

ADRC Directors' Meeting

National Institute on Aging

Virtual

October 2, 2020

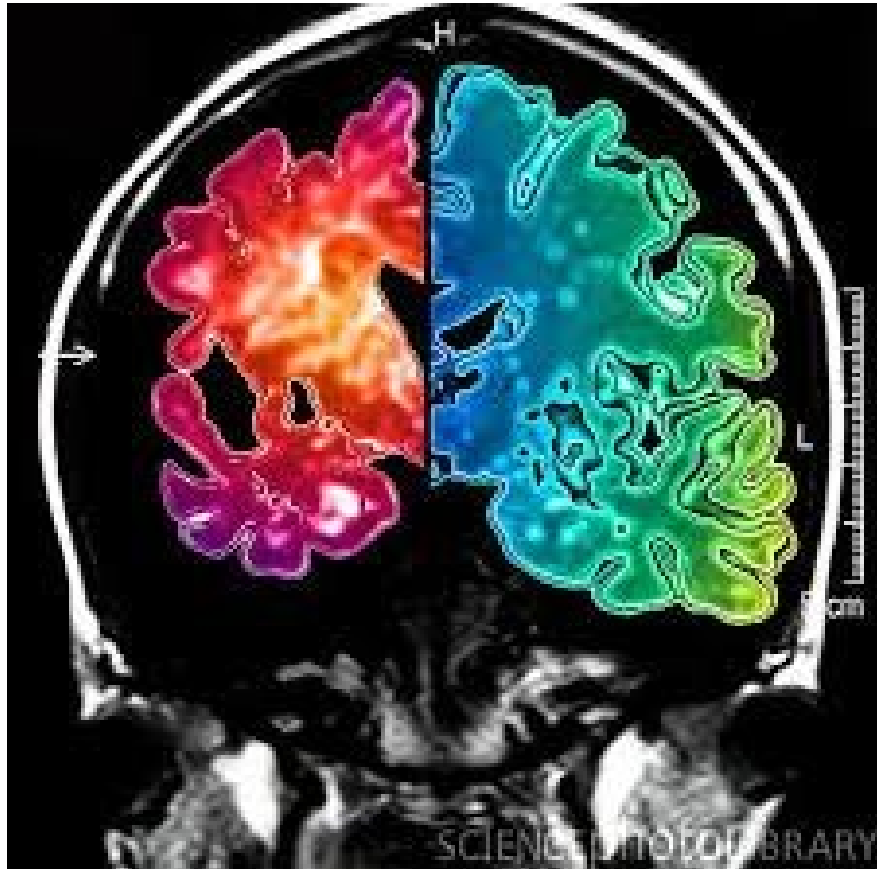
NIA Division of Neuroscience Update

Eliezer Masliah

Division of Neuroscience

NIA-NIH

NIA Division of Neuroscience




To support and advance research leading to better understanding of the mechanisms of brain aging and Alzheimer's Disease and related dementias

DN collaborates with other NIA Divisions, NIH institutes and the community to advance NAPA

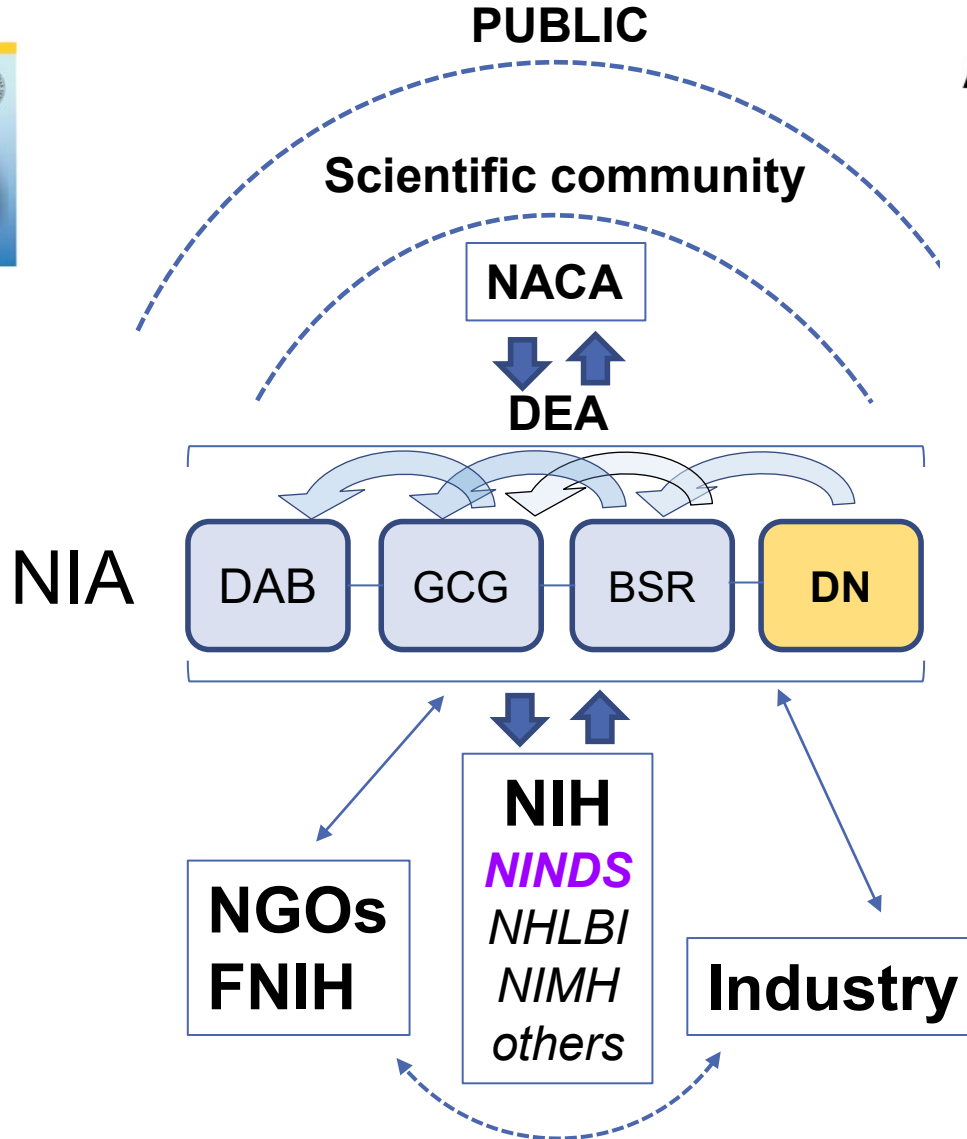
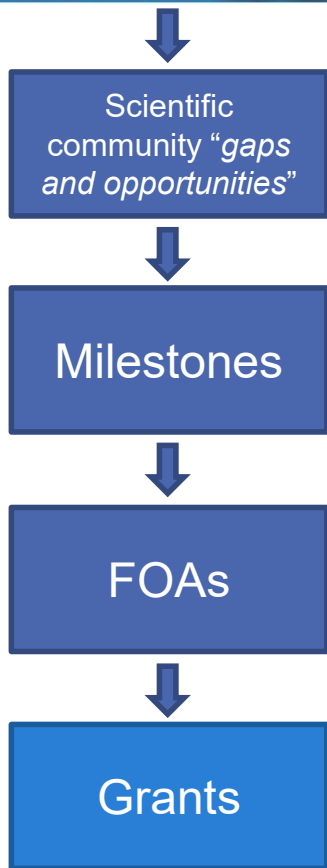
NAPA

