DIRECTOR’S REPORT

National Advisory Council for Human Genome Research

February 2017

Eric Green, M.D., Ph.D.
Director, NHGRI
### Director's Report-Related Documents: February 2017

<table>
<thead>
<tr>
<th>No.</th>
<th>Relevant Documents</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>20th Anniversary of Institute Status</td>
</tr>
<tr>
<td>2</td>
<td>Francis Collins &quot;Held Over&quot; as NIH Director</td>
</tr>
<tr>
<td>3</td>
<td>New Chief Executive Officer, NIH Clinical Center</td>
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<td>4</td>
<td>Kathy Hudson Departs as NIH Associate Director for Science, Outreach, and Policy</td>
</tr>
<tr>
<td>5</td>
<td>Phil Bourne Departs as NIH Associate Director for Data Science</td>
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<tr>
<td>6</td>
<td>21st Century Cures Act</td>
</tr>
<tr>
<td>7</td>
<td>Common Rule Revisions Finalized</td>
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</tbody>
</table>
Open Session Presentations

- NIH Data Commons
  Vivien Bonazzi

- NHGRI Data Sandbox
  Valentina Di Francesco

- Genomics and Society Working Group
  Lisa Parker

- Building Bonds between NHGRI and NICHD
  Diana Bianchi
I. General NHGRI Updates
II. General NIH Updates
III. General Genomics Updates
IV. NHGRI Extramural Research Program
V. NIH Common Fund/Trans-NIH
VI. NHGRI Division of Policy, Communications, and Education
VII. NHGRI Intramural Research Program
NHGRI celebrates 20 years

20th Anniversary of Institute Status
Transition of NHGRI Chief Information Officer

Ed Whitley
New NHGRI Chief Information Officer

Joe Henke
Retirement of Clinical Advisor, Division of Policy, Communications, and Education

Jean Jenkins, PhD, RN, FAAN
Workshop on the Use of Race and Ethnicity in Genomics and Biomedical Research

- Co-sponsored by NHGRI and NIMHD
- Examined the complex relationships between individual identity, genetics, and health
Director’s Report Outline

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VI. NHGRI Division of Policy, Communications, and Education
VII. NHGRI Intramural Research Program
Francis Collins “Held Over” as NIH Director

Francis Collins, M.D., Ph.D.
## 2017 Congressional Leadership

### NIH Oversight Committees

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<th></th>
<th><strong>House</strong></th>
<th><strong>Senate</strong></th>
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<tr>
<td><strong>Appropriation</strong></td>
<td>Labor, HHS, &amp; Education</td>
<td>Labor, HHS, &amp; Education</td>
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<tr>
<td></td>
<td>Chairman Tom Cole (OK)</td>
<td>Chairman Roy Blunt (MO)</td>
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<tr>
<td></td>
<td>Ranking Rosa DeLauro (CT)</td>
<td>Ranking Patty Murray (WA)</td>
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<td></td>
<td>Chairman Greg Walden (OR)</td>
<td>Chairman Lamar Alexander (TN)</td>
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<tr>
<td></td>
<td>Ranking Frank Pallone (NJ)</td>
<td>Ranking Patty Murray (WA)</td>
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<tr>
<td><strong>Health Subcommittee</strong></td>
<td>Chairman Michael Burgess (TX)</td>
<td></td>
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<tr>
<td></td>
<td>Ranking Gene Green (TX)</td>
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Greg Walden (OR)

Michael Burgess (TX)
New Chief Executive Officer, NIH Clinical Center

Major General James Gilman, M.D.
Kathy Hudson Departs as NIH Associate Director for Science, Outreach, and Policy

Kathy Hudson, Ph.D.
Phil Bourne Departs as NIH Associate Director for Data Science

Philip Bourne, Ph.D.
The 21st Century Cures Act — A View from the NIH
Kathy L. Hudson, Ph.D., and Francis S. Collins, M.D., Ph.D.

