



National Institute of  
Neurological Disorders  
and Stroke

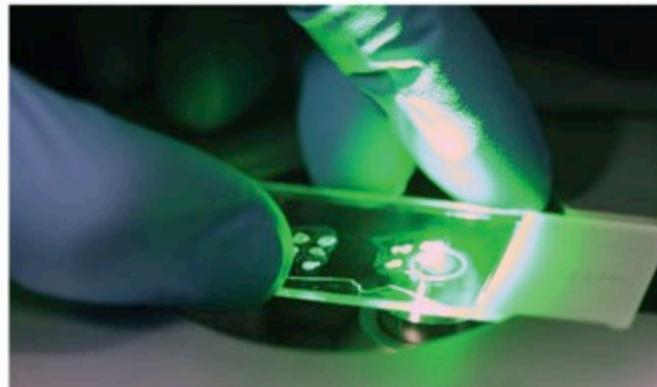
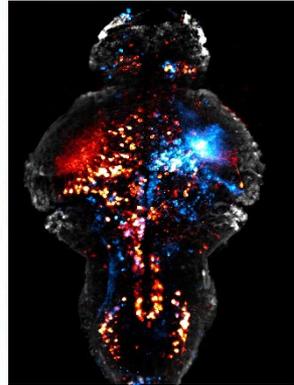
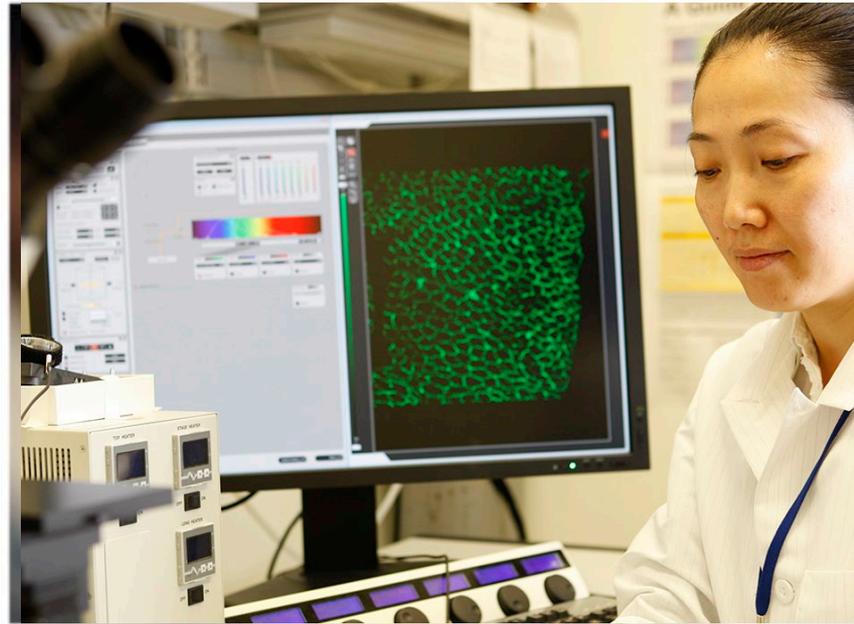
# NINDS Director's Report

*NANDS Council*

September 4, 2019

Walter J. Koroshetz, M.D.

Director, National Institute of  
Neurological Disorders and Stroke, NIH



# NINDS Director's Report

Thanks for the well wishes



Thanks to Dr. Nina Schor and NINDS  
Leadership

# Appropriation History

(Dollars in Thousands)

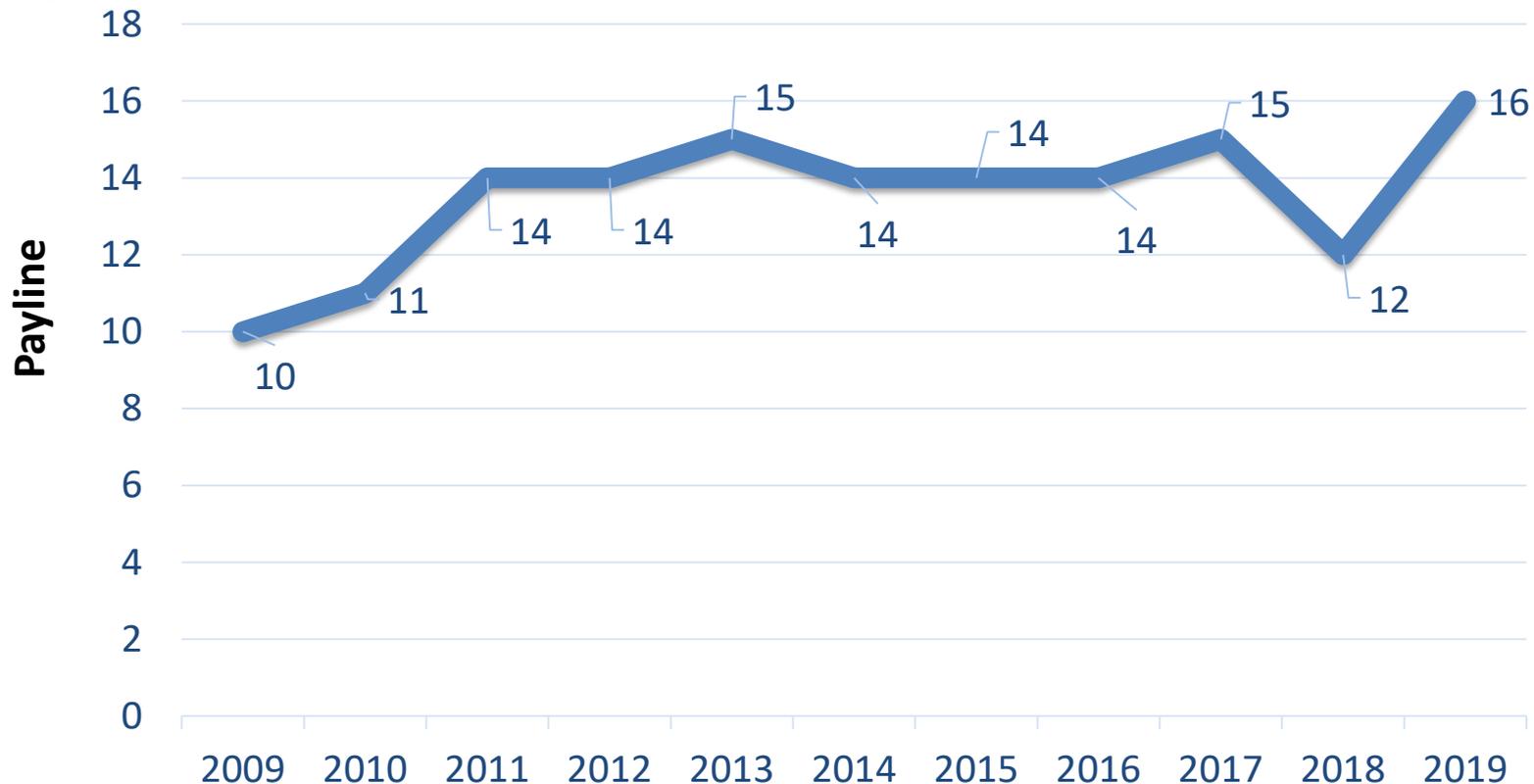
	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019 Appropriation	FY 2020 President's Budget	FY 2020 House Mark
<b>NINDS</b>	1,604,607	1,692,833	1,778,688	1,888,130*	1,966,913*	\$1,706,031*	\$2,053,346*
<b>NINDS % Change</b>	1.0%	5.5%	5.4%	6.15%	4.17%	-13.3%	4.4%
<b>NIH</b>	30,311,349	32,345,549	34,161,349	36,228,080**	38,023,000**	\$33,375,629**	\$40,108,000**
<b>NIH % Change</b>	0.5%	6.7%	5.6%	6%	4.9%	-12.2%	5.5%

- NIH FY 2020 House Mark is a \$2 billion increase over FY 2019's level.
- In FY 2019, NINDS received \$250m for Pain Research in part of the HEAL Initiative and \$57.5m in CURES Act fund for the BRAIN Initiative.
- In FY 2019, NINDS will co-manage approximately \$170 million of the AD/ADRD monies that NIA received.

