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NHGRI Funds Large-Scale Sequencing Centers

New Era of Sequencing for Cancer and Other Medical Purposes Begins

BETHESDA, Md., Mon., Nov. 20, 2006 **–** The National Human Genome Research Institute (NHGRI) today announced the results of the recent competition for support of its three large-scale sequencing centers, strengthening efforts to use the power of DNA sequencing to unlock the genomic secrets of human diseases. Also today, NHGRI and the National Cancer Institute (NCI), both part of the National Institutes of Health (NIH), announced that all three sequencing centers will devote a significant part of their efforts to The Cancer Genome Atlas (TCGA) Pilot Project, which is testing the feasibility of a large-scale, systematic approach to identify important genomic changes involved in cancer.

"Genomic sequencing has already made a substantial impact on both biological and medical research. A major focus of the next phase will be medical sequencing, which involves using sequencing technologies to identify genes that contribute to common human diseases, most of which have so far eluded gene hunters," said NHGRI Director Francis S. Collins, M.D., Ph.D. "These discoveries will shed new light on the biological pathways involved in human health and disease, which in turn will lead to better strategies for diagnosis, treatment and prevention. It is gratifying that our sequencing centers are going to play a major role in bringing the promise of personalized health care closer to reality."

The sequencing centers were selected through a competitive, peer-reviewed process based on scientific merit of each center's application, as well as costs and efficiency. The three NHGRI-supported, large-scale sequencing centers, their principal investigators and their approximate Fiscal Year (FY) 2007 funding levels are:

- Broad Institute Sequencing Platform, The Eli & Edythe L. Broad Institute of the Massachusetts Institute of Technology and Harvard University; Eric S. Lander, Ph.D.; Cambridge, Mass.; $48 million.

- Washington University Genome Sequencing Center, Washington University School of Medicine, Saint Louis; Richard K. Wilson, Ph.D.; $41 million.

- Human Genome Sequencing Center, Baylor College of Medicine, Houston; Richard Gibbs, Ph.D.; $27.6 million.

The sequencing centers will be funded under cooperative agreements in which substantial programmatic involvement is anticipated among NHGRI and the recipients during performance of the scientific activities. The cooperative agreements also require each sequencing center to participate in the NHGRI's Minority Action Plan by developing and implementing a training and education program to increase the number of under-represented minorities in genomic sciences.

Over the next four years, the centers in NHGRI's Large-Scale Sequencing Research Network will utilize existing technology to continue large-scale sequencing of important targets. Almost half of the sequencing capacity will be dedicated to medical sequencing. The sequencing centers will also pursue new ways to increase the speed and lower the cost of DNA sequencing by testing and implementing several new technologies, which could potentially revolutionize large-scale sequencing and expand the use of genomics in medical research and health care. The combined sequence output from the centers, using current technologies, is expected to be about 12 billion DNA base pairs per month – the equivalent of four human genomes.

A significant portion of NHGRI's medical sequencing program will be used for The Cancer Genome Atlas (TCGA), which was launched in December 2005 as a $100 million, collaborative three-year pilot project between NHGRI and NCI. TCGA consists of four integrated components: the Genome Sequencing Centers announced today, plus seven Cancer Genome Characterization Centers, a Data Collection Center, and the Biospecimen Core Resource. In the pilot phase of TCGA , the Genome Sequencing Centers will sequence a substantial number of selected gene targets to identify genomic changes, such as single base mutations and small insertion/deletions, in three types of tumors: brain (glioblastoma), lung (squamous cell), and ovarian.

"Cancer is an extremely complex disease. The Genome Sequencing Centers will play a pivotal role in our systematic effort to assess the range of genomic changes associated with malignancy," said Mark S. Guyer, Ph.D., director of NHGRI's Division of Extramural Research. "This genomic information will provide the research community with a powerful tool for uncovering new therapeutic targets and developing better strategies for diagnosing, treating and preventing cancer."

Other medical sequencing projects will use DNA sequencing to: discover new genes that are involved in common diseases; identify the genes responsible for dozens of relatively rare, single-gene (autosomal Mendelian) diseases; sequence all of the genes on the X chromosome from affected individuals to identify those involved in sex-linked diseases; and survey the range of variants in genes known to contribute to certain common diseases. The start of each project will depend on a number of factors, including the strategic selection of specific diseases and the availability of patient samples with appropriate informed consent.