NIH AD Research Summits:
Path to Treatment and Prevention

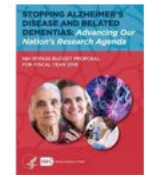
May 14-15, 2012
Feb 9-10, 2015
March 1-2, 2018



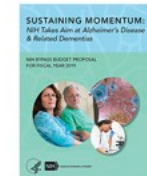
NIH National Institute on Aging
Turning Discovery Into Health



AD Bypass Budget



2018



2019



2020



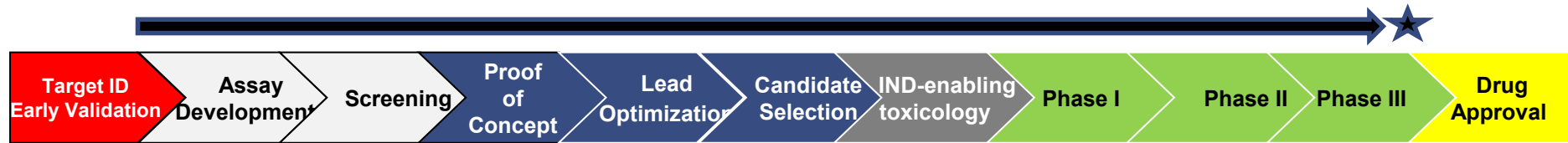
2021



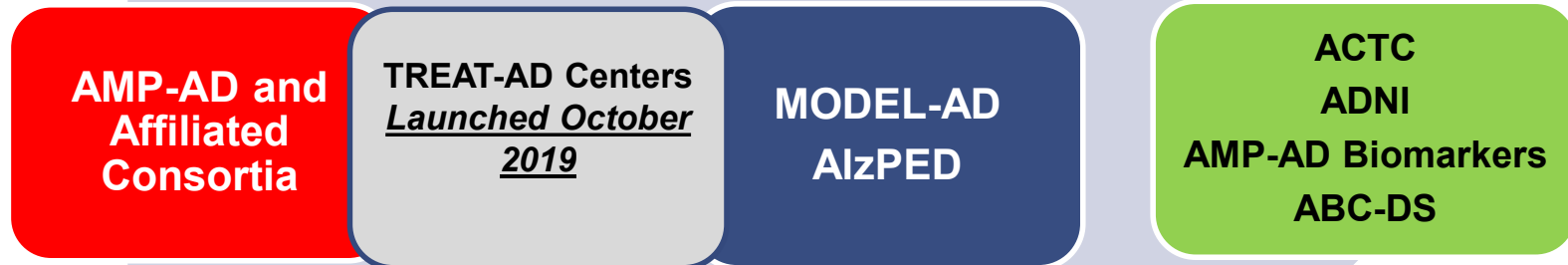
2022

NIA AD Translational Research Program: Diversifying the Therapeutic Pipeline

A Pipeline of Translational Research Funding Opportunities (R21/R01, U01, SBIR/STTR)



