Ushering in a New Era of Responsible Innovation

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Director, National Institutes of Health

Novel and Exceptional Technology & Research Advisory Committee (NExTRAC)

December 5, 2019

Emerging Biotechnologies: The Promise...

Science

Brian Madeux, who has Hunter syndrome, has received a treatment aimed at editing the genome of his liver cells. AP PHOTO/ERIC RISBERG

A human has been injected with gene-editing tools to cure his disabling disease. Here's what you need to know

By Jocelyn Kaiser | Nov. 15, 2017 , 6:00 PM

NIH National Institutes of Health
Turning Discovery Into Health

Friday, November 2, 2018

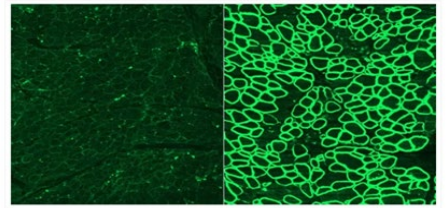
NIH greatly expands investment in BRAIN Initiative

NIH announces new round of awards for cutting-edge brain research.

NIH Director's Blog

Gene Editing in Dogs Boosts Hope for Kids with Muscular Dystrophy

Posted on September 11th, 2018 by Dr. Francis Collins



Untreated Treated

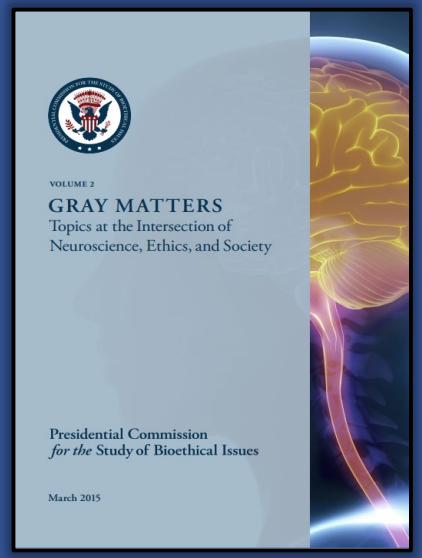
Caption: A CRISPR/cas9 gene editing-based treatment restored production of dystrophin proteins (green) in the diaphragm muscles of dogs with Duchenne muscular dystrophy.
Credit: UT Southwestern

CRISPR and other gene editing tools hold great promise for curing a wide range of devastating conditions caused by misspellings in DNA. Among the many looking to gene editing with hope are kids with Duchenne muscular dystrophy (DMD), an uncommon and tragically fatal genetic disease in which their muscles—including skeletal muscles, the heart, and the main muscle used for breathing—gradually become too weak to function. Such hopes were recently buoyed by a new study that showed infusion of the CRISPR/Cas9 gene editing system could halt disease progression in a dog model of DMD.

CRISPR treatment for rare genetic eye disorder gains FDA study approval

Damian Garde | STAT | December 10, 2018

Days after a Chinese researcher incensed the world of science with claims of editing the genomes of twin girls, an American company is plotting a CRISPR trial of its own. But in place of the secrecy and stagecraft that marked the Chinese experiment, Editas Medicine went the old-fashioned way: waiting for approval from the Food and Drug Administration.



VOLUME 2

GRAY MATTERS

Topics at the Intersection of Neuroscience, Ethics, and Society

Presidential Commission *for the* Study of Bioethical Issues

March 2015

WIRED

MEGAN MOLTENI SCIENCE 01.16.19 04:30 PM

ANTIBIOTICS ARE FAILING US. CRISPR IS OUR GLIMMER OF HOPE

Antibiotic overuse has led to a growth in drug-resistant infections, which sicken more than two million people in the US each year and kill upwards of 23,000.
BJARTE RETTEDAL/GETTY IMAGES

FDA U.S. FOOD & DRUG ADMINISTRATION

FDA approval brings first gene therapy to the United States

CAR T-cell therapy approved to treat certain children and young adults with B-cell acute lymphoblastic leukemia