\* These columns do not include the monies that NINDS received for the HEAL Initiative and CURES Act.

\*\* These columns do not include the monies that NIH received for the HEAL Initiative and CURES Act.

# NINDS Payline



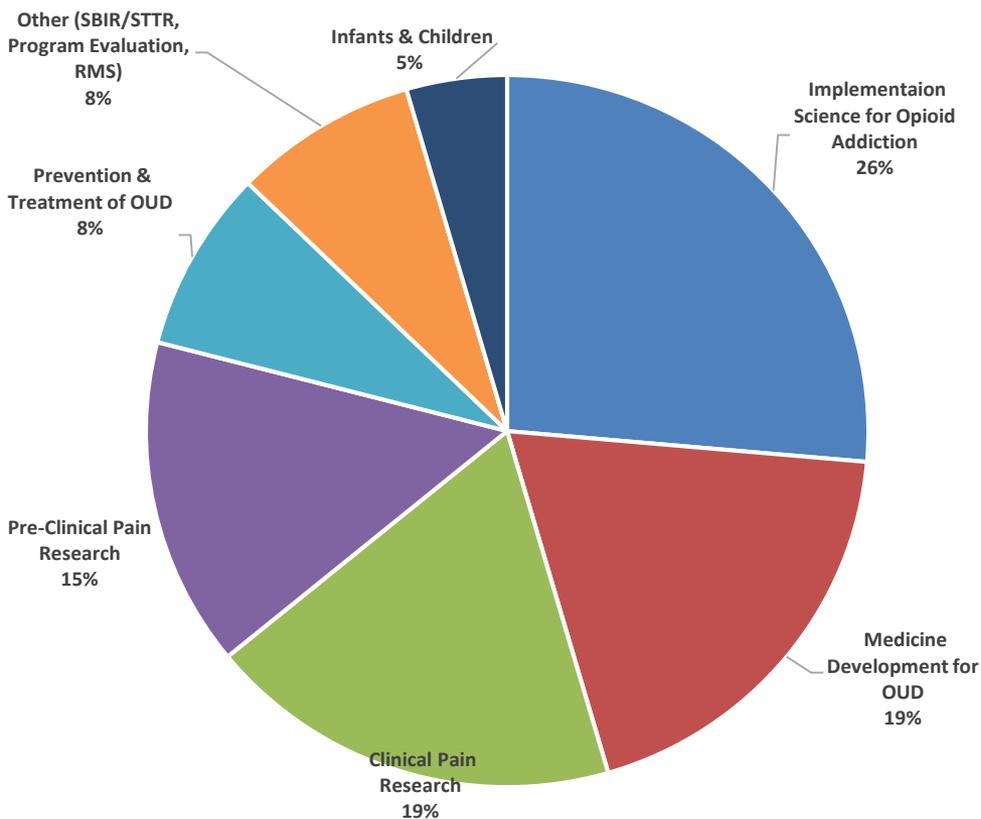
- We are adhering to the President's Budget until we get more clarity from Congress on final FY2020 budget
- Currently for FY 2020 - funding through 12%

# NINDS Commitment to Early Stage Investigators

FY (payline)	FY12 (15%)	FY13 (14%)	FY14 (14%)	FY15 (14%)	FY16 (15%)	FY17 (12%)	FY18 (15%)
<b>Total number of ESI awardees</b>	60	58	49	80	80	61	93
Number of ESI awardees above NINDS payline	24	28	21	36	35	34	28
Number ESI within the payline	36	30	28	44	45	27	65
<b>% of ESI applications paid to 25% tile</b>	88%	93%	87%	98%	98%	95%	98%
ESI Funding (TC) for applications above the payline	\$8.1M	\$9.8M	\$7.1M	\$12.9M	\$13.0M	\$13.3M	\$10.8M

# Trans-NIH Initiative Funding

# Helping to End Addiction Longterm (HEAL) Initiative Research FY 19 Tentative Spending Plan

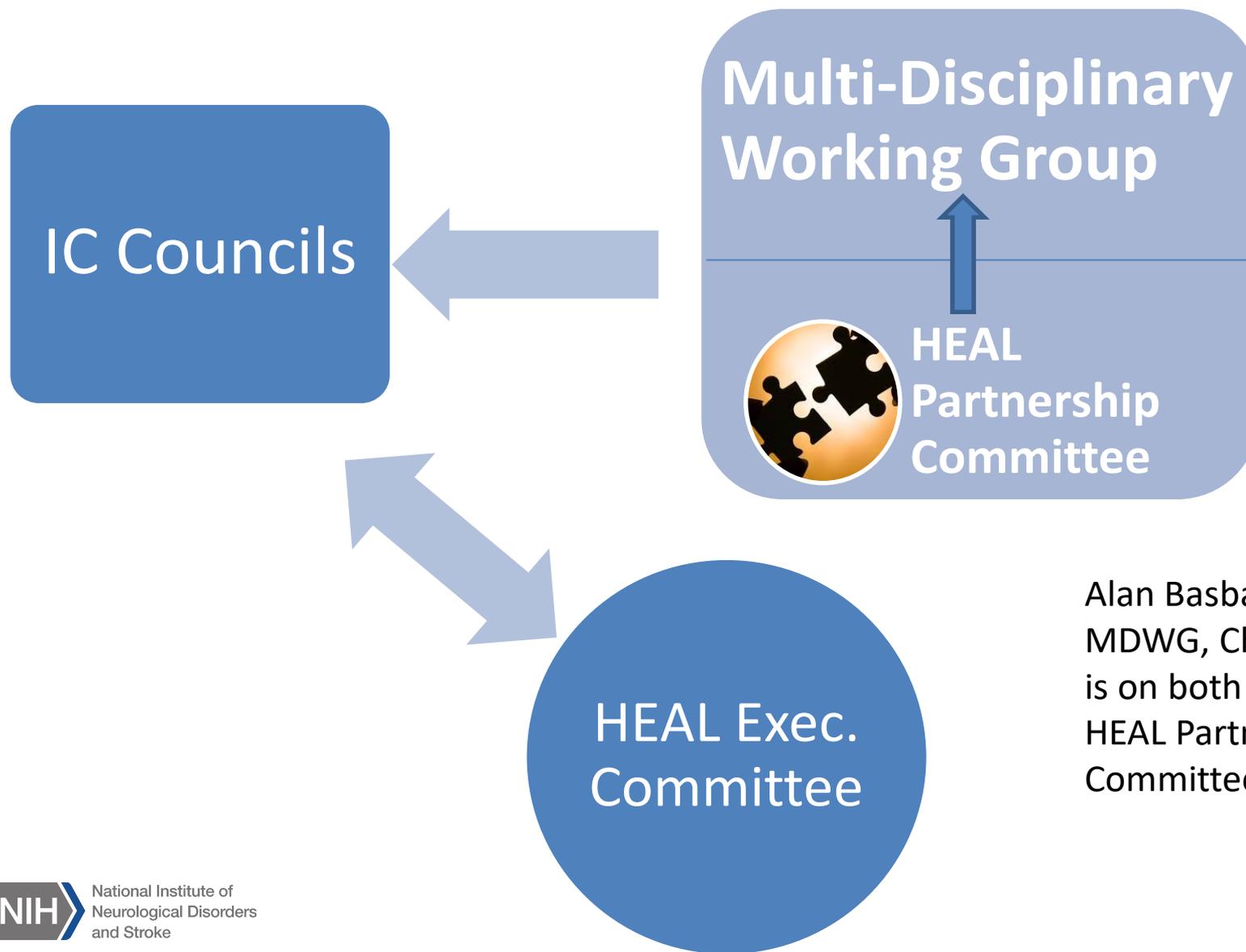


Note: OUD (Opioid Use Disorder)