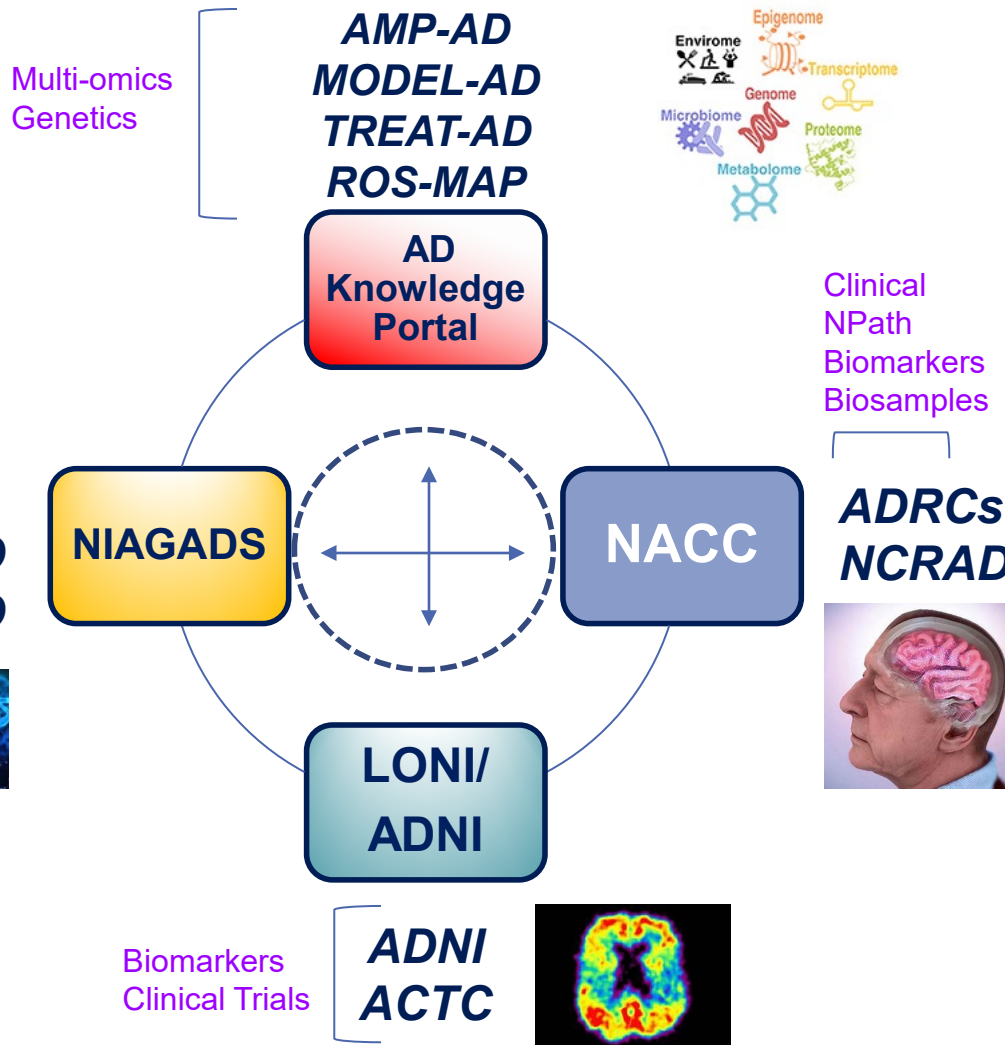
NACC/ADRCs



**ENABLING INFRASTRUCTURE FOR
DATA DRIVEN AND PREDICTIVE
DRUG DEVELOPMENT**

NIA resources for data sharing in support of 2025

NIA Program Directors: Nina Silverberg, Cerise Elliott, Laurie Ryan, Suzana Petanceska, Lorenzo Refolo, Marilyn Miller, Dallas Anderson, Kristina McLinden



- **ACTC** - AD Clinical Trials Consortium
- **ADSP** - AD Sequencing Program
- **ADGC** - AD Genetics Consortium
- **ADNI** - AD Neuroimaging Initiative
- **ADRCs** - AD Research Centers
- **AMP-AD** - Accelerating Medicines Partnership for AD
- **MODEL-AD** - Model Organism Develop and Evaluation for Late-Onset AD
- **NACC** - National AD Coordinating Center
- **NCRAD** - National Centralized Repository for AD and ADRD

NIA Division of Neuroscience New Organization

Offices

Directors Office

- Eliezer Masliah (Director) and Jennie Larkin (Deputy Director)
- Jean Tiong-Koehler, Toni Salazar, Donna Weaver, Sarita Chapman, LaKeisha Carroll, Alexander Bracy, Chelsea Dinneny

Leadership team

- Eliezer Masliah, Jennie Larkin, Bradley Wise, Molly Wagster, Suzana Petanceska, Laurie Ryan, Lorenzo Refolo

Strategic Development and Partnerships Office

- Suzana Petanceska (Director)
- Nadezda Radoja, Erika Tarver, Laurie Ryan, Jean Yuan,
- Alvin McKelvy

Population Studies and Genetics Branch

- *TBN Chief*
- Dallas Anderson, Marilyn Miller, Alison Yao, Jennie Larkin, Ananya Paria, Sharna Tingle

Neurobiology of Aging and Neurodegeneration Branch

- Brad Wise (Chief)
- Mack Mackiewicz, Paul Barrett, Amanda M. DiBattista, Austin Yang, Lisa Opanashuk, Elizabeth A. Newman

Behavioral and Systems Neuroscience Branch

- Molly Wagster (Chief)
- Luci Roberts, Coryse St. Hillaire-Clarke, Devon Oskvig, Matt J Sutterer, Dave Frankowski

Translational Research Branch

- Lorenzo Refolo (Chief)
- Suzana Petanceska, Zane Martin, Jean Yuan, Shreaya Chakroborty,
- Ali Sharma

Clinical Interventions and Diagnostics Branch

- Laurie Ryan (Chief)
- Nina Silverberg, John Hsiao, Cerise Elliot, Yuan Luo, Kristina McLinden, Akanni Clarke, Grayson Donley, Alvin McKelvy

Branches

Director's Office



Eliezer Masliah (Director) and **Jennie Larkin (Deputy Director)**

Jean Tiong-Koehler, Toni Salazar, Donna Weaver,

Sarita Chapman, LaKeisha Carroll, Alex Bracy, Chelsea Dinneny



Office for Strategic Development and Partnerships

Enable an integrated approach to program development on all aspects of brain aging, Alzheimer's disease, and related dementias to accelerate therapy development and to facilitate the Division of Neuroscience's collaborations.