For Immediate Release November 22, 2017

Gene Drives on the Horizon

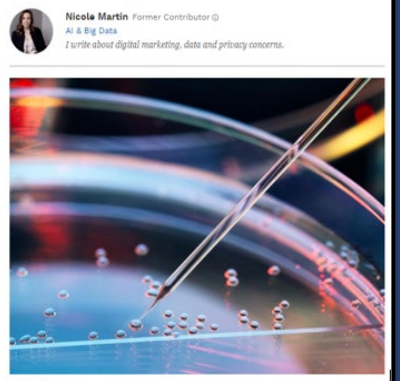
Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values

The National Academies of SCIENCES · ENGINEERING · MEDICINE

Forbes

4,396 views | Oct 18, 2019, 01:56pm

How Artifical Intelligence Is Advancing Precision Medicine



null, getty

Emerging Biotechnologies: The Peril...

The New York Times

As D.I.Y. Gene Editing Gains Popularity, 'Someone Is Going to Get Hurt'

By Emily Baum

May 14, 2018

The Telegraph

GM mosquitoes: playing with God or the only way to wipe out malaria?

By Sophie

5 FEBRUARY

The Guardian

Nicola Davis

First human-monkey chimera raises concern among scientists

Researchers reprogrammed human cells before injecting them in the monkey embryo

Daily Mail .com

Controversial 'gene drive' research sparking ethical debate

By AFP

PUBLISHED:

New Scientist

DAILY NEWS 14 February 2017

Human genome editing shouldn't be used for enhancement – yet

cnet

The CRISPR machines that can wipe out entire species

Science

CRISPR—a weapon of mass destruction?

By Kelly Servick

The New York Times

How to Stop Rogue Gene-Editing of Human Embryos?

SCIENTIFIC AMERICAN

Racial Bias Found in a Major Health Care Risk Algorithm

Black patients lose out on critical care when systems equate health needs with costs

The New York Times Magazine

The Biotech Death of Jesse Gelsinger

By SHERYL GAY STOL

Newsweek

HUMAN MINI-BRAINS CREATED IN LAB MAY BECOME SENTIENT AND ABLE TO FEEL PAIN, SCIENTISTS WARN

BY ROSIE MCCALL ON 10/21/19 AT 10:10 AM EDT

The New York Times

Chinese Scientist Claims to Use Crispr to Make First Genetically Edited Babies

The researcher, He Jiankui, offered no evidence or data to back up his assertions. If true, some fear the feat could open the door to "designer babies."

By Gina Kolata, Sui-Lee W

November 26, 2018

The Guardian

Philip Ball

Sun 8 Jan 2017

Designer babies: an ethical horror waiting to happen

The Guardian

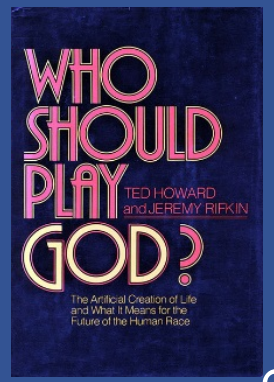
Ian Sample *Science editor*

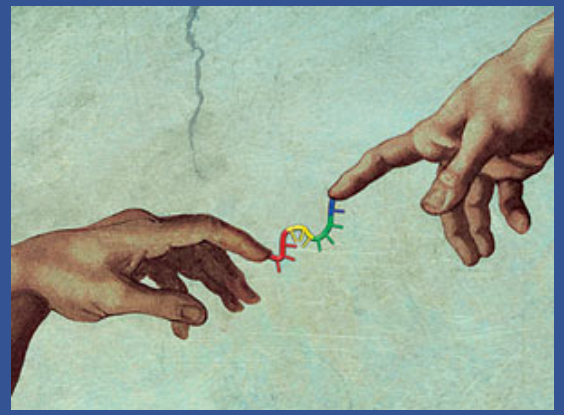
Scientists 'may have crossed ethical line' in growing human brains

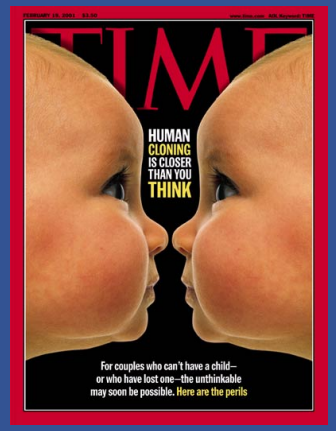
Debate needed over research with 'potential for something to suffer', neuroscientists say

But what about the ethical issues?

