January 5, 2016

Happy New Year! We have many things to celebrate as we begin 2016, including a budget increase for NIH! On December 18, President Obama signed the Fiscal Year 2016 Omnibus Bill into law, which provides NIH an additional $2 billion in funding. As our first substantive budget increase in a very long time, all NIH leaders are celebrating the much-needed additional funds for biomedical research. For example, see NIH Director Dr. Francis Collins' statement at nih.gov/about-nih/who-we-are/nih-director/statements/statement-fy2016-omnibus-bill.

Beyond this great budget news, we have plenty of things to highlight as we start the new year. In this month's *The Genomics Landscape*, I feature the next stage of NHGRI's ENCyclopedia of DNA Elements (ENCODE) Project. See various details below, along with other information items that I hope will be of interest to you.

Specifically, January's *The Genomics Landscape* features stories about:

- Future of ENCODE: Looking Deeper into Genome Function
- *Genome: Unlocking Life's Code* Travels to Milwaukee, WI
- 25th Anniversary of Human Genome Project's Launch: Seminar Series Video Available
- Welcoming New NHGRI Advisors
- NIH Unveils 2016-2020 Strategic Plan

All the best,

Watch here for current and upcoming locations of the Smithsonian-NHGRI exhibition "Genome: Unlocking Life's Code" as it tours North America!

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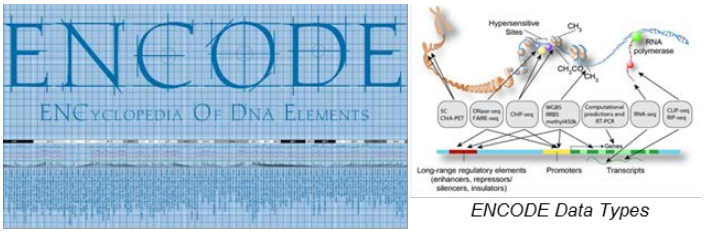
~To access past editions, see: genome.gov/27541196~

Future of ENCODE: Looking Deeper into Genome Function

The billions of chemical units of DNA that make up a human genome work in often mysterious ways in providing the instructions to build and operate all the cells in the human body. The Human Genome Project, which determined the order of those chemical units (also called nucleotides or bases), was completed nearly 13 years ago. So, what is left to understand? As it turns out – a ton! In fact, genome scientists are just beginning to scratch the surface of understanding all the intricacies of human genome function and how genomic differences influence health and disease.

The genome is not organized in a simple way – for example, it does not partition into a 'protein' part, a 'regulatory' part, a 'cancer' part, or a 'heart disease' part. Rather, different functions are encoded by bits of DNA that are essentially interspersed across the genome. This leaves researchers the challenging task of scanning the genome base-by-base, looking for clues in the DNA that might indicate the presence of functional elements. Such elements include genes that code for proteins and regulatory sequences that turn those genes on and off.

NHGRI's largest program dedicated to understanding how the human genome works is the ENCyclopedia of DNA Elements (ENCODE) Project. ENCODE was conceived just as the Human Genome Project was ending, aiming to build a robust understanding about the human genome beyond its sequence. The overarching goals of ENCODE included identifying and developing the best laboratory and computational techniques for finding functional DNA elements, applying them to analyze the human genome, and making the resulting data widely available.



ENCODE Data Types

Because the human genome is large and complex, ENCODE was started as a pilot in 2003, with an initial focus on a defined 1% of the human genome. After completing the pilot, ENCODE expanded in 2007 to work on the entire human genome, publishing a large set of findings in 2012. Substantial amounts of additional data and insights have been generated since then. At the same time, there is a growing need to understand what the genomic elements catalogued by ENCODE actually do.

