph.D. “Not only will these technologies substantially reduce the cost of sequencing a genome, but they will provide a quantum leap in the scope and scale of research aimed at uncovering the genomic contributions to common diseases, such as cancer, heart disease and diabetes.”

Over the past decade, DNA sequencing costs have fallen more than 50-fold, fueled in large part by tools, technologies and process improvements developed as part of the successful effort to sequence the human genome. However, it still costs about \$10 million to sequence 3 billion base pairs – the amount of DNA found in the genomes of humans and other mammals.

NHGRI’s near-term goal is to lower the cost of sequencing a mammalian-sized genome to \$100,000, which would enable researchers to sequence the genomes of hundreds or even thousands of people as part of studies to identify genes that contribute to common, complex diseases. Ultimately, NHGRI’s vision is to cut the cost of whole-genome sequencing to \$1,000 or less, which will enable the sequencing of individual genomes as part of routine medical care. The ability to sequence an individual genome cost-effectively could enable health care professionals to tailor diagnosis, treatment and prevention to each person’s unique genetic profile.

The new grants balance NHGRI’s sequencing research portfolio by supporting more investigators working on technologies that would make it feasible to sequence a genome for \$1,000. The majority of researchers who received NHGRI’s initial sequencing technology grants, issued in October 2004, are working on technologies to sequence a genome for \$100,000. Both approaches have many complementary elements that integrate biochemistry, chemistry and physics with

engineering to enhance the whole effort to develop the next generation of DNA sequencing and analysis technologies.

“It is very important that we encourage and support the variety of sequencing technology projects that hold the most promise for revolutionizing genome sequencing. Each research team brings a unique set of skills and expertise to solving difficult scientific and engineering problems,” said Jeffery Schloss, Ph.D., NHGRI’s program director for technology development. “The different approaches will likely yield several successful and complementary technologies. It is going to be interesting to see how each technology progresses and which of them can ultimately be used by the average researcher or physician.”

### **“\$1,000 Genome” Grants**

NHGRI’s “Revolutionary Genome Sequencing Technologies” grants have as their goal the development of breakthrough technologies that will enable a human-sized genome to be sequenced for \$1,000 or less. Grant recipients and their approximate total funding are:

**Richard B. Fair, Ph.D., Duke University, Durham, N.C.**

**\$510,000 (2 years)**

**“Droplet-Based Digital Microfluidic Genome Sequencing”**

The near-term goal of this group is to demonstrate how existing droplet-based microfluidic electro-wetting technology can be modified to perform sequencing by synthesis reaction chemistry. This method allows for smaller volumes of materials to be used as well as the decoupling of synthesis and detection steps, resulting in more efficient automation.

**M. Reza Ghadiri, Ph.D., The Scripps Research Institute, La Jolla, Calif. and  
Hagan P. Bayley, Ph.D., Oxford University, UK.**

**\$4.2 million (5 years)**

**“Single-Molecule DNA Sequencing with Engineered Nanopores”**

This project is a collaborative effort between two laboratories that have experience in nanopore research, protein engineering and molecular recognition. The group will engineer a device with the ability to recognize a nucleotide on the basis of changes in electrical current, as it passes through a membrane with tiny channels known as nanopores.

**Jene A. Golovchenko, Ph.D., Harvard University, Cambridge, Mass.**

**\$5.2 million (3 years)**

**“Electronic Sequencing in Nanopores”**

The objective of this project is to develop a general utility instrument to provide inexpensive sequencing that can also be used for projects to recognize genome variation. The group will design novel nanopores articulated with probes to sequentially, and directly, identify nucleotides in very long fragments of genomic DNA based on their unique electronic signals.

**Susan H. Hardin, Ph.D., VisiGen Biotechnologies, Inc., Houston.**  
**\$4.2 million (3 years)**  
**“Real-Time DNA Sequencing”**

This group is developing a sequencing system in which polymerase (an enzyme used to synthesize DNA molecules) and nucleotides act together as direct molecular sensors of DNA base identity. The key to the system is the interaction between a fluorescent polymerase and the nucleotide, which emits a signature detectable in real-time.