- **NAPA milestones, AD Summit, ADBB, Public-Private Partnerships, IADRP**

Suzana Petanceska (Director)

Laurie Ryan

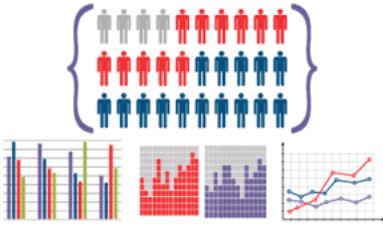
Nadezda Radoja

Erika Tarver

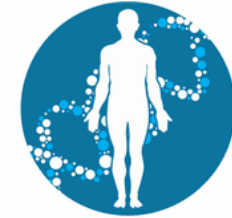
Jean Yuan

Alvin McKelvy





Population Studies and Genetics Branch



Understanding the contributions of population and genetics studies in brain aging and neurodegeneration

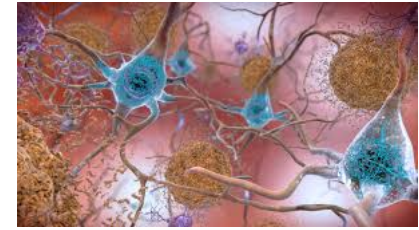
- **Trajectory of cognitive decline-** *MCI/AD, potential risk and protective factors*
- **Morbidity/mortality-** *in general populations and race/ethnic subpopulations*
- **Novel genomic elements-** *functional roles driving heterogeneity*
- **Integrated genomics-** *machine learning, functional genomics, harmonization*
- **ADSP, NIAGADS, CGAD, GCAD**

Dallas Anderson,
Damali Martin
Marilyn Miller,
Alison Yao,
Jennie Larkin,
Ananya Paria,
Sharna Tingle





Neurobiology of Aging and Neurodegeneration Branch



Understanding how the nervous system is affected by normal as well as pathological aging

- **Fundamental Neuroscience-** *functional changes, selective vulnerability, plasticity*
- **Basic Science of AD/ADRD-** *molecular and cellular mechanisms, repair, neurovirology*
- **Integrative Neurobiology-** changes between organ systems and the CNS
- **Sleep and Biological Rhythms** - sleep-wake cycles/disordered biorhythmicity
- **BRAIN initiative, Stem cells, human connectome, Blueprint, single cell atlas**

Brad Wise (Chief)

Mack Mackiewicz

Amanda M. DiBattista

Lisa Opanashuk

Austin Yang

Paul Barrett

Elizabeth A. Newman

Rachel Sare





Behavioral and Systems Neuroscience Branch



Neural and psychological mechanisms underlying age-related changes in cognition, emotion, sensory and motor function

- **Cognitive neuroscience-** *learning, memory, attention, executive function, language*
- **Sensory processes-** *visual, auditory, somatosensory, pain, vestibular*
- **Motor function-** *neuromuscular, sensory-motor, balance, and movement disorders*
- **Affective Neuroscience-** *interface between emotion and cognition*
- **NIH Toolbox, HEAL Initiative, Delirium, Resilience, Super-Agers**

Molly Wagster (Chief)

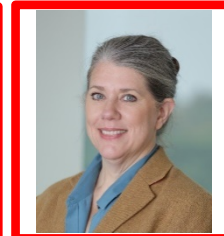
Luci Roberts

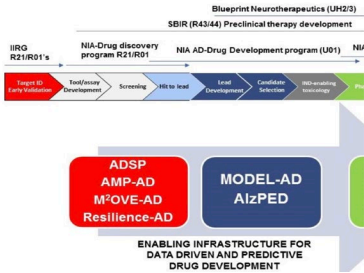
Coryse St. Hillaire-Clarke

Devon Oskvig

Matt J Sutterer

Dave Frankowski





Translational Research Branch

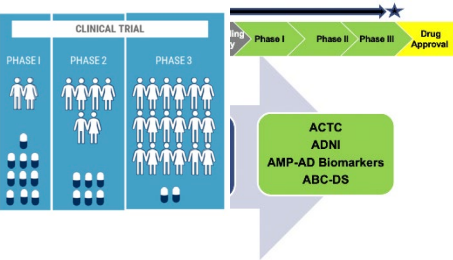


Supports the spectrum of drug discovery and preclinical drug development from target discovery and validation through securing Investigational New Drug (IND)

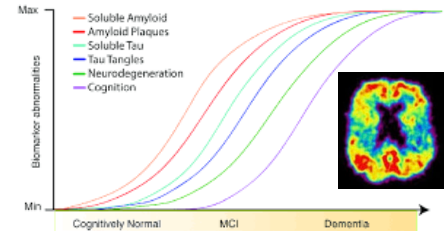
- **Target discovery and validation** – systems and network biology approaches
- **Drug discovery and preclinical drug development** – *development of small molecules and biologics for a diverse set of therapeutic targets*
- **Drug repositioning and combination therapy development** – *integrated computational and experimental approaches*
- **Translational Infrastructure and Training** – *open science consortia and centers, resources for increasing research rigor, reproducibility, and translatability*
- **ADDP, SBIR-STTR, Blueprint Neurotherapeutics, AMP-AD and Affiliated Consortia (M²OVE-AD, Resilience-AD, Psych-AD), MODEL- AD Consortium, TREAT-AD Centers, AD Knowledge Portal/Agora, ALzPED**

Larry Refolo (Chief)
 Suzana Petanceska
 Zane Martin
 Jean Yuan
 Shreaya Chakroborty
 Ali Sharma





Clinical Interventions and Diagnostics Branch



Supports research aimed at prevention, treatment, and management of individuals with or at-risk for cognitive decline, AD/ADRD

- **Biomarkers-** *diagnostic procedures instruments, imaging, fluid and digital biomarkers, and clinical and neuropsychological instruments for diagnosis*
- **Pharmacological and non-pharmacological clinical trials-** *Phases I-III, small molecules, biologics, combination therapies, neurostimulation, behavioral, lifestyle*