To take stock of ENCODE's accomplishments to date and to help frame NHGRI's future research efforts in this area, the Institute held the program review workshop "From Genome Function to Biomedical Insight: ENCODE and Beyond" in March 2015. The recommendations emanating from this workshop included continuing genome-wide

Genome: Unlocking Life's Code Travels to Milwaukee, WI

The *Genome: Unlocking Life's Code* exhibition is now on its way to Discovery World in Milwaukee, WI. The exhibition will be in Milwaukee from January 18 to April 25, 2016. Discovery World has several exhibition-related programs planned, including hands-on activities, visitor exploration of their own personal ancestry stories, and a visiting genealogist. Programming will be designed to offer families and students an opportunity to explore genome science more deeply and to allow Discovery World to expand its role as a leader in workforce development.

25th Anniversary of Human Genome Project's Launch: Seminar Series Video Available

From the left: Drs. Elke Jordan, Mark Guyer, and Eric Green at the opening seminar.

Last month, the NHGRI History of Genomics Program kicked off a seminar series celebrating the 25th anniversary of the launch of the Human Genome Project (HGP). The six-part, monthly series is entitled "A Quarter Century after the Human Genome Project's Launch: Lessons Beyond the Base Pairs." The first installment in December was a panel discussion with former NHGRI Deputy Directors Dr. Elke Jordan and Dr. Mark Guyer. As the 2nd and 4th employees of the Office of Human Genome Research in the NIH Office of the Director (this Office later became what is now NHGRI), Drs. Jordan and Guyer provided unique perspectives on the early days of the Institute and the establishment and management of the HGP. A video recording of this opening

identification and cataloging of functional elements in the human genome – activities that were pursued in all previous phases of ENCODE. A new high-priority recommendation called for expanding efforts to understand how the functional genomic elements actually work. Such an effort will require that researchers test the catalogued elements to determine what roles, if any, they play in human biology. In addition, future efforts should examine the function of the elements in a range of biological conditions and diseases.

Following the workshop's recommendations, NHGRI will issue funding opportunity announcements (FOAs) for a five-part ENCODE program that includes: Functional Element Mapping Centers, Functional Element Characterization Centers, Computational Analysis Centers, a Data Analysis Center, and a Data Coordination Center. Through awards issued in response to these FOAs, expected to be made later this year, NHGRI hopes to continue ENCODE's strong tradition as a dynamic and productive research program.

In 2015, NHGRI launched two other programs to explore the function of the human genome. The Genomics of Gene Regulation (GGR) program aims to decipher the language of how and when genes are turned on and off, and how the molecules that regulate this activity work together. GGR will thus help scientists understand how regulatory elements and genes interact. In another program, NHGRI and the National Cancer Institute have awarded grants for developing new computational approaches that integrate data from many sources to help determine the functional consequences of genomic variants – differences in DNA between individuals. Such data would narrow the set of genomic variants, millions of which are known, down to a smaller number that might be relevant to human health and disease.

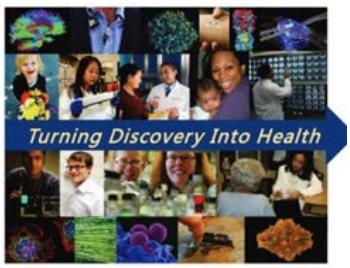
Through all these efforts, NHGRI hopes to foster research that increases our knowledge about functional elements in the human genome by cataloguing them, determining what they do, and establishing their connection to human biology. This body of work reflects yet another layer of complexity associated with the human genome. Fully understanding all of the genome's complexity will require the effort of multiple generations of scientists – well beyond my lifetime – but NHGRI envisions playing a leadership role for these efforts over the long haul.

event is now available on GenomeTV. Subsequent seminars by other HGP participants will follow this month through May 2016; these will also be video recorded and made available on GenomeTV. For the full seminar series schedule, see genome.gov/27562713.