- $4.8 billion for NIH innovation projects
- Data sharing can be required
- Protection of identifiable and sensitive information: FOIA exemption
- Privacy protection for human research subjects: Certificates of Confidentiality
<table>
<thead>
<tr>
<th></th>
<th>FY2016 Enacted</th>
<th>FY2017</th>
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<tbody>
<tr>
<td>NIH</td>
<td>$32.3 B</td>
<td>CR through April 28, 2017</td>
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<tr>
<td>NHGRI</td>
<td>$513.2 M</td>
<td>CR through April 28, 2017</td>
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</table>
SBIR/STTR Reauthorization

SBIR · STTR
America’s Seed Fund™
POWERED BY SBA
Common Rule Revisions Finalized

- Improve informed consent
- Calibrate review to study risks
- Allow broad consent for secondary use of biospecimens
- Does not require consent for the use of de-identified biospecimens
- Streamline IRB review
Regulatory Updates

- FDA’s Laboratory Developed Test (LDT) guidance delayed
- NIH Single-IRB Policy: Effective date extended to Sept. 25, 2017
New dbGaP Data Browser

The database of Genotypes and Phenotypes (dbGaP) was developed to archive and distribute the data and results from studies that have investigated the interaction of genotype and phenotype in Humans.

Access dbGaP Data
- Advanced Search
- Controlled Access Data
- Public FTP Download
- Collections
- Summary Statistics

Resources
- dbGaP Data Browser
- Phenotype-Genotype Integrator
- dbGaP RSS Feed
- Software
- dbGaP Tutorial

Important Links
- How to Submit
- FAQ
- Code of Conduct
- Security Procedures
- Contact Us

Latest Studies

NCBI

NIH National Human Genome Research Institute
RFI on dbGaP Streamlining

- Will solicit feedback on data-submission and data-access processes
- Also will include policy-related questions:
  - Alternate controlled-access models
  - Benefits and risks associated with sharing genomic summary statistics
  - Use of genomic research data held in dbGaP for clinical reference purposes
NIH-ACMG Fellowship in Genomic Medicine Program Management

- Goal to increase the pool of physicians trained in managing research and implementation programs in genomic medicine

- Applications due March 1, 2017

- Fellowship begins July 2017
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Mourning the Loss of Oliver Smithies
Mourning the Loss of Allen Roses
Lasker-Koshland Special Achievement Award in Medical Science

Bruce Alberts, Ph.D.
2017 Breakthrough Prize in Life Sciences

Huda Zoghbi, M.D.
2016 ASHG Awards

Brendan Lee, M.D., Ph.D.

David Valle, M.D.
New Steering Committee Chair, Global Alliance for Genomics and Health

Ewan Birney, Ph.D.
New Senior Vice President of Global Oncology, Lilly

Levi Garroway, M.D., Ph.D.
Elected to the National Academy of Medicine

Anita Allen
Leslie Biesecker
Rob Califf
Joseph DeRisi
Allison Goate
Mark Musen
Kenneth Offit
Craig Venter
Huntington Willard
Xiaoliang Sunney Xie
David Walt
Elected to the AAAS

Paul Aristoff
Stephen Fodor
Monica Justice
Craig Lindsley

Clifton Poodry
Gary Stormo
Sharlene Weatherwax
2016 *Science* Breakthrough of the Year
Runner Up

Pocket-Size DNA Sequencer
The Scientist’s Top Ten Innovations 2016

3. Pacific Biosciences >> The Sequel System

5. Thermo Fisher Scientific >> LentiArray CRISPR Libraries

10. Thermo Fisher Scientific >> GeneArt Platinum Cas9 Nuclease
Genomes In The News…
I. General NHGRI Updates
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III. General Genomics Updates
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Genome Sequencing Program

- Centers for Common Disease Genomics (CCDGs)
  - Cardiovascular Diseases
  - Neuropsychiatric Diseases
  - Autoimmune/Inflammatory Diseases
  - ~ 18,000 whole genomes sequenced
  - ~ 19,000 whole exomes sequenced

- Centers for Mendelian Genomics (CMGs)
  - ~ 200 articles published
  - ~ 1,000 genes discovered
  - ~ 19,000 whole exomes sequenced
TCGA Unified Ensemble "MC3" Call Set

This wiki page provides documentation for the panCan merged.v0.2.6.PUBLIC.maf dataset. This is the public, open-access, dataset of somatic mutation calls (SNVs and indels) produced as part of the capstone project based on the full complement of cases in The Cancer Genome Atlas (TCGA). The file was produced using six different algorithms from four centers on over 10,000 tumor/normal pairs in TCGA. This effort is referred to within the TCGA Network as MC3 ("Multi-Center Mutation Calling in Multiple Cancers").

Members of the TCGA PanCanAtlas project should go syn5917296 for the working files (both open-access and controlled-access) for the PanCanAtlas project.