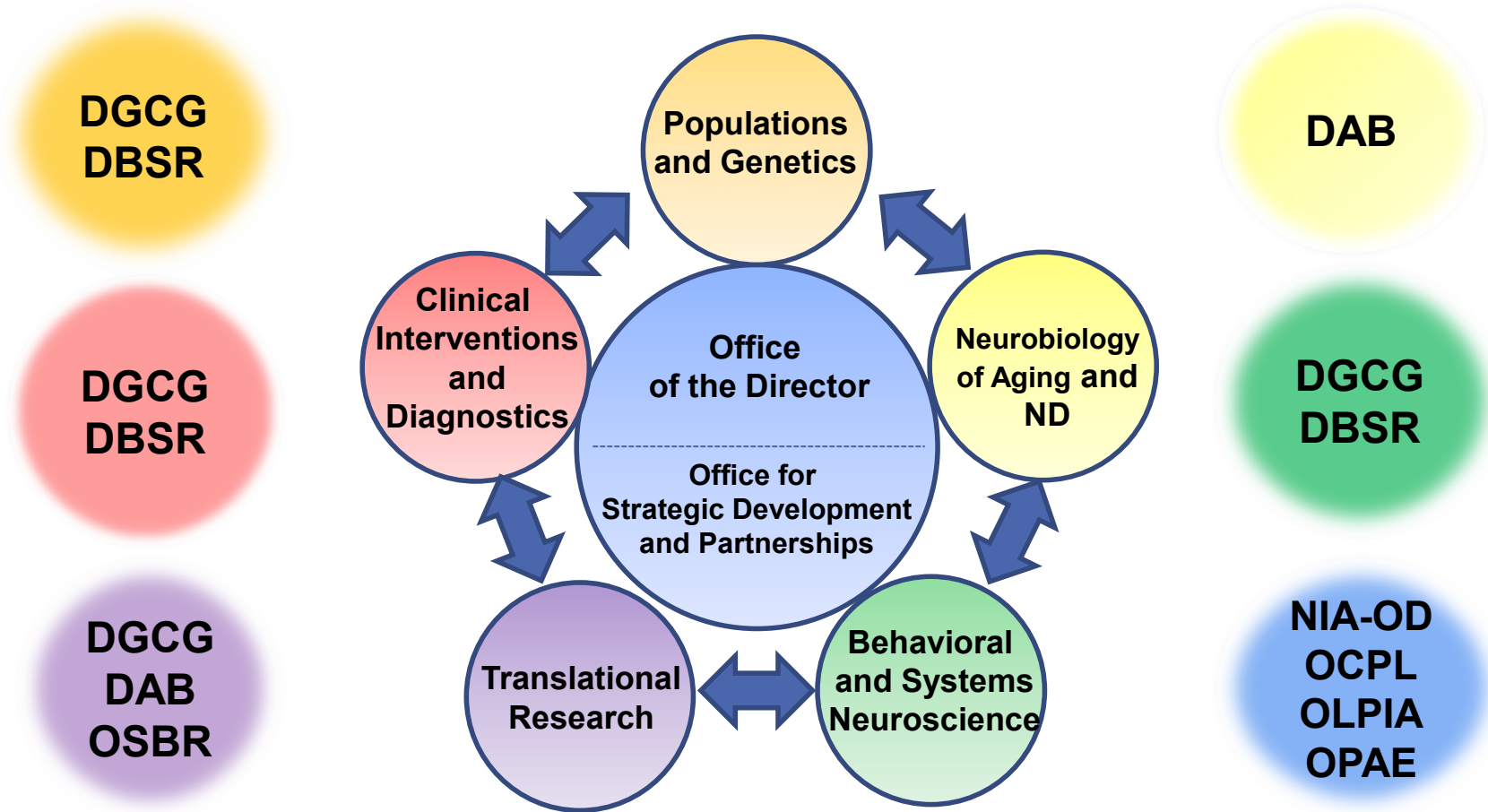
Clinical Trials Infrastructure and Training

- **ADRCs, NACC, NCRAD, ADNI, ACTC, DIAN, DIAN-TU, ABC-DS**

Laurie Ryan (Chief)
 Nina Silverberg
 John Hsiao
 Cerise Elliot
 Yuan Luo
 Kristina McLinden
 Akanni Clarke
 Grayson Donley
 Alvin McKelvy



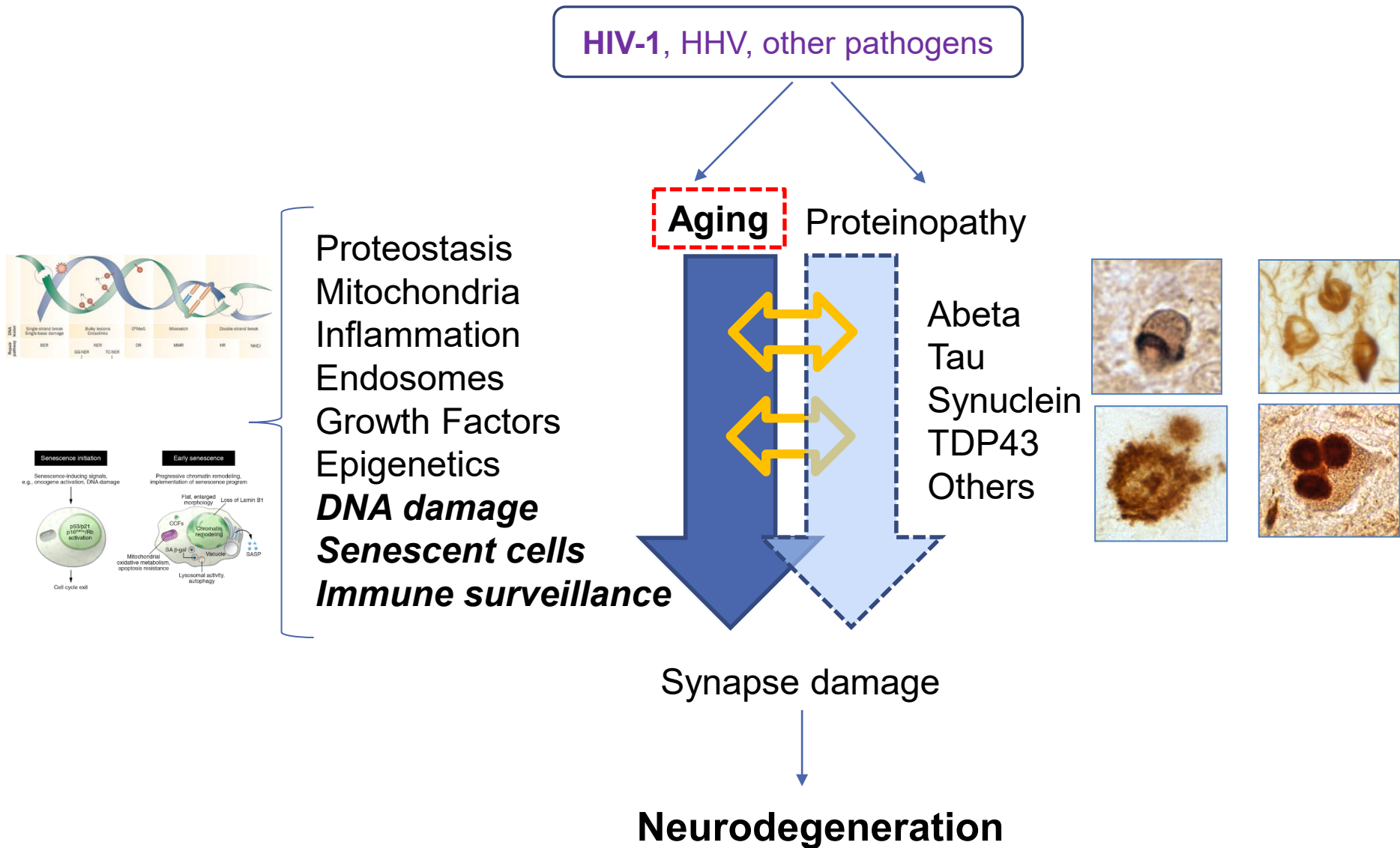
NIA Division of Neuroscience Collaborations