- HEAL launched in response to the opioid epidemic for addiction/pain research funded from '18-'19 \$'s
- Dr. Collins (OD) invited all ICs to propose HEAL programs
- OD chose the research priorities
- RFAs released and reviewed in approved areas
- Presentations/discussion MDWG and HEAL Executive Committee
- Final decisions by Dr. Collins

FY 2019 total: ~\$930M

# HEAL Decision-Making



Alan Basbaum is on the MDWG, Christin Veasley, is on both MDWG and the HEAL Partnership Committee

# HEAL Programs for Pain

## Pre-Clinical Research in Pain

- Target Discovery/Validation
- Devices/SPARC\*
- Therapy Development
- Preclinical Screening Platforms (animal models and **NCATS** human cells)

## Clinical Research in Pain Management

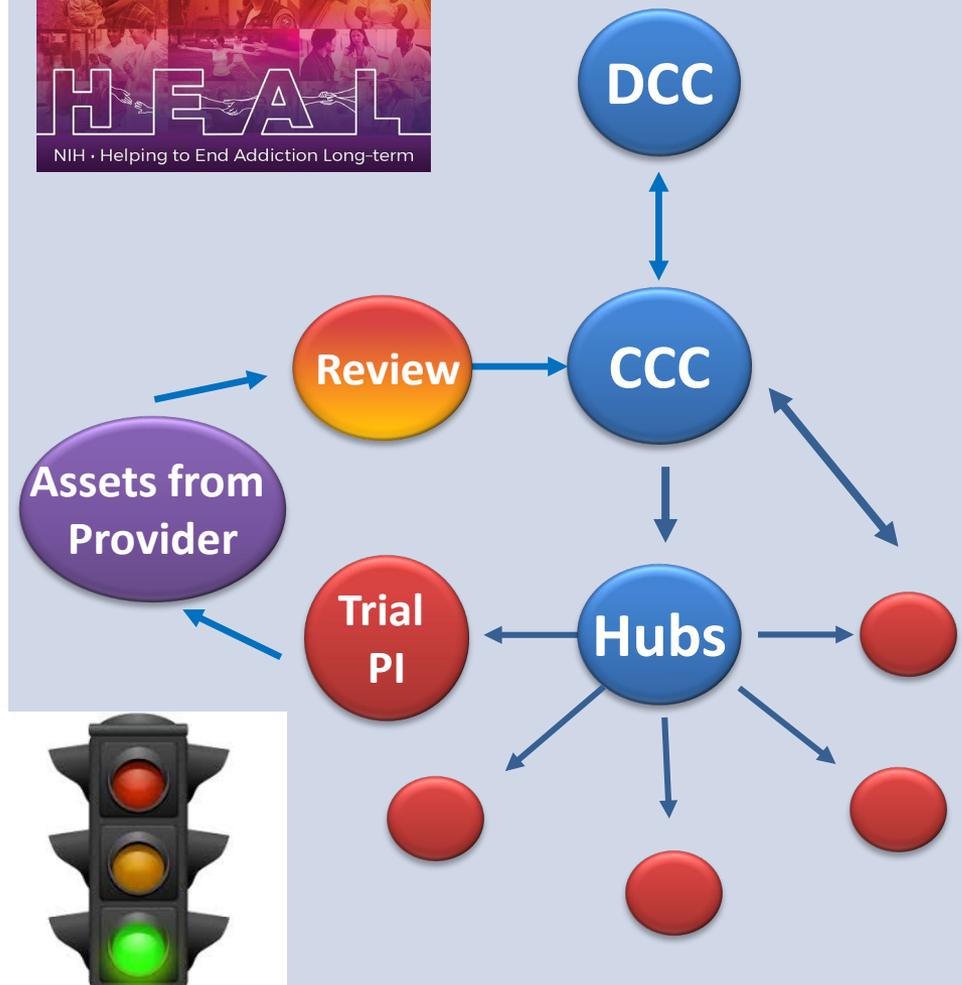
- Early Phase Pain Investigation Clinical Network EPPIC-NET
- Back Pain Consortium (**NIAMS**)
- Comparative Effectiveness
  - Effectiveness Research Network (**Multiple ICs**)
  - Pragmatic & Implementation Studies for the Management of Pain (PRISM) (**NCCIH**)
  - Hemodialysis pain consortium (**NIDDK**)
- Biomarkers
- Acute to Chronic Pain Transition (NINDS and **NIDA**)\*

\* Programs that receive NIH Common Fund support

# EPPIC Net Infrastructure

## Goals for **EPPIC-Net** (Early Phase Pain Investigation Clinical Network):

- Provide academia/industry with expert infrastructure to test early-phase pain therapeutics (drugs/devices) for conditions of unmet need
- Accelerate, high quality early-phase clinical trials of biomarkers and non-addictive pain therapeutics in deeply phenotyped cohorts with different pain conditions.



# Thank You to the Many NINDS Staff who Participated in the HEAL Initiative!

- Amir Tamiz
- Amy Adams
- Ana Garcia Orellana
- Barbara Karp
- Becky Roof
- Brian Klein
- Brooks Gross
- Carlos Faraco
- Cheryse Sankar
- Chris Boshoff
- Christine Lam
- Chuck Cywin
- Clint Wright
- Cristina Saugar Lanchas
- Danielle Haney
- Eric Hudak
- Ernie Lyons
- Jackie Ward
- Jeremy Brown
- Jimok Kim
- John Kehne
- Joonil Seong
- Julia Bachman
- Kari Ashmont
- Karrah Benson
- Leah Pogorzala
- Linda Porter
- Liza Litvina
- Margo Warren
- Maria Charlier
- Marilyn Moore-Hoon
- Mary Ann Pelleymounter
- Michael Oshinsky
- Mohamed Hachicha
- Nick Langhals
- Paul Myers
- Quynh Ly
- Ranga Rangarajan
- Sarah Woller
- Smriti Iyengar
- Stephanie Fertig
- Tim Lyden