**Xiaohua Huang, Ph.D., University of California, San Diego, La Jolla.**  
**\$750,000 (3 years)**  
**“Massively Parallel Cloning and Sequencing of DNA”**

The goal of this project is to develop two innovative technologies: massively parallel, whole-genome amplification and DNA sequencing by denaturation. The resulting system amplifies DNA directly on a microchip, enabling the process of sequencing to be done on a single miniaturized device.

**Jingyue Ju, Ph.D., Columbia University, New York.**  
**\$970,000 (3 years)**  
**“Modulating Nucleotide Size in DNA for Detection by Nanopore”**

This group will design and synthesize modified nucleotides of different sizes, which can be incorporated into DNA. When passed through nanopores, the differences between these modified nucleotides will be easier to detect, producing clean sequencing data.

**Bhubaneswar (Bud) Mishra, Ph.D., New York University, New York.**  
**\$585,000 (2 years)**  
**“Haplotype Sequencing Via Single Molecule Hybridization”**

Investigators from this group will hybridize short DNA probes to genomic DNA fragments to determine sequence information. In addition, they will use optical mapping to create restriction maps to help assemble the genome once it is sequenced. The group will then demonstrate how to combine the sequence and maps into distinct haplotype sequences.

**Gregory L. Timp, Ph.D., University of Illinois at Urbana-Champaign.**  
**\$2.1 million (3 years)**  
**“Sequencing a DNA Molecule Using a Synthetic Nanopore”**

This group will explore the feasibility of sequencing a DNA molecule using a type of silicon integrated circuit. The circuit incorporates a nanopore mechanism with a molecular trap that forces the DNA molecule to oscillate back and forth between electrodes, measuring the electrical signal associated with each specific base.

**Stephen W. Turner, Ph.D., Nanofluidics, Menlo Park, Calif.**  
**\$6.6 million (3 years)**  
**“Real-Time Multiplex Single-Molecule DNA Sequencing”**

This group will leverage their “zero-mode waveguide” technology to detect single nucleotides in real-time, as they are incorporated by a DNA polymerase into a growing DNA molecule. The ultimate goal is to create a real-time, multiplex single-molecule DNA sequencing system that produces sequence reads containing hundreds of thousands of nucleotides.

### **“\$100,000 Genome” Grants**

NHGRI’s “Near-Term Development for Genome Sequencing” grants will support research aimed at sequencing a human-sized genome at 100 times lower cost than is possible today. There is strong potential that, five years from now, some of these technologies will be at or near commercial availability. Grant recipients and their approximate total funding are:

**Gina L. Costa, Ph.D., Agencourt Personal Genomics., Beverly, Mass.  
\$1.2 million (2 years)  
“Bead-Based Polony Sequencing”**

Supplemental funding is expected to accelerate commercialization of this technology that will use oligonucleotide ligation to read DNA sequence, using bead-based, polymerase colony (polony) sequencing technology.

**Vera B. Gorfinkel, Ph.D., The State University of New York (SUNY),  
Stony Brook, N.Y.  
\$1.5 million (2 years)  
“Ultra High Throughput DNA Sequencing System Based on Two-Dimensional  
Monolith Multi-Capillary Arrays and Nanoliter Reaction Volume”**

This group will develop and implement an efficient method capable of sequencing mammalian size genomes by amplifying single template molecules, and subjecting the product to Sanger sequencing and a highly parallel, capillary electrophoresis separation system.

**Greg Kellogg, Ph.D., Network Biosystems, Woburn, Mass.  
\$4.5 million (3 years)  
“\$100,000 Genome Using Integrated Microfluidic Capillary Electrophoresis”**

This group will work to improve performance of Sanger sequencing and PCR as compared to that attainable using capillary electrophoresis systems. To do so, it will miniaturize and integrate current sequencing technologies, building on its microfluidics platform.

For more details about the NHGRI sequencing technology development grants, go to:  
| <http://www.genome.gov/15015202>. NHGRI is one of 27 institutes and centers at NIH, an agency of the Department of Health and Human Services. Information about NHGRI can be found at: [www.genome.gov](http://www.genome.gov).

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