FY19 Budget Status – Funding Increases Across the Board

$39 Billion for the NIH

$40M for Universal Flu Vacc

$169M for BRAIN

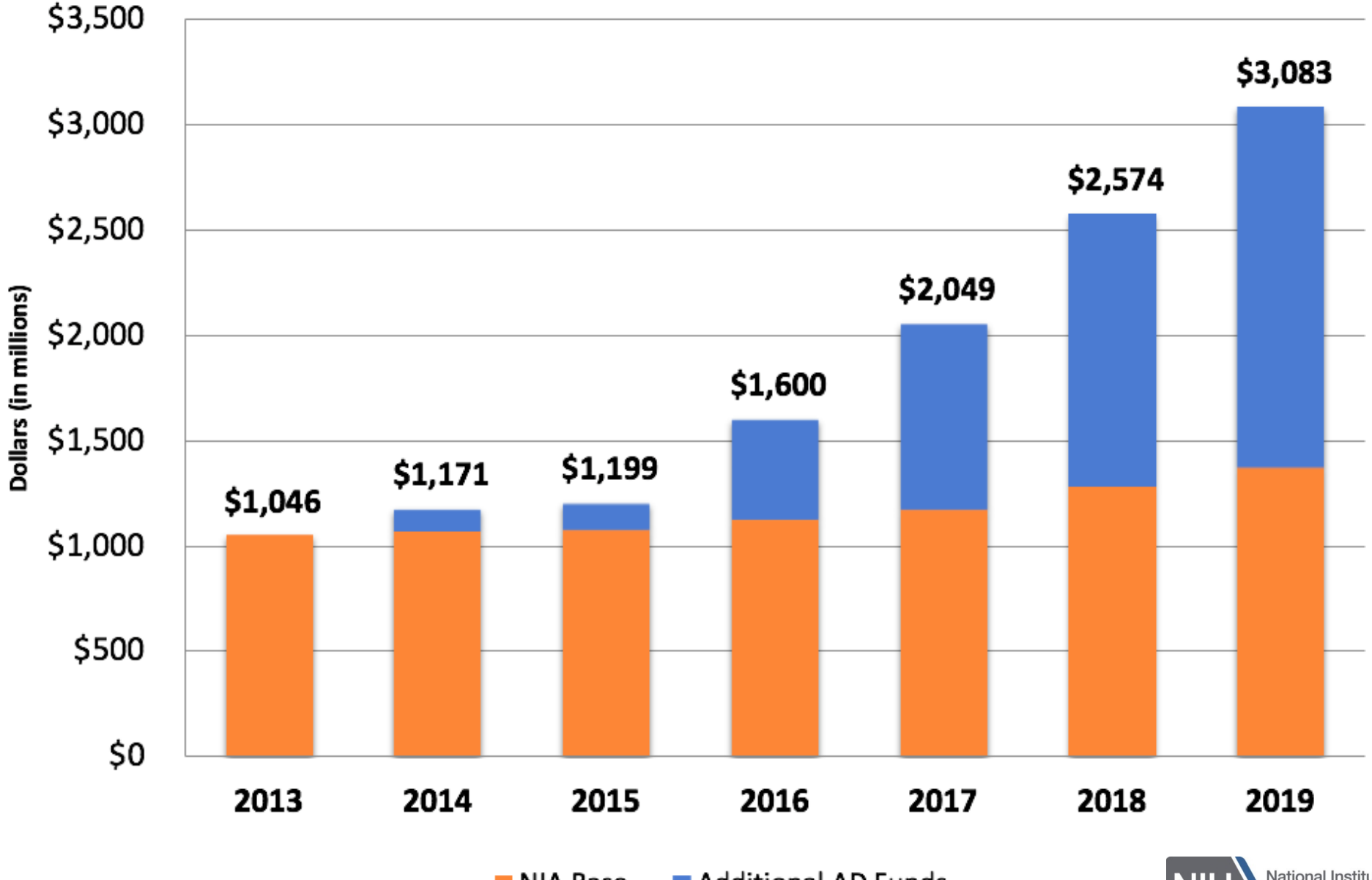
$149M for All of US

$425M to NIA for AD

- **$3.1B for the NIA**
- $84M increase for non-targeted NIA research; percent increase comparable to other ICs