# NINDS Leadership Changes



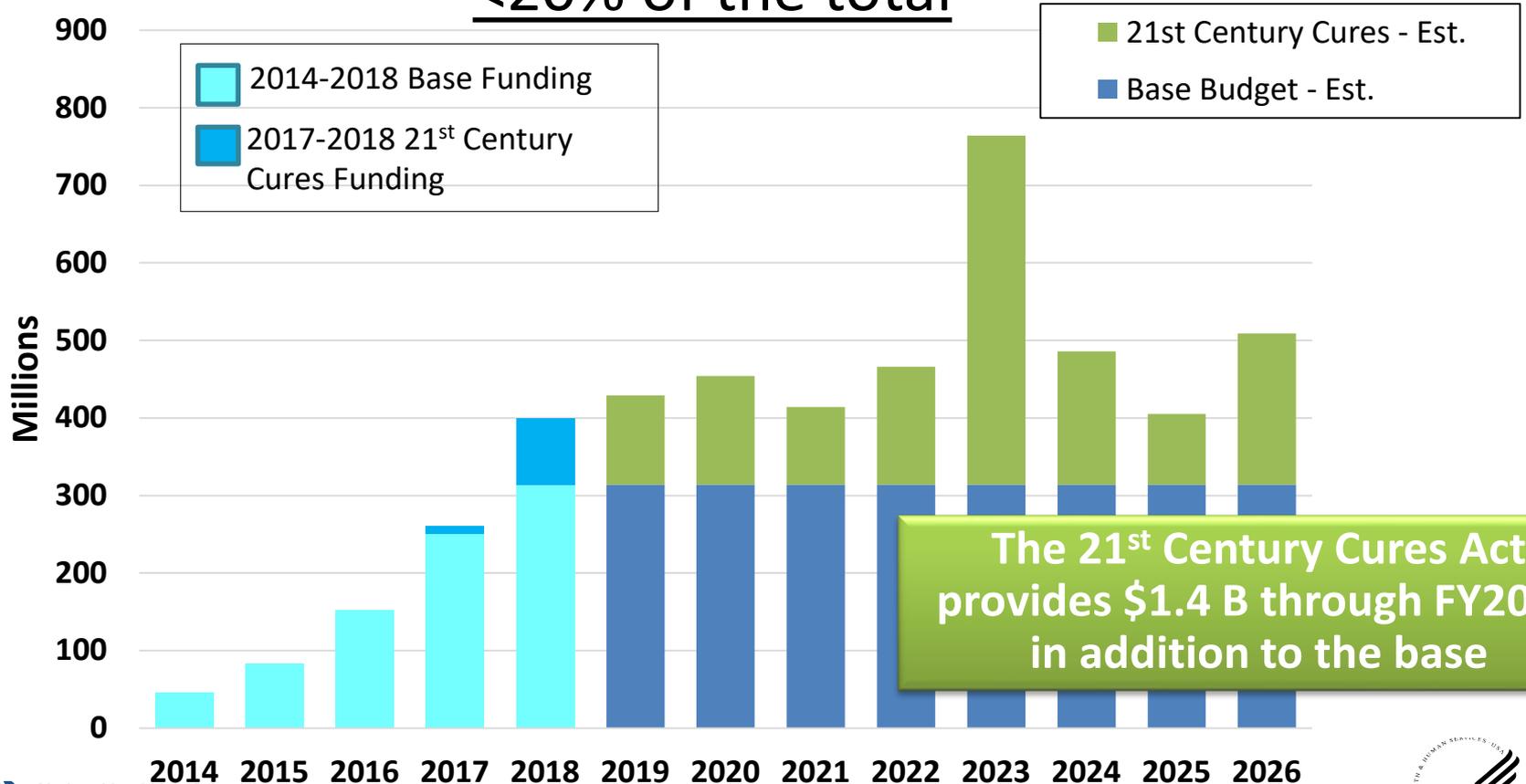
**Linda Porter, Ph.D.**  
**Director, Office of Pain Policy and Planning**  
*Previously: Director, Office of Pain Policy*

# BRAIN is Just Getting Started!

**\$4.9B** Projected total for lifetime of BRAIN

**~\$950M** BRAIN Funding through 2018

<20% of the total



# ACD BRAIN Working Group 2.0 and BRAIN Neuroethics Subgroup

- BRAIN Initiative WG 2.0 and BRAIN Neuroethics Subgroup specifically and separately convened to review scientific progress and develop Neuroethics Roadmap
- Currently finalizing reports with NIH staff, based on ACD feedback
- Reports and video of their presentations available on NIH ACD website: <https://acd.od.nih.gov/meetings.html>



# NIH Topics

# Foreign Influences

- ACD Working Group on Foreign Influences on Research Integrity
- NIH concerned about threats to the integrity of the U.S. biomedical research enterprise, specifically:
  - Failure to disclose substantial contributions of resources from other organizations, including foreign governments, which threatens to distort decisions about the appropriate use of NIH funds.
  - Diversion of intellectual property in grant applications or produced by NIH-supported biomedical research to other entities, including other countries.
  - Sharing of confidential information by peer reviewers with others, including in some instances with foreign entities, or otherwise attempting to influence funding decisions.

# Neuroscience in a Global Era



## LETTERS

Edited by Jennifer Silts

### Racial profiling harms science

On behalf of the Society of Chinese Bioscientists in America (SCBA), the Chinese American Hematologist and Oncologist Network (CAHON), and the Chinese Biological Investigators Society

of interest. Such policies have been further enhanced in recent years with more detailed and specific requirements from various federal and state agencies, including the National Institutes of Health (NIH) (4). The vast majority of scientists and students of Chinese descent are law-abiding citizens, residents, or visitors who have followed these rules.

must be established through official channels. NIH also suggests more disclosure requirements for foreign collaborators than domestic colleagues (pp. 12-13 in (2)), which could hinder collaborations.

In recent decades, there have been several high-profile cases in which Chinese-American scientists were wrongfully accused of spying (e.g., (6-10)).

## NIH Response:

*We are determined to maintain the integrity of the NIH research enterprise, but we are also deeply concerned about the issues raised by these three societies. NIH is committed to avoiding overreaction, stigmatization, harassment, and profiling.*

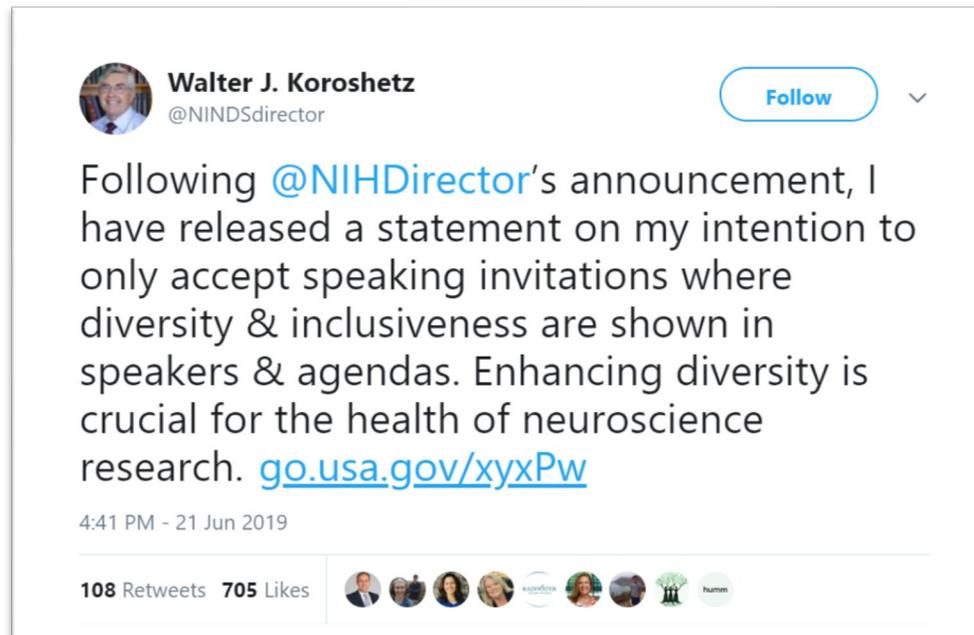
Francis S. Collins\*, Lawrence A. Tabak, Carrie D. Wolinetz, Michael S. Lauer, Michael M. Gottesman, *Science* 22 Mar 2019: Vol. 363, Issue 6433, pp. 1292-1294

“As to the concerns raised by scientists of Chinese descent who feel they are being targeted by increased scrutiny, I hear you. Please know that this is not the intent and we are sensitive to the perception that this is happening. Importantly, I want you to know that NINDS deeply appreciates the scientific contributions of the many neuroscientists around the globe who are from China or are of Chinese descent”.