Is biotechnology "playing God"?







Recombinant DNA

Genetic Engineering

Cloning

Human Genome Project

Genome Editing

70s 80s 90s 00s 10s Present

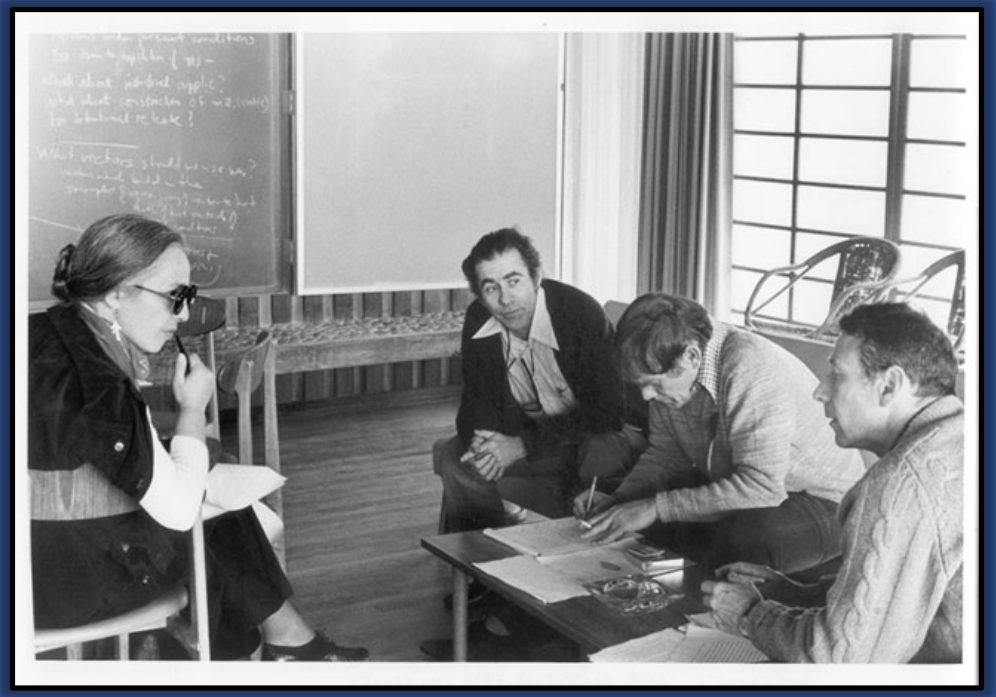
Overarching Considerations

- How to anticipate emerging biotechnologies that will create policy/safety/ethical/security challenges?
- How to develop a flexible/dynamic oversight framework that evolves with the biotechnology?
- When has an emerging biotechnology emerged?
- How do you keep the focus on the applications of the biotechnology, vs. biotechnology itself?
- And… how do you do this in the real world?

What's Past is Prologue:

Lessons from Past Approaches to Emerging Biotechnologies, Through Today

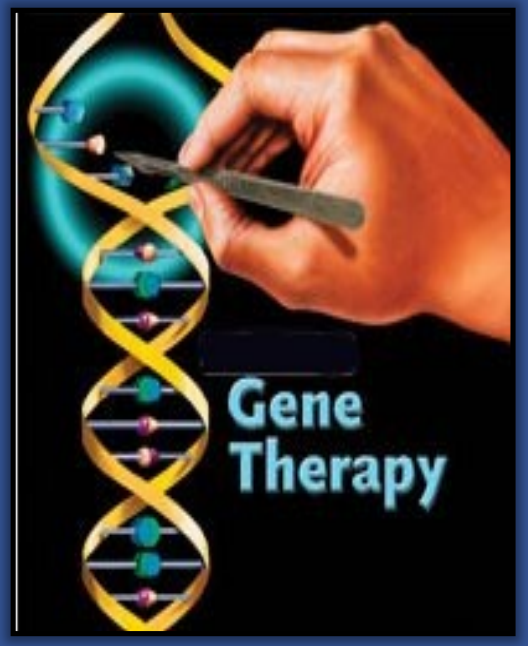
Lessons From The Past…
Recombinant DNA and Asilomar



The *NIH Guidelines*

The Recombinant DNA Advisory Committee (RAC)

Human Gene Therapy



- **1989:** First gene transfer protocol reviewed by the RAC and approved by NIH Director
- **1997:** NIH Director no longer approves protocols to eliminate duplication with FDA regulatory authority; RAC role continues for in-depth review and public discussion
- **2002:** NIH harmonizes serious adverse event requirements with FDA regulations
- **2016:** NIH implements IOM recommendations to limit RAC review to novel and exceptional individual protocols
- **2019:** Streamlining of oversight framework

We've Come a Long Way …

Current State of Human Gene Therapy (HGT) Oversight

Rewriting Life

FDA Approves Groundbreaking Gene Therapy for Cancer

The treatment will be sold by Novartis for $475,000.

by Emily Mullin August 30, 2017

A **revolutionary cancer therapy that uses genetically engineered** immune cells has been approved by the U.S. Food and Drug Administration, ushering in a new era of cancer treatment.

Revised Common Rule

The U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies have issued final revisions to the Federal Policy for the Protection of Human Subjects (the Common Rule). A final rule was published in the *Federal Register* (FR) on January 19, 2017, and was amended to delay the effective and compliance dates on January 22, 2018 and June 19, 2018.

The revised Common Rule is effective July 19, 2018; note that from July 19, 2018 through January 20, 2019 institutions are not permitted to implement the entirety of the revised Common Rule. This is explained in the transition provision (45 CFR 46.101(l), as amended June 19, 2018).

In order to understand the regulatory text of the revised Common Rule, OHRP recommends reviewing the preamble and regulatory text from:

- The final rule to revise the Common Rule - PDF (published January 19, 2017)

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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Home > Search Results

Modify Search Start Over

4151 Studies found for: **gene therapy**

Also searched for **Treatment**, **Therapeutic**, **Gene transfer** and more. See Search Details

Search Details

Showing: 1-10 of **4,151** studies 10 ▾ studies per page

Row	Saved	Status	Study Title	Conditions	Interventions
1	☐	Recruiting	HSV-tk + Valacyclovir + SBRT + Chemotherapy for Recurrent GBM	• Glioblastoma Multiforme • Astrocytoma, Grade III	• Drug: ADV/HSV-tk (**gene therapy**)
2	☐	Not yet recruiting	TAC Chemotherapy and Pembrolizumab Plus Interleukin-12 **Gene Therapy** and L-NMMA in Triple Negative Breast Cancer	• Triple Negative Breast Cancer	• Drug: Docetaxel • Drug: Doxorubicin • Drug: Cyclophosphamide • (and 3 more...)
3	☐	Recruiting	HSV-tk and XRT and Chemotherapy for Newly Diagnosed GBM	• Glioblastoma • Anaplastic Astrocytoma	• Drug: ADV/HSV-tk (**gene therapy**)

Emerging Biotechnologies of Today

What technologies (and applications) are we talking about?