Acknowledgement:

In addition to citing the dataset, people who use the MC3 file should include the following in their acknowledgements: "The results <published or shared> here are in whole or part based upon data generated by the TCGA Research Network http://cancergenome.nih.gov/ as outlined in the TCGA publications guidelines http://cancergenome.nih.gov/publications/publicationguidelines

Questions or concerns should be directed to Discussion Board"
Technology Development Program

- Novel Nucleic Acid Sequencing Technology Development
  RFA-HG-15-031 (to 33; R01, R21, and R43/44)
  Upcoming due date: June 15, 2017

- Novel Genomic Technology Development
  PAR-16-14 (to 17; R01, R21, R43/44, and R44)
  Upcoming due date: October 31, 2017
Encyclopedia of DNA Elements (ENCODE)

- ENCODE Outreach and Collaboration
  
  ENCODE-DREAM In Vivo Transcription Factor-Binding Site Prediction Challenge

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**Publications Using ENCODE Data**

- ENCODE Community Publications
- ENCODE Consortium Publications

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Encyclopedia of DNA Elements (ENCODE)

- 4th phase of ENCODE grants
- Expand the catalog
- NEW Functional Characterization Centers

<table>
<thead>
<tr>
<th>Funded Initiative</th>
<th># of Awards</th>
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<tbody>
<tr>
<td>Mapping Centers</td>
<td>8</td>
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<tr>
<td>Functional Characterization Centers</td>
<td>5</td>
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<tr>
<td>Computational Centers</td>
<td>6</td>
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<tr>
<td>Data Analysis Center (DAC)</td>
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<tr>
<td>Data Coordinating Center (DCC)</td>
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</tbody>
</table>
Centers of Excellence in Genomic Science (CEGS) Program

Two new CEGS awards:

- Broad Institute
  Center for Cell Circuits

- University of Chicago
  Center for Dynamic RNA Epitranscriptomes
GWAS Catalog
The NHGRI-EBI Catalog of published genome-wide association studies

Nature commentary highlights GWAS Catalog data
Updated, comprehensive analysis underway

Ancestry Distribution of GWAS Participants

PhenX Toolkit

90 new and updated measures added

Integration by larger research programs

FOAs citing PhenX (cumulative)

dbGaP mapping

dbGaP Study containing PhenX “Alcohol 30 Day Freq” measure
Candidate Gene Association Resource (CARe)
NEIGHBOR Consortium Glaucoma GWAS
Genetic Multiple Sclerosis Association (GeneMSA)
The Vaginal Microbiome: Disease, Genetics, and the Environment
GenADA/LONG/Imaging (Genetic Alzheimer’s Disease Associations)

RFA-HD-17-001
NICHD Genomic Clinical Variant Expert Curation Panels

Consent to Share Genetic and Health Information
Your health history and your genetic information can help doctors and scientists understand how genes affect human health. Though you may not personally benefit, sharing this information helps:

- **Doctors** provide better care for their patients.
- **Labs** improve testing.
- **Researchers** make discoveries.

Right now, [LAB NAME] publicly shares general summary information about the changes in peoples’ genes that we find in our laboratory, as well as the reason(s) people were referred for testing.

With your permission, our lab would like to also share more specific information about your individual genetic and health information, including:
- All the information about your genes from your individual test results, and
- Health information that your doctor provides on the test order form.

Your privacy is very important to us, and we will take all appropriate measures to protect your privacy. We do not share any information like address, name, or contact information. All personal identifying information is replaced with a unique code.
Clinical Sequencing Exploratory Research Program

- Enrolled 5,135 adults and 1,320 children
- 288 publications, 18 working group publications
A survey of current practices for genomic sequencing test interpretation and reporting

Julianne M. O’Daniel, MS1, Heidi G. Wenzlau1, Sherri J. Bale, PhD4, Jonathan S. Beck5, Elizabeth C. Chao, MD7,8, Wendy K. Corrigan2, Soma Das, PhD12, Joshua L. Deignan5, Arezou A. Ghazani, PhD15
Kelly D. Farwell Hagman1, Lucia A. Hindorff, PhD, MPH3
Amy Knight Johnson, MS17, Lindsey Miller9, Sumit Punj, PhD22, C. Sue Richards7, Nancy B. Spinner, PhD11, Shalini V. Sukumar4
Yaping Yang4,11,18,19

Orthogonal confirmation practices among labs (n = 21)
MACE Risk Halved through PGx Prescribing

Cumulative MACE Rate (%)