"The availability of the human genome sequence, as well as other genomic resources produced by our sequencing centers, has transformed biomedical research everywhere," said NHGRI's Associate Director of Extramural Research Jane Peterson, Ph.D., who is also a program director for NHGRI's Large-Scale Sequencing Research Network. "The addition of medical sequencing projects is challenging and quite exciting. Making these data publicly available to researchers will build upon the past success of NHGRI's rapid data access model, and will continue to expand our knowledge of human health and disease."

The sequencing centers also will focus increased attention on sequencing the genomes of organisms, such as bacteria, fungi, parasites and insects, which cause or transmit human diseases. In addition, they will pursue promising new areas of health-related research. For example, the large-scale sequencing program has already started to sequence the genomes of 100 microorganisms found in the human gut, and will build on this by using genomic sequencing to characterize the complex microbial communities found at many sites in and on the human body. Microbes have a profound effect on many human physiological processes, such as digestion and drug metabolism, and play a vital role in disease susceptibility. It is hoped new information about these organisms will lead to improved methods for monitoring and maintaining human health.

In addition to medical sequencing and technology development efforts, the sequencing research network will continue its groundbreaking work in comparative genomics, which involves sequencing and comparing the genomes of various organisms. This has proven to be one of the most powerful ways of identifying the parts of the human genome that are most functionally important, and therefore most likely to be relevant for an understanding of disease. In addition to the large-scale sequencing centers, other important comparative sequencing data will be contributed by the NIH Intramural Sequencing Center (NISC) in Rockville, Md. NISC conducts sequencing projects for NIH investigators and also generates sequence data to support various NHGRI sequencing program activities. NISC funding will be around $7 million, with half of this coming from intramural funds.

Since the completion of the human genome sequence in 2003, the sequencing centers have sequenced and published analyses of the genomes of a wide range of animals, including the mouse, chimpanzee, chicken, dog, rat, honey bee and sea urchin. This has provided researchers with a powerful tool for understanding the structure and function of the human genome. For instance, DNA sequences that are shared, or conserved, between humans and another species may be essential for turning genes on and off during development.

NHGRI's process for selecting sequencing targets to enter the pipeline for the sequencing centers begins with three working groups comprised of experts from across the research community. Each of the working groups is responsible for developing a proposal for a set of genomes to sequence that would advance knowledge in one of three important scientific areas: identifying areas in genetic research where the application of high-throughput sequencing resources would rapidly lead to significant medical advances; understanding of the human genome; and understanding the evolutionary biology of genomes.

A coordinating committee then reviews the working groups' proposals, helping to fine-tune the suggestions and integrate them into an overarching set of scientific priorities. The intent of the target selection process is to maintain flexibility so the focus of the sequencing program can be adjusted as the state of knowledge improves over the next four years in order to pursue the most biomedically compelling sequencing targets. The recommendations of the coordinating committee are reviewed and approved by the National Advisory Council for Human Genome Research, which in turn forwards its recommendations to NHGRI leadership. For more on the selection process, go to: www.genome.gov/Sequencing/OrganismSelection.

In addition, each sequencing center may use up to 10 percent of its capacity to work on targets of its own choosing. This will afford the sequencing centers some flexibility to demonstrate innovative uses of sequence information.

A complete list of organisms and their sequencing status can be viewed at www.genome.gov/10002154. High-resolution photos of many of the organisms being sequenced in NHGRI's Large-Scale Sequencing Program are available at: www.genome.gov/10005141.

NHGRI is one of the 27 institutes and centers at the National Institutes of Health, an agency of the Department of Health and Human Services (DHHS). Additional information about NHGRI can be found at its Web site, www.genome.gov.

For more information about cancer and the National Cancer Institute, please visit the NCI Web site at www.cancer.gov or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

More information about The Cancer Genome Atlas Pilot Project is available at http://cancergenome.nih.gov/.

The National Institutes of Health (NIH) — *The Nation's Medical Research Agency* — includes 27 Institutes and Centers and is a component of the U. S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

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