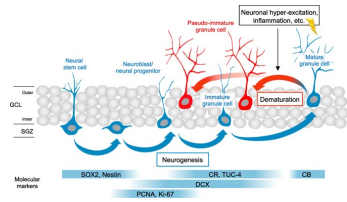
NINDS, NHLBI, NIMH, NICHD, NIDDK, NIDCD, NICHD, others

Cross-cutting: DISPARITIES, DIVERSITY, TRAINING

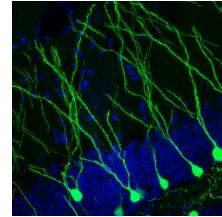
Understanding AD in the context of Aging



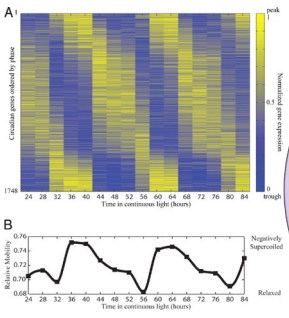
New FOAs in Aging related cellular and molecular mechanisms in AD/ADRD FY2020



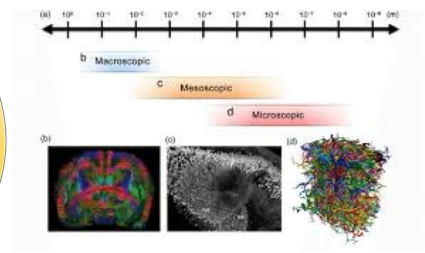
**Neurogenesis
In aging and
AD/ADRD
(FOA pending)**



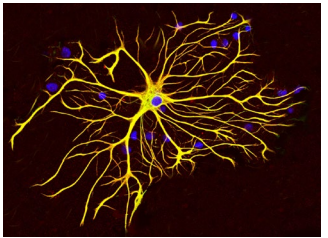
**Oscillatory
gene
expression in
aging and
AD/ADRD
(RFA-AG20-04)**



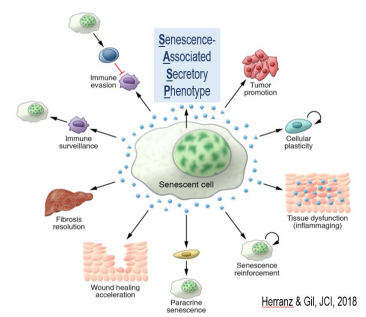
**Cellular scale
connectome
in aging and
AD/ADRD
(FOA
pending)**



**Glial cell
plasticity in
Aging and
AD/ADRD
(RFA-AG-21-010)**




**Cell
senescence in
Aging and
AD/ADRD
(RFA-AG-20-025)**



Recent conflicting reports on adult human neurogenesis raise controversy.

Published: 07 March 2018

Human hippocampal neurogenesis drops sharply in children to undetectable levels in adults

Shawn F. Sorrells, Mercedes F. Paredes, Arantxa Cebrian-Silla, Dashi Qi, Kevin W. Kelley, David James, Simone Mayer, Julia C. Chang, Edward F. Chang, Antonio J. Gutierrez, Arnold R. Kriegstein, Michael C. Oldham, Eric J. Huang, Jose Manuel Garcia-Verdugo & Arturo Alvarez-Buylla 



Nature 555, 377–381(2018) | [Cite this article](#)

LETTERS

<https://doi.org/10.1038/s41591-019-0375-9>

nature
medicine

Adult hippocampal neurogenesis is abundant in neurologically healthy subjects and drops sharply in patients with Alzheimer's disease

Elena P. Moreno-Jiménez^{1,2,3,6}, Miguel Flor-García^{1,2,3,6}, Julia Terreros-Roncal^{1,2,3,6}, Alberto Rábano⁴, Fabio Cafini⁵, Noemí Pallas-Bazarrá ^{1,3}, Jesús Ávila^{1,3} and María Llorens-Martin ^{1,2,3*}

Is Alzheimer's Disease a Neurogenesis Disorder?