Welcoming New NHGRI Advisors

NHGRI interacts extensively with external experts, who advise the Institute in setting and achieving its goals for advancing genomics research. I would like to welcome newly nominated/appointed members of our two major advisory groups – the National Advisory Council for Human Genome Research (NACHGR; see above photo), which mostly provides advice about our Extramural Research Program, and the Board of Scientific Counselors (BSC), which provides advice about our Intramural Research Program. Jonathan Pritchard, Ph.D., David Walt, Ph.D., Gail Henderson, Ph.D., Brenton Graveley, Ph.D., and Mark Johnston, Ph.D., have been nominated to become new NACHGR members. Brendan Lee, M.D., Ph.D. has been appointed to the BSC.

NIH Unveils 2016-2020 Strategic Plan



Last month, NIH submitted an NIH-wide Strategic Plan to Congress – an unusual occurrence given that it has been over 20 years since NIH last undertook an agency-wide strategic planning process. Traditionally, NIH operates as distinct Institutes, Centers, and Offices, most of which develop their own individual strategic plans aligned with their congressionally mandated missions. The new NIH-wide Strategic Plan complements the individual Institutes, Centers, and Offices plans, and outlines a vision for biomedical research that capitalizes on NIH's holistic strengths and capabilities. The Strategic Plan focuses on four objectives to help guide NIH's priorities over the next five years. For further details and to view the Strategic Plan, visit nih.gov/about/strategic-plan.

Spotlight on the Precision Medicine Initiative (PMI)

nih.gov/precisionmedicine

- Four PMI Funding Opportunities are still open, with closing dates in February.
- Frequently Asked Questions posted related to the PMI Cohort Program funding opportunities.
- Pursuing Precision Medicine for Chronic Kidney Disease – an example of identifying new biologically important indicators and testing them in cohorts.
- Precision Medicine and FDA – Emerging Cloud Platform in Beta.
- NIH Calls for Input on Strategies for Administering Physical Evaluations and Collecting Biological Samples from PMI Cohort Program Direct Volunteers – Request for Information open until January 15.
- In a Q&A for POLITICO, Drs. Francis Collins, Kathy Hudson, and Jim Ostell discuss the Precision Medicine Initiative.

Genomics Research

Link Between Congenital Heart Disease and Neurodevelopment Issues in Children Found

T-Cell Transcription Factor May Offer New Pathway for Vaccine Research

Study Uncovers Hard-to-Detect Cancer Mutations

Stunning Diversity of Gut Bacteria Uncovered by New Approach to Gene Sequencing Devised at Stanford

International Study Reveals New Genetic Clues to Age-Related Macular Degeneration

Genome Misfolding Unearthed as New Path to Cancer

Genomics News

Science's Breakthrough of the Year

Top Stories of 2015: Pluto, Gene Editing, a New Hominid and More

The Scientist: Top 10 Innovations 2015

Funding Opportunities

GTEx Legacy Project

Environmental Influences on Child Health Outcomes (ECHO): Patient Reported Outcomes Research Resource Center Core, Pediatric Cohorts, Data Analysis Center, and Coordinating Center

IDeA States Pediatric Clinical Trials Network: Clinical Sites and Data Coordinating and Operations Center

High-End Instrumentation Grant Program

Shared Instrumentation Grant Program

Request for Information

Second Draft Specification for Conformant Cloud Providers

NIH News of Interest

This Holiday Season, Resolve to Discover Your Family Health History

NHGRI Summarizes Proposed Changes to the Common Rule Relevant to Genomics Research

Funding News

Revised NIH Grants Policy Statement for FY 2016

Revised Instructions for Applications Due On and Between January 25 and May 24, 2016

Updates to Research Performance Progress Reports to Address Rigor and Transparency

Coming Requirements for Rigor and Transparency: Institutional Training Grants and Individual Fellowships

Notice to Extend Dissemination and Implementation Research in Health: PAR-13-055 (R01), PAR-13-054 (R21), and PAR-13-056 (R03)

Clarification of Eligibility for K99/R00 Applications

New Salary and Research Cost Allowances for K08 and K23 Career Development Awards

ASSIST Now an Option for All NIH Competing Grant Applications and Some Post-award Administrative Actions