Gene Editing Technologies

Technologies

• ZFNs • Meganucleases • TALENs •
• CRISPR-Cas9 • Prime Editing •

Gene Editing ≠ CRISPR ≠ Heritable Gene Editing

Applications

• Research Tool • Somatic Gene Therapy • Heritable Gene Editing•
Organism Creation/Modification (plants, insects, animal models of disease) •
• Antimicrobials • Gene Drives •

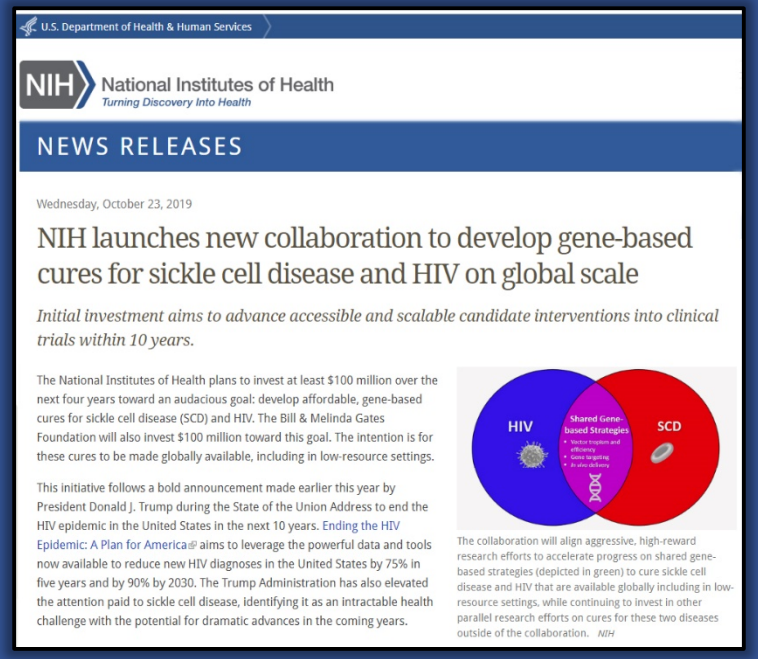
Different applications present different risks…

Human Gene Editing

Somatic cell gene editing

- Raises similar safety and ethical issues as earlier HGT approaches
- Well-established oversight framework
- NIH supports research and many initiatives

CURE SICKLE CELL.



U.S. Department of Health & Human Services

NIH National Institutes of Health
Turning Discovery Into Health

NEWS RELEASES

Wednesday, October 23, 2019

NIH launches new collaboration to develop gene-based cures for sickle cell disease and HIV on global scale

Initial investment aims to advance accessible and scalable candidate interventions into clinical trials within 10 years.

The National Institutes of Health plans to invest at least $100 million over the next four years toward an audacious goal: develop affordable, gene-based cures for sickle cell disease (SCD) and HIV. The Bill & Melinda Gates Foundation will also invest $100 million toward this goal. The intention is for these cures to be made globally available, including in low-resource settings.

This initiative follows a bold announcement made earlier this year by President Donald J. Trump during the State of the Union Address to end the HIV epidemic in the United States in the next 10 years. Ending the HIV Epidemic: A Plan for America aims to leverage the powerful data and tools now available to reduce new HIV diagnoses in the United States by 75% in five years and by 90% by 2030. The Trump Administration has also elevated the attention paid to sickle cell disease, identifying it as an intractable health challenge with the potential for dramatic advances in the coming years.

The collaboration will align aggressive, high-reward research efforts to accelerate progress on shared gene-based strategies (depicted in green) to cure sickle cell disease and HIV that are available globally including in low-resource settings, while continuing to invest in other parallel research efforts on cures for these two diseases outside of the collaboration. *NIH*

