September 6, 2017

In addition to late summer vacations and solar-eclipse viewing, August brought some great genomic science to the NIH campus. Specifically, NIH hosted a workshop entitled "The Human Microbiome: Emerging Themes at the Horizon of the 21st Century," which showcased the remarkable recent advances in human microbiome research. I would encourage you to view some of the video-recorded talks from this symposium, now available.

Meanwhile, we recently learned about some transitions within the NHGRI Intramural Research Program involving two long-time members of the Institute. Dr. Bill Pavan will become Chief of the Genetic Disease Research Branch, taking over the reins of this Branch from Dr. Pam Schwartzberg, who will be joining an exciting new research program at the National Institute of Allergy and Infectious Diseases (NIAID). I would like to congratulate both Bill and Pam on their new positions.

This month's *The Genomics Landscape* features stories about:

- Genome Editing: How, When, and Why?
- NHGRI Funds Research on Accelerating Genomics in Clinical Care
- A Fond Farewell to the NCCIH Director
- Native Graduate Health Fellows Visit NIH
- NHGRI Summer Interns

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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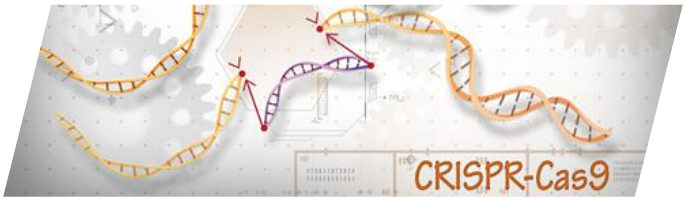
Genome Editing: How, When, and Why?

In parallel with scientific advances, public interest in genome editing is accelerating at a rapid pace. What was once science fiction can now be considered 'science fact.' The new tools of genome editing allow researchers to change the DNA of different organisms, such as plants, bacteria, and animals (including humans), which can lead to changes in physical traits.

Current genome-editing involves the use of technologies that act like scissors, cutting DNA at specific locations. After cutting, scientists can remove, add, or replace the DNA at that site. This then allows researchers to explore in greater detail the relationships between the DNA makeup of an organism (its genotype) and the manifestation of traits (its phenotype).

Some genome-editing technologies have been available for the past two decades, including homologous recombination, zinc-finger nucleases (ZFNs), and transcription activator-like effector nucleases (TALENs). While useful for some applications, these techniques can be time-consuming, expensive, and/or complicated to use; they also tend to be inefficient, causing 'off-target' edits (in which an area of the genome gets unintentionally edited).



A newer tool called CRISPR/Cas9 (CRISPR, for short), developed in 2009, has revolutionized the field of genome editing. CRISPR, which stands for Clustered Regularly Interspaced Short Palindromic Repeats, is simpler, faster, cheaper, and more accurate than older genome-editing methods, and has rapidly become the preferred technology for most scientists.

Using CRISPR, the genomes of animals (such as mice and zebrafish) can now be edited with much greater ease. This allows researchers to modify specific genes and study the resulting consequences to the animals' health. In particular, this allows animal-based disease models to be created and used for important research projects.

In the NHGRI Intramural Research Program, Dr. Shawn Burgess uses genome-editing techniques to investigate the causes of human deafness using zebrafish models. Working in the NHGRI Embryonic Stem Cell and Transgenic Mouse Core, Director Lisa Garrett has developed gene-editing protocols for efficiently generating transgenic mice, and she maintains an updated guide for protocols using CRISPR/Cas9 and other gene-editing tools. In addition, genome-editing tools are being tested for use in gene

NHGRI Funds Research on Accelerating Genomics in Clinical Care

In keeping with a mission to make genomic medicine a reality for all populations and individuals, NHGRI, in collaboration with the National Cancer Institute and the National Institute on Minority Health and Health Disparities, recently announced new grants that will support the Clinical Sequencing Evidence-Generating Research (CSER2) Consortium. These four-year awards, totaling $18.9 million in Fiscal Year 2017, will fund research to generate evidence about the utility of genome sequencing in clinical care. The new awards have an important focus on underserved populations and settings that extend beyond academic medical centers. For more information, see genome.gov/27568938.

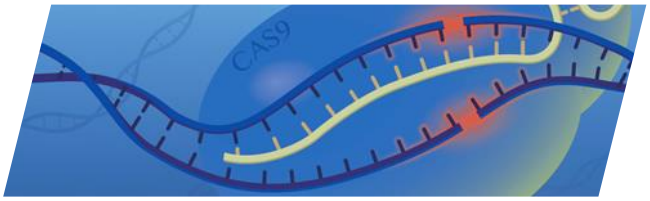
A Fond Farewell to the NCCIH Director

Later this fall, Josie Briggs, M.D. will be leaving her post as the Director of the National Center for Complementary and Integrative Health (NCCIH). In 1997, she was recruited from the University of Michigan to serve as the Director of the Division of Kidney, Urologic, and Hematologic Diseases in the National Institute of Diabetes and Digestive and Kidney Diseases. She briefly left NIH for a senior position at the Howard Hughes Medical Institute before returning as the NCCIH Director in 2008. NHGRI wishes her the best of luck in her new position as the Editor-in-Chief of the *Journal of the American Society of Nephrology*.

therapy to treat disease in humans; when the use of the technologies is limited to somatic (or non-reproductive) cells, like those in skin or liver, the DNA changes are not transmitted to future generations. For this application, minimizing off-target effects is critical since changes to the wrong portions of the genome could negatively affect other biological processes.