- [NINDS Director's Message](#)

# NIH Efforts to Change the Culture to End Sexual Harassment

- NIH ACD Working Group ACD Working Group on Changing the Culture to End Sexual Harassment – final report expected in Dec 2019
- Current NIH focus:
  - Demonstrating accountability
  - Clarifying expectations for institutions and investigators to ensure a safe workplace and inform the agency
  - Providing clear channels of communication to NIH



# Sexual Harassment at NIH



NATIONAL CANCER INSTITUTE

Nearly one in five NIH employees say they experienced gender harassment in the past year

By Meredith Wadman | Jun. 12, 2019, 5:30 PM

- NIH surveyed employees early this year
- Received ~16,000 responses (response rate of 44%)
- Overall, 21.6% of respondents said they experienced harassment
- 44.8% of transgender staff and those with other gender identities reported harassment

**NIH and NINDS rolled out a number of programs to combat harassment**

# Requirements for Human Fetal Tissue Research

- HHS announced changes to requirements for research involving human fetal tissue (HFT)
- The new requirements include:
  - specific justification of HFT use within applications or proposals,
  - additional details regarding procurement and costs, and
  - information about how HFT is used in the research
- Applications and proposals involving HFT that fall within a fundable scoring range will be assessed for policy compliance by an HHS ethics advisory board comprised of scientists, bio-ethicists and others

## Changes to NIH Requirements Regarding Proposed Human Fetal Tissue Research

Notice Number: NOT-OD-19-128

### Key Dates

Release Date: July 26, 2019

### Related Announcements

[NOT-OD-19-137](#)

### Issued by

NATIONAL INSTITUTES OF HEALTH (NIH)

### Purpose

The purpose of this notice is to inform the extramural research community of upcoming [HHS requirements](#) and review considerations regarding research that is supported by the NIH and involves the proposed use of human fetal tissue obtained from elective abortions (HFT) in extramural applications for grants, cooperative agreements and R&D contracts. These requirements are in addition to the existing requirements as detailed in the NIH Grants Policy Statement (4.1.14). In addition, NIH reminds the community of expectations to obtain informed consent from the donor for any NIH-funded research using HFT ([NOT-OD-16-033](#)).

# NIH Leadership Changes



**Linda Birnbaum, Ph.D., D.A.B.T., A.T.S.**, is retiring as Director of the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP)  
*Richard Woychik, Ph.D. will serve as NIEHS Acting Director*



**Paul Sieving, M.D., Ph.D.**, recently retired as Director of the National Eye Institute (NEI)  
*Santa Tumminia, Ph.D. is serving as NEI Acting Director*



# NINDS Topics

# 2019 Landis Award for Outstanding Mentorship



**Heather Broihier, Ph.D.**  
Case Western  
Reserve University



**Jonah Chan, Ph.D.**  
University of California,  
San Francisco



**Mel Feany, M.D., Ph.D.**  
Brigham and Women's  
Hospital



**Miriam Goodman, Ph.D.**  
Stanford University



**Louise McCullough, M.D., Ph.D.**  
University of Texas Health  
Science Center



**Matthew Rasband, Ph.D.**  
Baylor College of Medicine



**Bernardo Sabatini, M.D., Ph.D.**  
Harvard Medical School

**2020 Landis Award** nominations now open for **senior faculty!**  
Researchers who are **21 years or more from the start of their first** tenure-track  
or equivalent faculty positions are eligible

# Upcoming Workshops



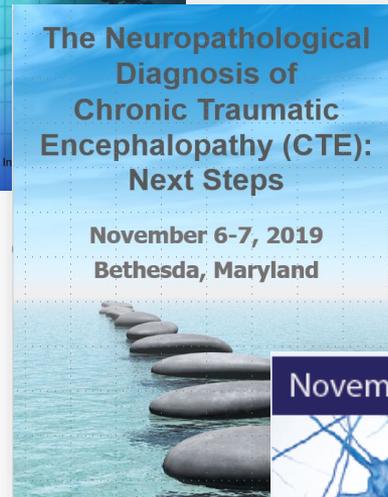
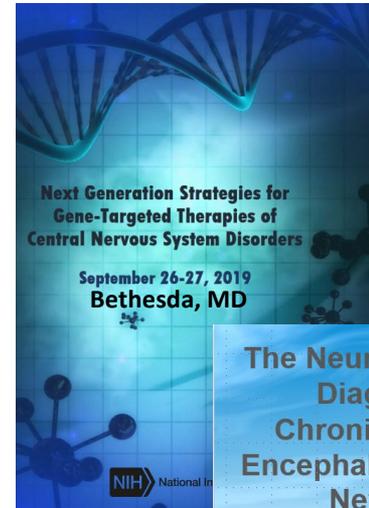
**HEAL Initiative  
Investigator's Meeting  
January 16-17,  
Bethesda MD**



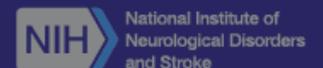
**Workshop on Future  
VCID Clinical Trials  
November 3-4  
Bethesda, MD**



**InTBIR 8th Conference  
October 24-25,  
Bethesda, MD**

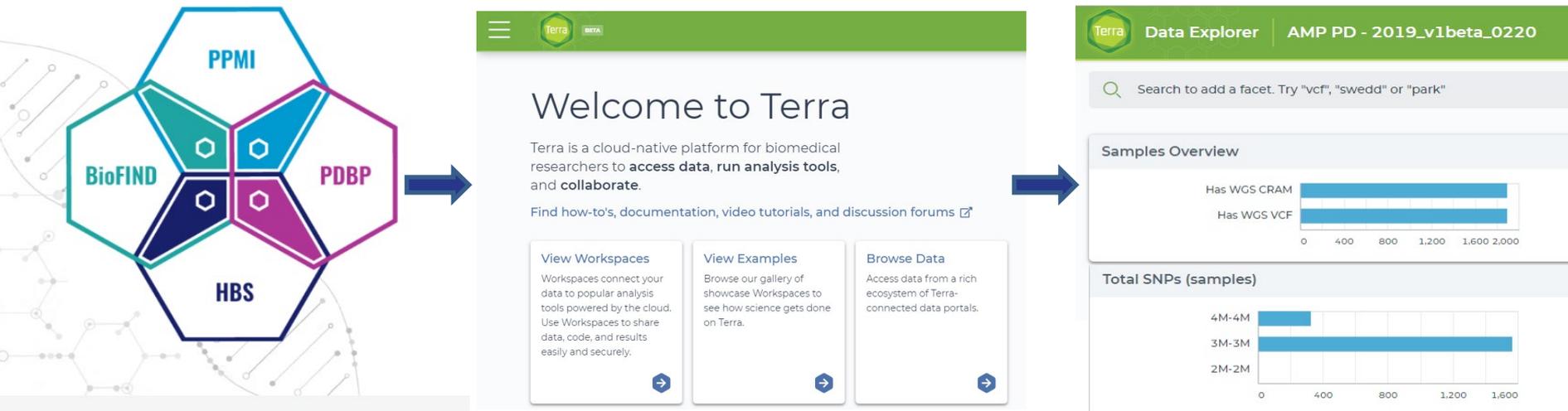


**Improving the Identification  
of Disease Modification  
PD Targets and Their Testing  
in Early Phase Clinical Trials**