Time (months)

LOF_CLOP
NON-LOF
LOF_ALT

Log-rank p=0.02
Log-rank p=0.2

Adjusted Hazard Ratio
LOF-CLOP vs LOF Alt.: 2.21
LOF-Alt. vs non-LOF: 0.81

Kaplan-Meier Survival Curve

LOF = Loss of function
Newborn Sequencing in Genomic Medicine and Public Health

Jonathan S. Berg, MD, PhD, a Pankaj B. Agrawal, MD, MMSc, b, c Donald B. Bailey Jr., PhD, d Alan H. Beggs, PhD, e Steven E. Brenner, PhD, e Amy M. Brower, PhD, f Julie A. Cakici, BA, BSN, g Ozge Ceyhan-Birsoy, PhD, h Kee Chan, PhD, f Flavia Chen, MPH, i Robert J. Currier, PhD, k Dmitry Dukhovny, MD, MPH, j Robert C. Green, MD, MPH, m Julie Harris Wai, MPH, PhD, l,n Ingrid A. Holm, MD, MPH, c Brenda Iglesias, o Galen Joseph, PhD, p Stephen F. Kingsmore, MD, DSc, q Barbara A. Koenig, PhD, r Pui-Yan Kwok, MD, PhD, s,t John Lantos, MD, v Steven J. Leeder, PharmD, PhD, w Megan A. Lewis, PhD, x Amy L. McGuire, JD, PhD, y Laura V. Milko, PhD, z Sean D. Mooney, PhD, f Richard B. Parad, MD, MPH, u Stacey Pereira, PhD, v Joshua Petrkin, MD, t Bradford C. Powell, MD, PhD, x Cynthia M. Powell, MD, y Jennifer M. Puck, MD, w Heidi L. Rehm, PhD, x Neil Risch, PhD, y Myra Roche, MS, y Joseph T. Shieh, MD, PhD, z,x Narayanan Veeraraghavan, PhD, e Michael S. Watson, MS, PhD, f Laurel Willig, MD, MS, t Timothy W. Yu, MD, PhD, c Tiina Urv, PhD, y Anastasia L. Wise, PhD a
4th ELSI Congress

Expanding the ELSI Universe #ELSICon

- Co-sponsored by NHGRI, the Jackson Laboratory, Columbia University Medical Center, and UCONN Health

- Keynote Speakers:
  - Eric Dishman
  - Alondra Nelson
  - Wylie Burke
  - James Evans
  - Pearl O’Rourke

- Topics:
  - Precision medicine
  - Genome sequencing enters the clinic
  - Genes, ancestry, and identity
Computational Genomics and Data Science Program

- Workshop in Bethesda September 2016
  Co-chairs: Mike Boehnke, Carol Bult, Trey Ideker, Aviv Regev, and Lincoln Stein

- Goal: Elicit discussion about NHGRI’s future extramural computational genomics and data science portfolio

- Final report will be presented at May Council meeting
# Small Business Grants

<table>
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<th>Small Business</th>
<th>Phase I Proof of Principle</th>
<th>Phase II Pre-Commercialization</th>
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<tr>
<td>Innovation Research (SBIR)</td>
<td>18</td>
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<td>Technology Transfer (STTR)</td>
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<tr>
<td>Total</td>
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Director’s Report Outline

I. General NHGRI Updates
II. General NIH Updates
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VII. NHGRI Intramural Research Program
Enrollment complete (965 donors)

Version 7 data release in summer 2017

>600 whole-genome sequences

RNA-Seq data on >12,000 samples
- >9,000 registered users from >90 countries
- 48,826 gene-expression profiles downloaded
- >220 papers using GTEx data, mostly from non-consortium members

**Papers Published Annually**

- Portal data - Consortium
- dbGaP data - Consortium
- Portal data - Non-Consort
- dbGaP data - Non-Consort

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<th>Year</th>
<th>Portal data - Consortium</th>
<th>dbGaP data - Consortium</th>
<th>Portal data - Non-Consort</th>
<th>dbGaP data - Non-Consort</th>
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<td>2015</td>
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<td>30</td>
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<tr>
<td>2016</td>
<td>120</td>
<td>40</td>
<td>70</td>
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Human Heredity and Health in Africa (H3Africa)

- 9th Consortium Meeting in October 2016
  Opening by Dr. Ameenah Gurib-Fakim, President of Mauritius

- Last Consortium meeting of Phase 1: May 2017
- Review of Phase 2 applications: March 2017
Undiagnosed Diseases Network (UDN)

Highlights

Undiagnosed Diseases Network sticks around

The Undiagnosed Diseases Network, an NIH Common Fund program aimed at solving challenging medical mysteries, isn’t going anywhere anytime soon. The program has just approved funding through 2022. With this investment, the UDN will continue to accept participants with undiagnosed conditions and hopes to better understand how to become self-sustaining in the future. Funding announcements are planned for Summer 2017, pending available funds.