The NHGRI Extramural Research Program just awarded a new Centers of Excellence in Genomic Science (CEGS) award to Dr. Jennifer Doudna at the University of California-Berkeley and collaborators. Building on the CRISPR-Cas9 genome-engineering technology, these investigators aim to create methods for detecting, altering, and recording the sequence and output of the genome in individual cells and tissues.

At the same time, exciting new laboratory advances have raised numerous questions: How is genome editing currently used, and how might it be used in the future? What are the ethical issues surrounding genome editing? What does the scientific community and the general public think about the advances in genome editing?



To provide information relevant to these questions, the Policy and Program Analysis Branch of NHGRI's Division of Policy, Communications, and Education has developed a web resource on genome editing. The resource describes the technical aspects of different genome-editing techniques as well as pertinent ethical issues, such as safety, informed consent, justice and equity, and research involving embryonic cells.

Since the public has a variety of perspectives on, and concerns about, genome-editing tools, this resource aims to provide information to facilitate the ongoing discussions. The resource concentrates relevant information into a single location for those interested in learning more about genome editing. For more information and to view the genome-editing resource, see genome.gov/27569222/genome-editing/.

Native Graduate Health Fellows Visit NIH

In July, a group of graduate students participating in the National Congress of American Indians (NCAI) Native Graduate Health Fellowship visited NIH. The NCAI Native Graduate Fellowship is a program that works to increase the number of Native health professionals who can address the health needs of American Indians and Alaska Natives. The group met with Dr. David Wilson, Director of the NIH Tribal Health Research Office, along with NHGRI staff. They participated in tours of the NHGRI Zebrafish Core and NIH Clinical Center. The day's agenda was designed to help participants increase their knowledge of how research translates into improved health practice and policies; the impact of research on national, state, and tribal policy; and opportunities available for research and training at the NIH.

NHGRI Summer Interns

Office of Intramural TRAINING & EDUCATION

Each summer, NIH hosts myriad trainees from high school to professional levels as part of the NIH Summer Internship Program (SIP). The SIP experience enables trainees to spend a summer working at NIH side-by-side with biomedical researchers. The trainees conduct research, attend scientific lectures, attend career/professional development workshops, and participate in other activities hosted by the NIH Office of Intramural Training and Education and by individual Institutes and Centers (e.g., the NHGRI Intramural Training Office). To learn more about three of the NHGRI summer interns, who all happen to have worked on enhancing the Atlas of Human Malformations in the laboratory of Dr. Max Muenke, see genome.gov/27569457.

Spotlight on the All of Us Research Program

allofus.nih.gov

- The *All of Us* Research Program released its Initial Research Protocol. The first version of the protocol includes the program's enrollment and data collection plans, consent forms, and surveys.
- The *All of Us* Research Program Advisory Panel established a new working group to help inform the program's genomics strategy. NHGRI Director Eric Green is serving on this group, which is considering issues related to the evolving nature of genome-sequencing technologies, the analysis of genomic data on a large scale, and the program's commitment to returning genomic information to participants.
- The August 2017 *All of Us* Research Program Advisory Panel Meeting is now available.
- The *All of Us* Research Program expanded its national network of medical centers. Awardees will help enroll participants in long-term precision medicine research efforts.
- The Child Enrollment Scientific Vision Working Group of the *All of Us* Advisory Panel seeks public input (with a deadline of September 12) on the pediatric research that the *All of Us* Research Program may be uniquely positioned to enable through the enrollment of children.

Genomics Research

NCI Study Identifies Essential Genes for Cancer Immunotherapy

Breakthrough Method Yields Trove of Neuron Subtypes, Gene Regulators

Experimental Treatment for Niemann-Pick Disease Type C1 Appears Safe, Effective

Sequencing All 24 Human Chromosomes Uncovers Rare Disorders

Notable Accomplishments in Genomic Medicine

Upcoming Videocasts & Webinars

Trent Lecture in Cancer Research: Bringing Genomics to the Pediatric Oncology Clinic – Sep 6

Applicant Information Webinar for The NHGRI Genomic Data Science Analysis, Visualization, and Informatics Lab-space (AnVIL) – Sep 7

NCATS Toolkit for Patient-Focused Therapy Development: Demonstration and Dissemination Meeting – Sep 8

Eight-first Meeting: National Advisory Council for Human Genome Research – Sepr 11

UDN Phase II Applicant Information Webinar – Sep 14

Funding Opportunities

National Metabolomics Data Repository

Metabolomic Data Analysis and Interpretation Tools

Stakeholder Engagement and Program Coordination Center

Funding Opportunities for the NIH Common Fund's Undiagnosed Diseases Network

Funding News

Guidance on Full-Time Training for Ruth L. Kirschstein National Research Service Awards

Salary Supplementation and Compensation on Mentored Research Career Development Awards

Policy Supporting the Next Generation Researchers Initiative

New Videos

The Human Microbiome: Emerging Themes Workshop – Day 1, Day 2, & Day 3

Discovery Documentary: First In Human

Jim Parsons on Documentary First In Human

NIH & NHGRI News

ASHG Weighs in on Human Genome Editing

Coleman Minority Health and Health Disparities Research Innovation Award

Kids First Announces the Third Set of Patient Cohorts for Whole Genome Sequencing

How Can You Take Part in Clinical Research? Looking Beyond "First in Human"

Dr. Collins Speaks to AP about How DNA Test Results Can Encourage Healthier Habits

Workshop on NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

IRDiRC Goals 2017-2027: New Rare Disease Research Goals for the Next Decade

Unlocking Life's Code: August 2017 Newsletter