# Accelerating Medicines Partnership: Parkinson's Disease

Collaborating toward **biomarker discovery** to advance the development of **Parkinson's disease therapies**



Planned AMP-PD demonstration at **Neuroscience of Movement Disorders Symposia Meeting, SFN Satellite**  
*Friday, October 18 @ 5 PM*



# Events at Neuroscience 2019

AMP-PD demonstration at **Neuroscience of Movement Disorders Symposia Meeting**  
*Friday, October 18 @ 5 PM*

*SfN Annual Meeting Mini-Symposium: “BRAIN Initiative: Cutting-Edge Tools and Resources for the Community”*  
*Saturday, October 19 @ 1:30 PM*

## **Diversity Poster Session**

*Saturday, October 19 @ 6:30 PM*

Featuring participants of the Neuroscience Scholars Program, ENDURE, and other diversity fellowship programs

## **NIH Funding and You: A Practical Guide for a Trainee to Survive and Thrive in Your Research Career**

*Sunday, October 20 @ 6:30 PM*

## **Reception: Tools & Tech: A BRAIN Initiative Alliance Social**

*Sunday, October 20 @ 6:30 PM*

## **Neuroethics Social**

*Sunday, October 20 @ 6:45 PM*



# NINDS Strategic Planning

## Timeline:



## NINDS Mission:

To seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

## Strategic Goals:

- Be a model of excellence for supporting and performing significant, innovative, and rigorous neuroscience research.
- Be a model of excellence for funding and conducting neuroscience research training and career development programs and ensuring a vibrant, talented, and diverse neuroscience work force.
- Promote the timely dissemination of accurate and rigorous information about scientific discoveries and their implications for neurological health.
- Promote a supportive work culture for biomedical research and the neuroscience community.

# NINDS Strategic Planning

**Please contribute your input to the new NINDS Strategic Plan!**

**NOT-NS-19-079**

**Request for Information:  
Input into the National Institute of Neurological Disorders and Stroke Strategic Planning Process**

NINDS is initiating a new strategic planning process. As a first step, we are seeking broad public input on how we can best achieve our mission. Please submit your perspective to this Request for Information!

<https://grants.nih.gov/grants/guide/notice-files/NOT-NS-19-079.html>



# Science Advances

# BRAIN Science Advance

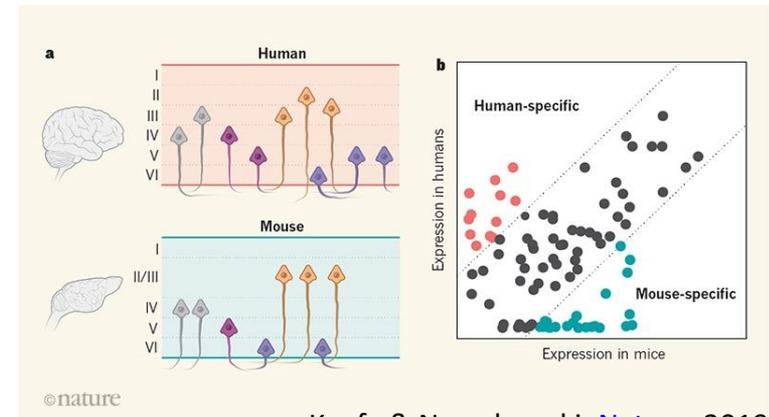
## Human cortical census

### Conserved cell types with divergent features in human versus mouse cortex

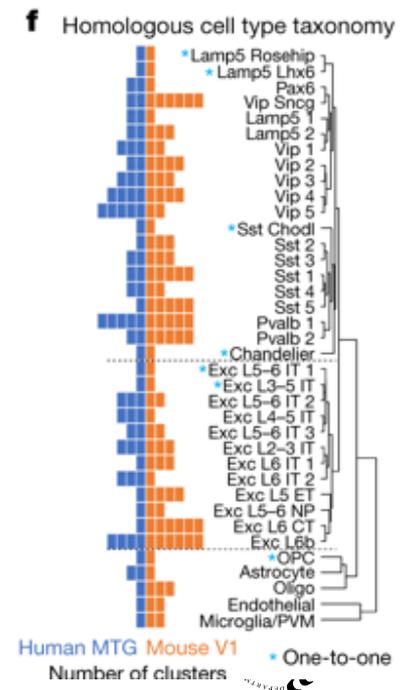
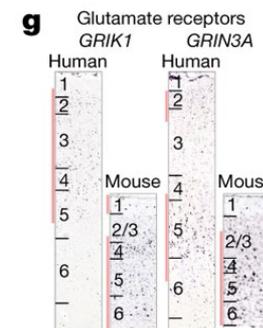
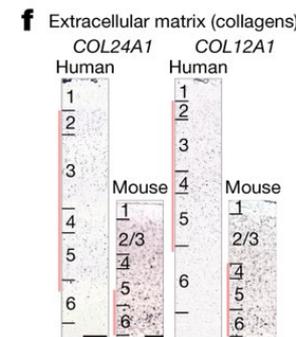
Ed Lein, Allen Institute for Brain Science

Hodge, Bakken, et al, [Nature](#), 2019

- Single cell RNA-seq from post-mortem human brain to catalog cell types in the middle temporal gyrus of the cortex
- Species level conservation (compared to mouse visual/motor cortex) in cellular architecture as predicted by anatomy
  - No major classes had missing homologous cell types.
- Differences in gene expression patterns in homologous cell types, especially in genes associated with cell signaling
  - Suggests major differences may be in the microcircuitry.
- Non-neuronal cells demonstrated the most divergent gene expression compared to mouse
- Differences in the proportion of inhibitory neurons



Keefe & Nowakowski, [Nature](#), 2019

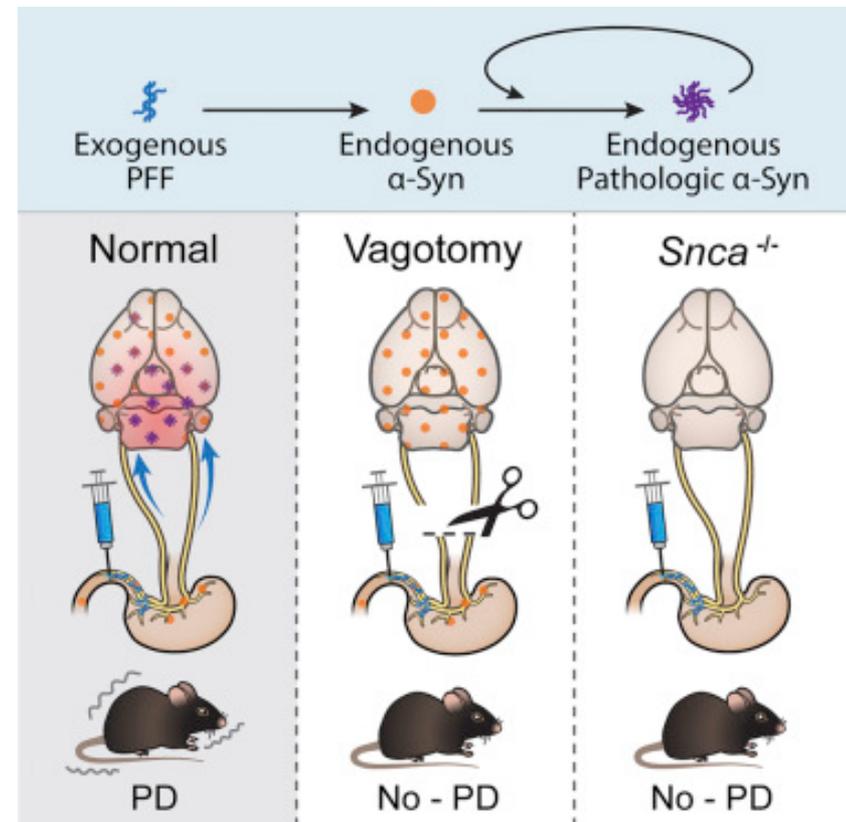
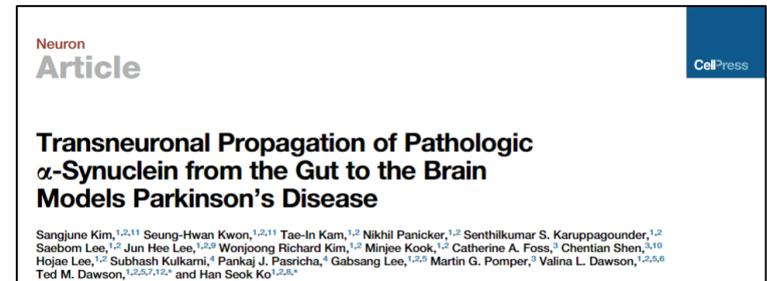