CGE
Somatic Cell Genome Editing

Human Gene Editing

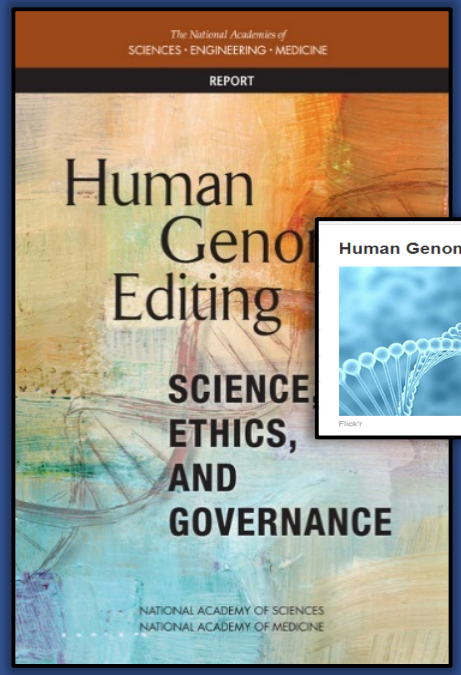
Heritable gene editing

- **NIH does not fund any use of gene editing technology in human embryos**
- Safety – risk of unintended mutations
- Medical – are there needs that only heritable gene editing could meet?
- Societal, ethical, moral issues: consent, justice/equity, philosophical, theological
- Global challenge for governance and oversight


COMMENT

Adopt a moratorium on heritable genome editing

Eric Lander, Françoise Baylis, Feng Zhang, Emmanuelle Charpentier, Paul Berg and specialists from seven countries call for an international governance framework.


The National Academies of SCIENCES · ENGINEERING · MEDICINE

REPORT

Human Genome Editing

SCIENCE, ETHICS, AND GOVERNANCE

NATIONAL ACADEMY OF SCIENCES
NATIONAL ACADEMY OF MEDICINE


Human Genome editing

WHO establishing expert panel to develop global standards for governance and oversight of human genome editing

14 December 2018 -- WHO is establishing a global multi-disciplinary expert panel to examine the scientific, ethical, social and legal challenges associated with human genome editing (both somatic and germ cell). The panel will review the current literature on the state of the research and its applications, and societal attitudes towards the different uses of this technology. WHO will then receive advice from the panel on appropriate oversight and governance mechanisms, both at the national and global level. Core to this work will be understanding how to promote


NATIONAL ACADEMY OF MEDICINE AND NATIONAL ACADEMY OF SCIENCES THE ROYAL SOCIETY

May 22, 2019

New International Commission Launched on Clinical Use of Heritable Human Genome Editing


THE NIH DIRECTOR

March 13, 2019

NIH supports international moratorium on clinical application of germline editing

Today, leading scientists and ethicists from seven countries have called for an international moratorium on the use of genetic editing to modify the human germline for clinical purposes. The call comes in the wake of irresponsible and unethical research in China, in which twins were born after alterations to their DNA before implantation. This unexpected and unwelcome revelation roiled the scientific community and the general public, and crystalized the need for guiding international principles. Research on the potential to alter the very biological essence of humanity raises profound safety, ethical, and philosophical issues. I expressed NIH's position on the incident in November 2018.

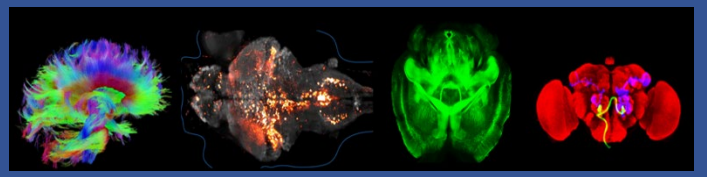
CRISPR-Cas9 is a customizable tool that lets scientists cut and insert small pieces of DNA at precise areas along a DNA strand. This lets scientists study our genes in a specific, targeted way. *Ernesto del Aguila III, NHGRI.*