Se Hoon Choi¹ and Rudolph E. Tanzi^{1,*}

¹Genetics and Aging Research Unit, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA

*Correspondence: tanzi@helix.mgh.harvard.edu
<https://doi.org/10.1016/j.stem.2019.06.001>



Dual Perspectives

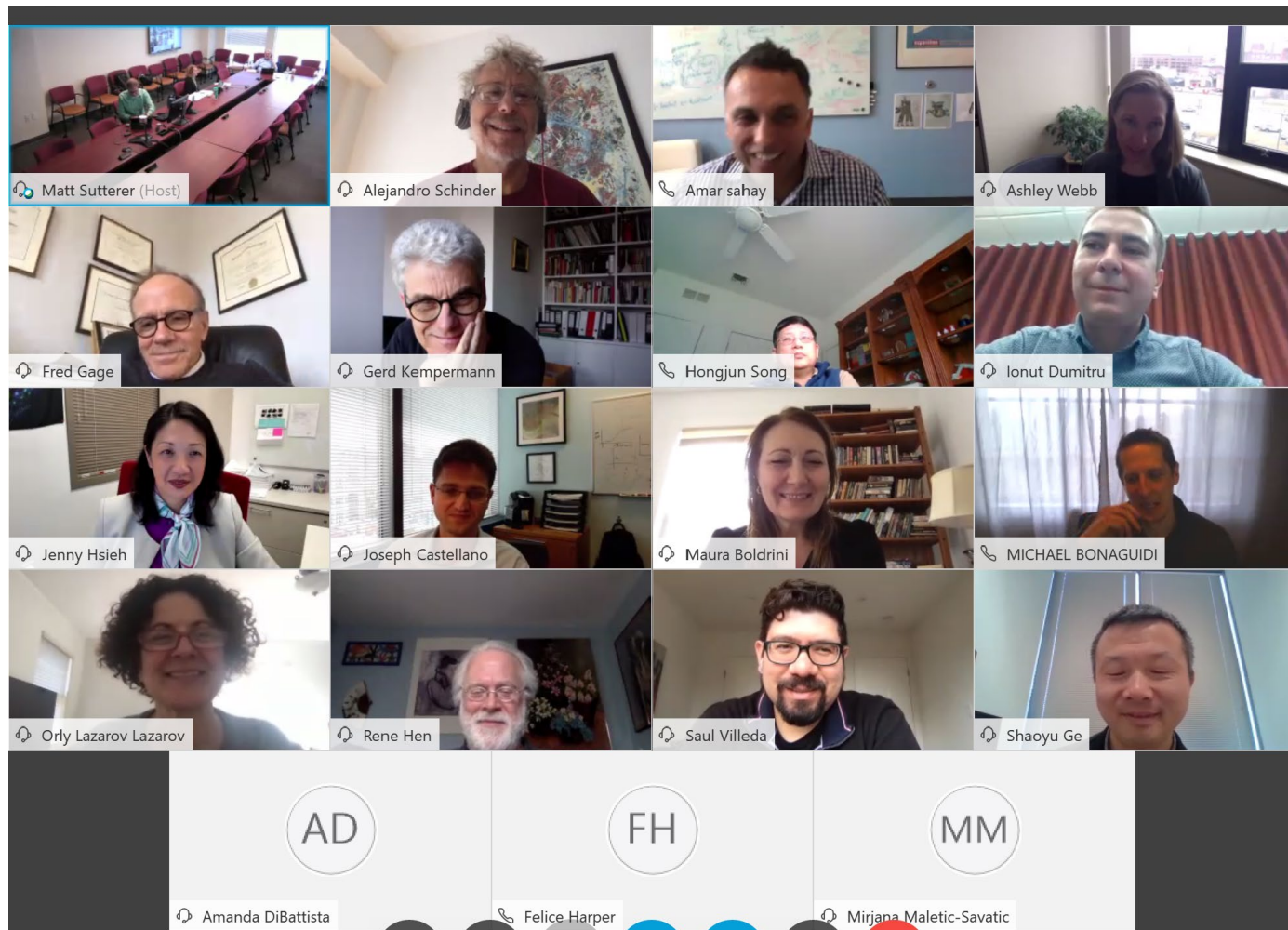
Does Adult Neurogenesis Occur in the Human Brain?

Presenters: Arturo Alvarez-Buylla, PhD; Maria Llorens-Martin, PhD

NIA Workshop on Neurogenesis and Aging

March 16-17, 2020 Bethesda MD (VIRTUAL)

NIH leads- Molly Wagster, Brad Wise, Amanda Dibattista, Matt Sutterer



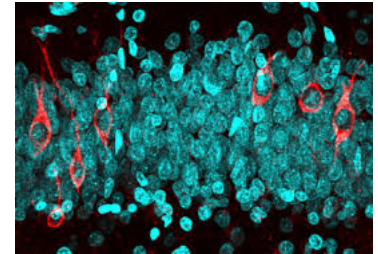
NIA Workshop on Neurogenesis and Aging

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NIH leads- Molly Wagster, Brad Wise, Amanda Dibattista, Matt Sutterer

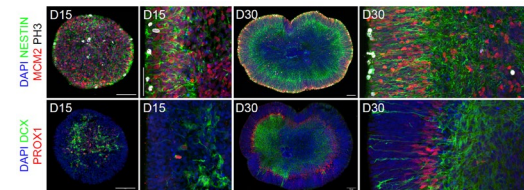
Session I. Neurogenesis in the Adult Human Brain.

- Hippocampal neurogenesis linked cognitive deficits and AD
- Solving human neurogenesis in vivo toward therapy of brain disorders



Session II. Regulation of Neurogenesis in the Aging Brain.

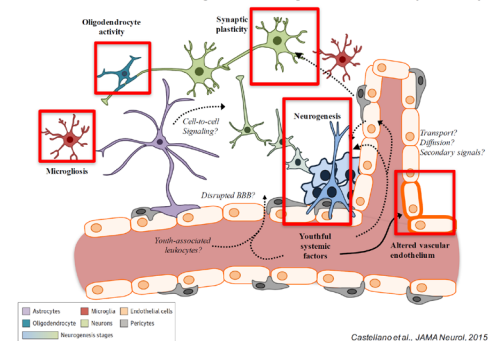
- Regulation of neural stem cell aging with single cell
- Enhanced plasticity of new neurons in the hippocampus
- Blood-borne regulators of the hippocampal neurogenic niche



Session III. Functional Significance of Adult Neurogenesis.