### Transneuronal Propagation of Pathologic $\alpha$ -Synuclein from the Gut to the Brain Models Parkinson's Disease

Han Seok Ko & Ted Dawson, Johns Hopkins University

Kim et al, [Neuron](#), 2019

- Injection of synuclein fibrils into the wall of stomach/duodenum leads to propagation of synuclein aggregation in brainstem nuclei, and then progression through brain over months
  - In accord with Braak hypothesis of PD.
- Dopamine neurons degenerate in this  $\alpha$ -synuclein gut-to-brain model of PD
- Gut injection of pathologic  $\alpha$ -synuclein causes PD-like motor and non-motor symptoms
- PD-like pathology and symptoms require endogenous  $\alpha$ -synuclein which is triggered to aggregate by the seeding into the gut wall (myenteric nerve plexus)



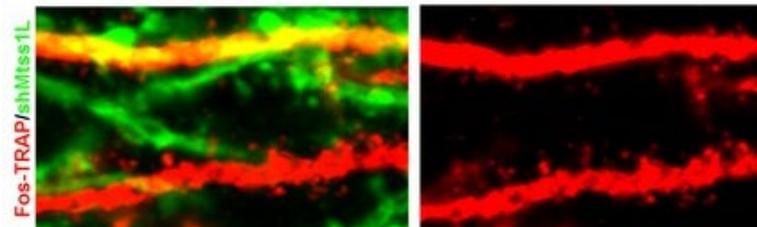
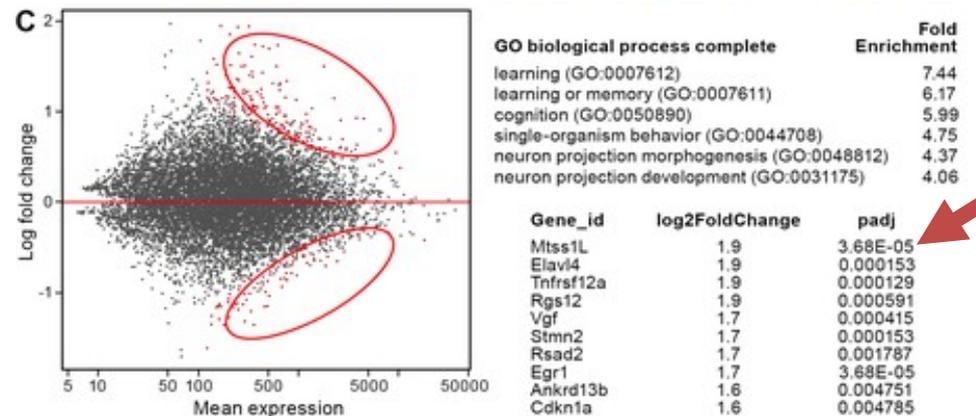
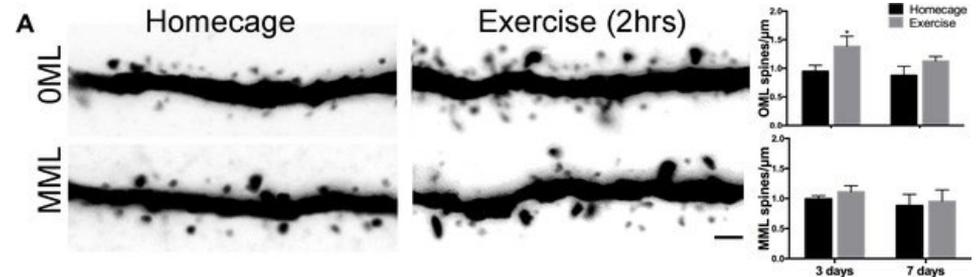
## Cellular effects of exercise on neurons

### Exercise-induced enhancement of synaptic function triggered by the inverse BAR protein, *Mtss1L*

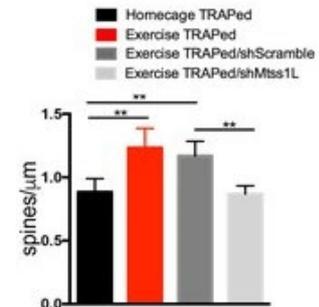
Gary Westbrook, Oregon Health & Science University

Chatzi et al, *eLife*, 2019

- Marked activated mature hippocampal dentate granule cells using conditional Fos-TRAP
- Input-selective increase in dendritic spines and excitatory postsynaptic currents at 3 days post-exercise
- Most highly induced transcript was *Mtss1L*
  - Could be involved in membrane curvature and dendritic spine formation



**Mtss1L knockdown: fewer spines**

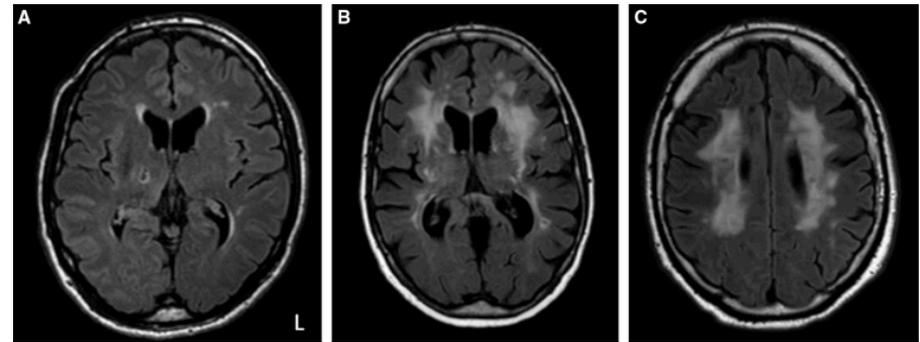


# Science Advances

## Blood pressure control in brain health

### Association of Intensive vs Standard Blood Pressure Control With Cerebral White Matter Lesions

The SPRINT MIND Investigators for the SPRINT Research Group, [JAMA](#), 2019



- 449 hypertensive patients received brain MRIs at baseline and after 4 years; randomized to systolic BP goal of less than 120 mm Hg (intensive) or 140 mm Hg (standard)
- Group with more intensive BP control (120) was significantly associated with a smaller increase in cerebral white matter lesion volume and a greater decrease in total brain volume