Neurotechnologies

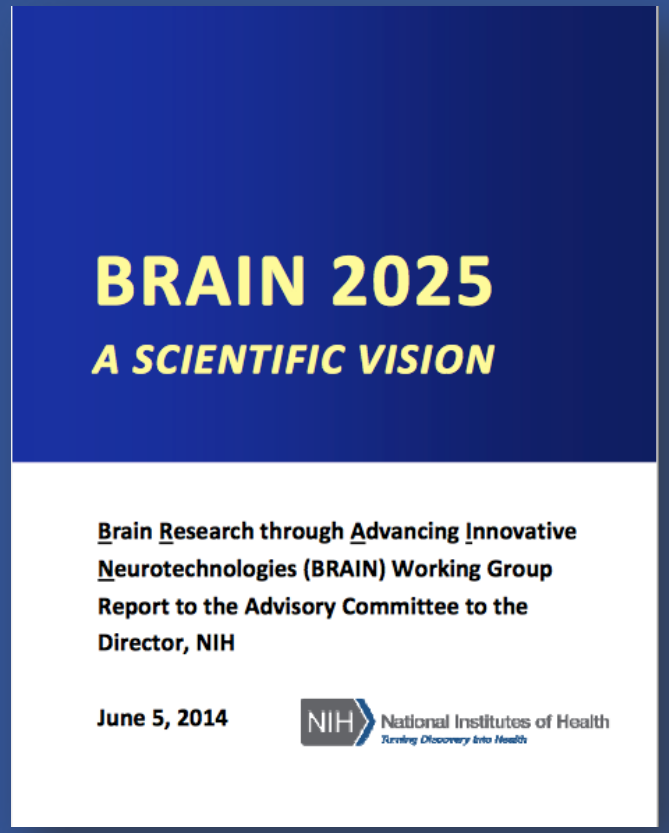
“Although brain research entails ethical issues that are common to other areas of biomedical science, it entails special ethical considerations as well. Because the brain gives rise to consciousness, our innermost thoughts and our most basic human needs, mechanistic studies of the brain have already resulted in new social and ethical questions.”