1062 Applications
414 Acceptances

Document 41
"These survey results suggest that people from all walks of life will be interested in the cohort program."

—Dave Kaufman, Ph.D., Program Director, National Human Genome Research Institute

RESEARCH ARTICLE
A Survey of U.S Adults’ Opinions about Conduct of a Nationwide Precision Medicine Initiative® Cohort Study of Genes and Environment

David J. Kaufman1*, Rebecca Baker2*, Lauren C. Milner2*, Stephanie Devaney2, Kathy L. Hudson2*

1 National Human Genome Research Institute, Division of Genomics and Society, National Institutes of Health, Rockville, MD, United States of America, 2 National Institutes of Health, Office of the Director, Bethesda, MD, United States of America
Recruitment at VA Hospitals
Direct volunteer recruitment nationwide

Mayo Clinic Biobank
Rochester, MN

University of Arizona - Banner Health Enrollment Center
Tucson, AZ

Cherokee Health Systems
Knoxville, TN

Trans-American Consortium for the Health Care Systems Research Network
Detroit, MI

Jackson-Hinds Comprehensive Health Center
Jackson, MS

Illinois Precision Medicine Consortium
Chicago, IL

Eau Claire Cooperative Health Center
Columbia, SC

Vanderbilt/Broad/Verily Data and Research Support Core
Nashville, TN

San Ysidro Health Center
San Ysidro, CA

San Ysidro Health Center, Inc.
Middletown, CT

New England Precision Medicine Consortium
Boston, MA

Columbia/Cornell/Harlem Hospital HPO
New York, NY

Community Health Center, Inc.
Middletown, CT

Geisinger Health System
Danville, PA

California Precision Medicine Consortium
San Diego, CA

Scripps and Vibrant Participant Technologies/ Direct Volunteer Opps
La Jolla, CA

Vanderbilt/Broad/Verily Data and Research Support Core
Nashville, TN

Illinois Precision Medicine Consortium
Chicago, IL

Precision Approach to healthCARE Enrollment Site
Pittsburgh, PA

Vanderbilt/Broad/Verily Data and Research Support Core
Nashville, TN

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ASHG-NHGRI Fellowships

2017-2018 Application Process Open

- Genetics and Public Policy Fellowship
- Genetics and Education Fellowship
- Application deadline: April 24, 2017
Genome: Unlocking Life’s Code Exhibition

Travel Schedule

2017

April 1-May 29
Peoria Riverfront Museum
Peoria, IL

June 12-September 11
Health Museum
Houston, TX

September 30-January 1
Science North
Sudbury, Ontario, Canada
Genome: Unlocking Life’s Code Exhibition

Website Award
Genomic Literacy, Education, and Engagement (GLEE) Initiative

- Possible launching of a national campaign to enhance genomic literacy
- Proposed target audiences: K-16, public, and healthcare professionals
- Strategic Visioning Meeting: March 2017
2017 NHGRI Short Course in Genomics

K-12, Community College, and Tribal College Faculty

Applications Open: Feb. 2017

Nurses, Physician Assistants, and Educators

Applications Open: March 2017
My Family Health Portrait

- Family history tool website revised to improve the user experience
- ‘NLM Hackathon’ to extend interoperability and expose programmers to family history and relevant resources
International Summit in Human Genetics and Genomics

- Five-year initiative (2016-2020)
- Help developing nations build expertise in genetics and genomics
- September 2016: 19 participants from 13 countries across the globe
Master, American College of Rheumatology

Dan Kastner, M.D., Ph.D.
Biallelic hypomorphic mutations in a linear deubiquitinase define otulipenia, an early-onset autoinflammatory disease

Systemic AAV9 gene therapy improves the lifespan of mice with Niemann-Pick disease, type C1

Extracellular Hsp60 triggers tissue regeneration and wound healing by regulating inflammation and cell proliferation
Thanks!

Special Thanks!
Advancing human health through genomics research