- Blood: at the interface of aging and adult neurogenesis
- Re-engineering and Rejuvenating aging memory circuits
- Harnessing Neurogenesis to Improve Pattern Separation in Aging

Blood-borne factors regulate neurogenic niche in myriad ways



Castellano et al., JAMA Neurol, 2015

NIA Workshop on Neurogenesis and Aging

March 16-17, 2020 Bethesda MD (VIRTUAL)

NIH leads- Molly Wagster, Brad Wise, Amanda Dibattista, Matt Sutterer

Develop Tools and Resources.

Develop new genetic and molecular markers for human neurogenesis.

Establish new models to study adult neurogenesis (e.g., non-mouse animal models, organoids, computational models), and identify species differences.

Improve live imaging approaches for adult neurogenesis.

Establish New Collaborations.

Create multi-laboratory consortia to establish “virtual labs” across fields.

Evaluate the Costs and Benefits to Increased Neurogenesis.

Test the impact of new neurons on circuits and behavior.

Collectively evaluate the neurogenic niche.

Evaluate the ideal balance of neurogenesis and mature neuron maintenance in humans.

NIA FOAs investigating the cross talk between pathogens and aging and AD/ADRD research

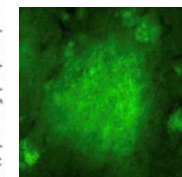
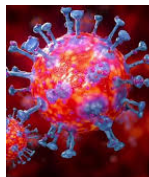
J Neuropathol Exp Neurol
Vol. 00, No. 00, 2020, pp. 1–6
doi: 10.1093/jnen/nlaa109

INVITED REVIEW

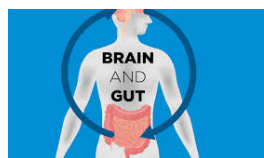
OXFORD

Risk of Transmissibility From Neurodegenerative Disease-Associated Proteins: Experimental Knowns and Unknowns

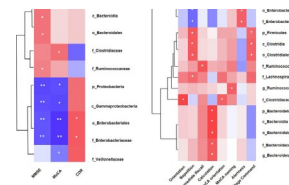
David M. **Asher**, MD, Ermias **Belay**, MD, Eileen **Bigio**, MD, Sebastian **Brandner**, MD, Scott A. **Brubaker**, BA, Byron **Caughey**, PhD, Brychan **Clark**, MD, Inger **Damon**, MD, PhD, Marc **Diamond**, MD, Michelle **Freund**, PhD, Bradley T. **Hyman**, MD, PhD, Mathias **Jucker**, PhD, C. Dirk **Keene**, MD, PhD, Andrew P. **Lieberman**, MD, PhD, Miroslaw **Mackiewicz**, PhD, Thomas J. **Montine**, MD, PhD, Susan **Morgello**, MD, Creighton **Phelps**, PhD, Jiri **Safar**, MD, PhD, Julie A. **Schneider**, MD, MS, Lawrence B. **Schonberger**, MD, MPH, Christina **Sigurdson**, DVM, PhD, Nina **Silverberg**, PhD, John Q. **Trojanowski**, MD, PhD, and Matthew P. **Frosch**, MD, PhD



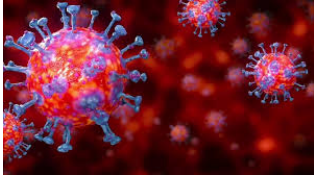
Downloaded from <https://academic.oup.com/jnen>



(RFA-AG-20-030)



Notice of Special Interest (NOSI): NIA Availability of Administrative Supplements and Revision Supplements on COVID-19



Notice Number: NOT-AG-20-022

Key Dates

Release Date: April 2, 2020

First Available Due Date: April 06, 2020

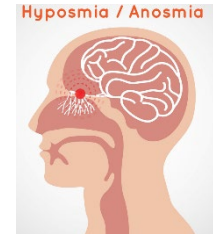
Expiration Date: May 01, 2021

Related Announcements

[PA-18-591](#) Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp Clinical Trial Optional)

[PA-18-935](#) Urgent Competitive Revision to Existing NIH Grants and Cooperative Agreements (Urgent Supplement - Clinical Trial Optional)

[NOT-AG-20-031](#)



Wesley Ely, 3R01AG058639-02S1 - Evaluate if hospitalized adult COVID-19 survivors have a high burden of Post-Intensive Care Syndrome (PICS)-related AD, PTSD, and depression at 6-months. Secondly, we will also determine if hydroxychloroquine versus placebo improves these outcomes

Eric Reiman- 3P30AG019610-20S1 - Neuropathological consequences of CNS SARS-CoV-2 in infected humans. investigations of 100 or more consecutive autopsies spanning the pandemic period.

Panagiotis Roussos– 3R01AG065582-01S1 - This supplement proposes to evaluate the molecular and neuropathological effects of SARS-CoV-2 in neurons and glial cells

Todd Golde – 3U01AG046139-08S1 - This supplement proposes to assess the potential mechanisms for the highly divergent immune responses to the SARS-CoV-2 infection

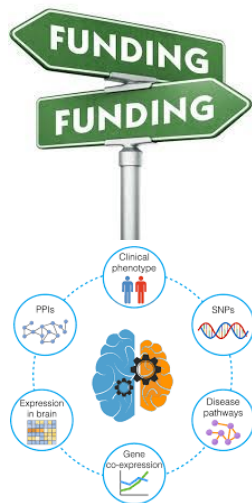
Suzanne Craft – 3P30AG049638-05S2 - Impact of COVID-19 related social distancing and stress on individuals with cognitive impairment as compared to older adults with normal cognition in the WF ADRC center cohort.

THANKS



Concept Approvals:

<https://www.nia.nih.gov/approved-concepts>

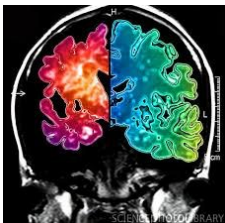


General FOAs:

<https://www.nia.nih.gov/research/funding>

Alzheimer's Disease and Related Dementias FOAs:

<http://www.nia.nih.gov/AD-FOAs>



NIA- Division of Neuroscience

<https://www.nia.nih.gov/research/dn>