– Authors of BRAIN 2025

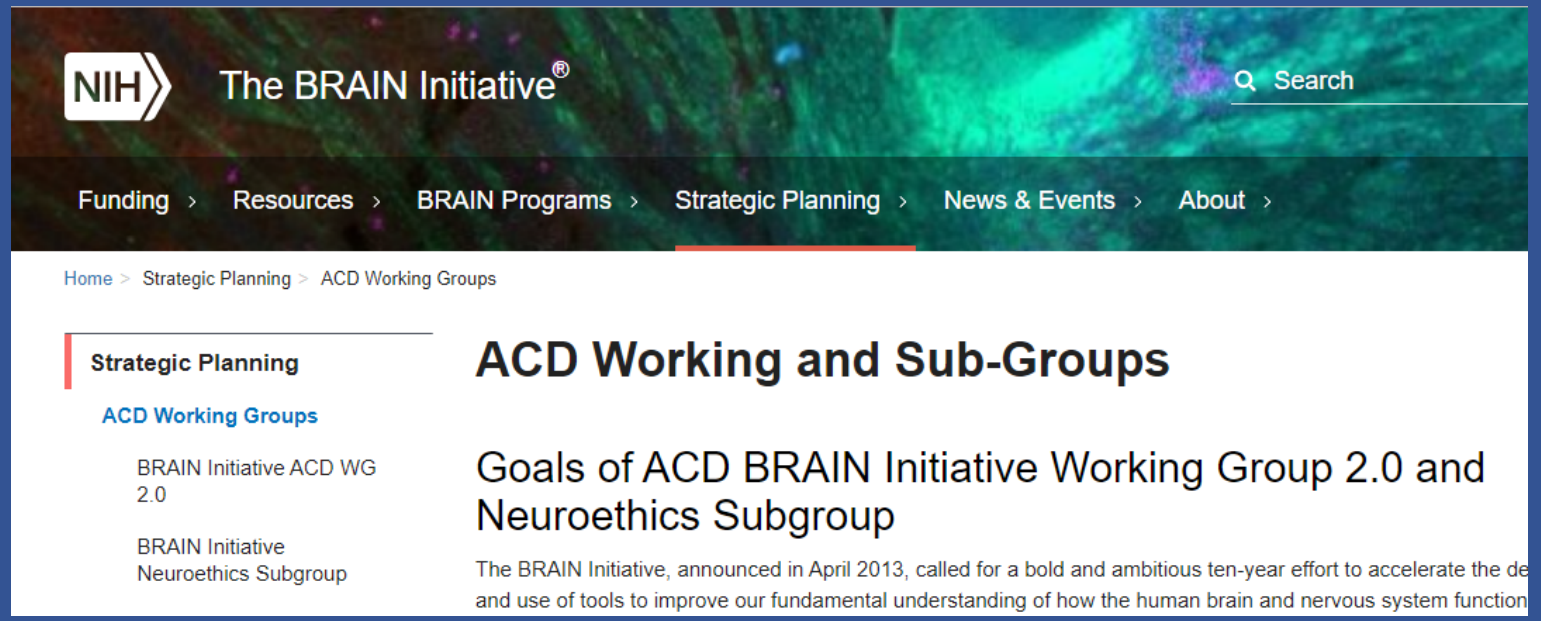
NIH and the U.S. BRAIN Initiative



- 2014: *BRAIN 2025*



- 2019 mid-course review
  - *BRAIN Initiative 2.0: From Cells to Circuits, Toward Cures*
  - *BRAIN Initiative and Neuroethics: Enabling and Enhancing Neuroscience Advances for Society*



Human neuroscience in BRAIN

BRAIN investigators are conducting *in vivo* neuroscience research with patients undergoing neurosurgery for clinical indications. This research offers no benefit to the patients but can provide extraordinary insight into how the human brain works.

Speech synthesis from neural decoding of spoken sentences

Gopala K. Anumanchipalli, Josh Chartier & Edward F. Chang

Nature **568**, 493–498(2019) | Cite this article

BRAIN–Neuroethics

NIH BRAIN Initiative's Neuroethics Working Group (NEWG)

- Identify & navigate neuroethical challenges
- Identify neuroethics research questions for further research inquiry

Workshops:

- Research with Human Neural Tissue (March 2018)
- Research with Invasive & Non-Invasive Neural Devices in Humans (October 2017)

ACD Neuroethics Subgroup:

- 2019 Neuroethics Roadmap

Additional neuroethics efforts coordinated with neuroscience initiatives across the globe!

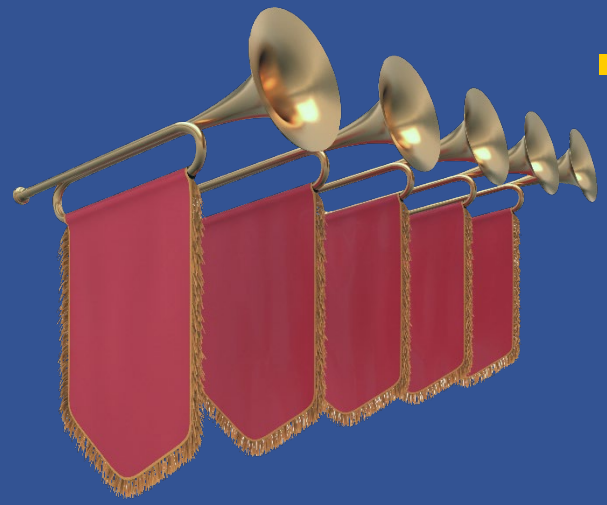
RAC ⟶ NExTRAC

How does this committee fit in?

Evolution of the RAC

- For over 40 years, the RAC has evolved to address issues associated with scientific advances
  - Recombinant DNA in 1970s
  - HGT in 1990s
- 2019 Evolution
  - Return to focus on the research involving the emerging biotechnologies (of today)

Introducing the NExTRAC: Novel and Exceptional Technology and Research Advisory Committee



- Focus on scientific, safety, and ethical issues associated with emerging biotechnologies
  - E.g., gene editing, gene drives, synthetic biology, neurotechnology
  - Cutting edge clinical applications?
- Continue roles as
  - Public forum for transparent discourse on challenging issues
  - Source of advice to NIH Director
  - Resource for scientific community and public


We must never allow our technology
to eclipse our humanity.




NIH... *Turning Discovery Into Health*

www.nih.gov/hope

directorsblog.nih.gov

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