Table 2. Estimated Changes in Structural Magnetic Resonance Imaging Outcomes by Treatment Group<sup>a</sup>

Outcome	Volume (95% CI), cm <sup>3</sup>		Intensive	Standard		Estimated Difference in Change	P Value	
	Intensive Treatment	Follow-up		Standard Treatment	Follow-up			
WML volume, asinh	1.99 (1.86 to 2.13)	2.14 (2.01 to 2.28)	0.15 (0.11 to 0.19)	1.96 (1.82 to 2.10)	2.25 (2.10 to 2.39)	-0.13 (-0.19 to -0.07)	<.001	
WML volume	4.57 (4.00 to 5.14)	5.49 (4.91 to 6.07)	0.92 (0.69 to 1.14)	4.40 (3.80 to 5.00)	5.85 (5.23 to 6.47)	1.45 (1.21 to 1.70)	-0.54 (-0.87 to -0.20)	
Annualized change			0.23 (0.17 to 0.29)			0.37 (0.30 to 0.43)		
Total brain volume	1134.5 (1125.1 to 1144.0)	1104.0 (1094.5 to 1113.4)	-30.6 (-32.3 to -28.8)	1134.0 (1124.4 to 1143.6)	1107.1 (1097.4 to 1116.8)	-26.9 (-28.8 to -24.9)	-3.7 (-6.3 to -1.1)	.006
Annualized change			-7.7 (-8.1 to -7.3)			-6.8 (-7.3 to -6.3)		

Abbreviations: WML, white matter lesion; asinh, inverse hyperbolic sine transformation,  $f(x) = \log(x + (x^2 + 1)^{0.5})$ .

<sup>a</sup> Estimates based on a linear mixed model, adjusting for intracranial volume and days since randomization, with random effects for participant and magnetic resonance imaging facility. All estimates computed using the baseline mean intracranial volume of 1382.03 cm<sup>3</sup>, with follow-up estimates computed at 1452 days (3.98 years)

after randomization. For change estimates, negative values denote decreases from baseline; positive values, increases from baseline. Difference in change represents intensive treatment group minus standard treatment group.

# Stroke Hyperglycemia Insulin Network Effort (SHINE)

Research

Karen Johnston, PI

JAMA | Original Investigation

## Intensive vs Standard Treatment of Hyperglycemia and Functional Outcome in Patients With Acute Ischemic Stroke The SHINE Randomized Clinical Trial

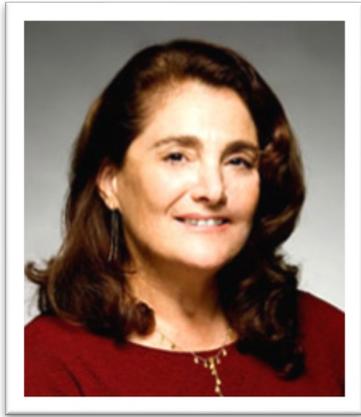
Karen C. Johnston, MD; Askiel Bruno, MD; Qi Pauls, MS; Christiana E. Hall, MD; Kevin M. Barrett, MD; William Barsan, MD; Amy Fansler, MPH; Katrina Van de Bruinhorst, MA; Scott Janis, PhD; Valerie L. Durkalski-Mauldin, PhD; for the Neurological Emergencies Treatment Trials Network and the SHINE Trial Investigators



# Introduction

# NINDS Intramural Program

## Annual Report of the NINDS Intramural Program



**Lorna Role, PhD**

**NINDS Scientific Director**

*Previously: SUNY Distinguished Professor*

# ALZHEIMER'S DISEASE-RELATED DEMENTIAS SUMMIT 2019



## Summit Goals

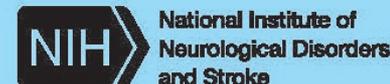
- Present rationale, including progress, for draft research recommendations
- Solicit feedback and opinions from audience and group experts
- Modify draft recommendations based on feedback

## 2 PM Today - ADRD Summit 2019 Report to Council

- ❖ Dr. Julie Schneider, Scientific Chair
- ❖ Dr. Roderick Corriveau, NIH Lead

## Council Members

- ❖ Susan Dickinson, Steering Committee
- ❖ Aaron Gitler, Emerging Scientific Topics Committee



# Working Group for ME/CFS Research *Charge*

## Goal: Reduce the burden of illness due to ME/CFS

Provide scientific guidance to the NANDS Council on how best to advance research on ME/CFS at NIH, including:

- Using the P2P workshop and the IOM reports as a guide:
  - Assess current NIH ME/CFS research activities and the extent to which they address opportunities and gaps in ME/CFS research
  - Suggest specific goals to further address opportunities and gaps in ME/CFS research, given the evolving scientific landscape
- Consider unique opportunities for NIH-supported ME/CFS research to train and empower a pipeline of young investigators, as well as investigators new to the field
- Identify an effective potential structure to enhance ongoing biomedical research collaboration and communication between relevant advocacy organizations, individuals with ME/CFS, researchers, and federal agencies

# Working Group for ME/CFS Research

## *Roster*



### **CHAIR**

Steven Roberds, Ph.D.  
Tuberous Sclerosis Alliance

### **MEMBERS**

- Armin Alaedini, Ph.D.  
*Columbia University*
- Lucinda (Cindy) Bateman, M.D.  
*Bateman Horne Center*
- Jennifer Brea/Rochelle Joslyn, Ph.D.  
*ME Action*
- Dane Cook, Ph.D.  
*University of Wisconsin*
- Carol Head / Sadie Whittaker, Ph.D.  
*Solve ME/CFS Initiative*

- Anthony (Tony) Komaroff, M.D.  
*Brigham & Women's Hospital*
- Amrit Shahzad, MBBS, MBA  
*University of California, San Diego*
- Steven Schutzer, M.D.  
*Rutgers New Jersey Medical School*

### **EX OFFICIO MEMBERS**

- Elizabeth (Beth) Unger, M.D., Ph.D.  
*CDC*  
Joseph Breen, Ph.D.  
*NIH/NIAID*  
Vicky Whittemore, Ph.D.  
*NIH/NINDS*

### **EXECUTIVE SECRETARY**

- Andrew Breeden, Ph.D.  
*NIH/NINDS*

# Thank You!

**Walter J. Koroshetz, M.D.**

**Director**

**National Institute of Neurological Disorders and Stroke**

**Email: [koroshetzw@ninds.nih.gov](mailto:koroshetzw@ninds.nih.gov)**

**Website: <http://www.ninds.nih.gov/>**



**Follow me @NINDSdirector**

- extras

# Stroke Preclinical Assessment Network (SPAN): Testing the benefits of neuroprotection

**Goal: Create a novel translational model that will accelerate the identification of the most promising neuroprotective therapies for future pivotal clinical trials and span the gap between preclinical and clinical testing, in a cost- and time-effective manner**

- Seven centers have been funded:
  - **Coordinating Center:** Cedars Sinai Medical Center; PI: Patrick Lyden
  - University of Texas Health Center; PI: Jaroslaw Aronowski (Tacilizumab, immunosuppressive drug)
  - Massachusetts General Hospital; PI: Cenk Ayata (Fasudil, vasodilator)
  - Augusta University; PI: David Hess (Remote Ischemic Conditioning)
  - Johns Hopkins University; PI: Raymond Koehler (Veliparib, anti-cancer drug)
  - University of Iowa; PI: Enrique Leira (uric acid)
  - Yale University School of Medicine; PI: Lauren Sansing (Fingolimod, immunomodulatory drug)
- The funding estimate for the network is \$4 million over 3 years