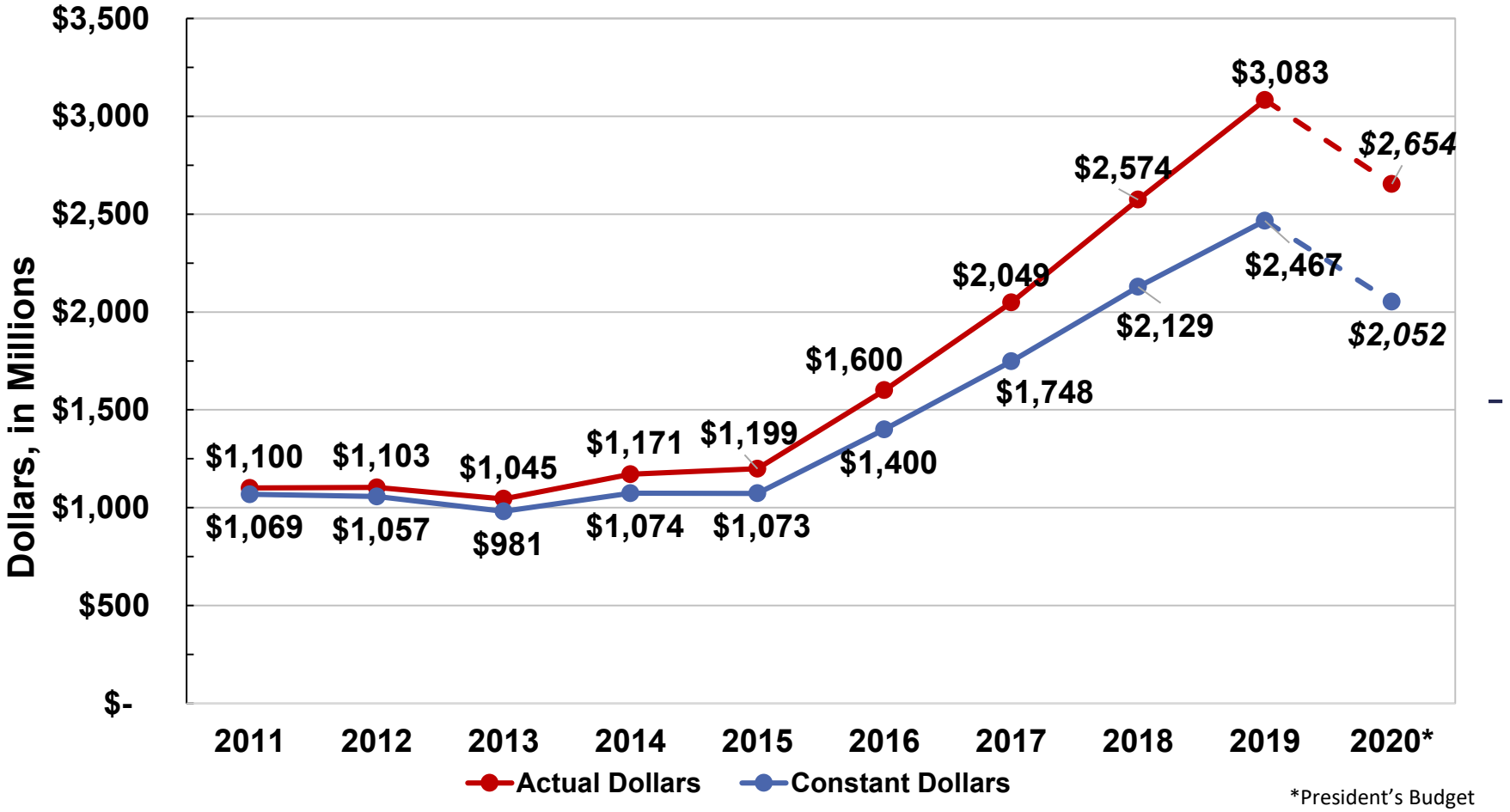
NIH National Institute on Aging

NIA Appropriations, Fiscal Years 2013-2019



NIH National Institute on Aging

NIA Appropriations and President's Budget Fiscal Years 2011-2020



*President's Budget

Appropriations Budget Growth since FY2011-2019

Actual Dollars: +$1,983.0 M (+180.2%) **Constant Dollars: +$1,398.2M (+130.9%)**

NIH National Institute on Aging

Allocations for Competing Research Grant Awards, FY 2019

CSR-reviewed Research Applications				
	General Pay line, <$500k	General Pay line, =>$500k	AD/ADRD pay line, <$500k	AD/ADRD pay line, =>$500k
All applications except as noted below	15	12	28	25
N.I. R01s	18	15	31	28
E.S.I. R01s	20	17	33	30

New investigator: An applicant who has not received a prior R01 award or its equivalent.
Early-Stage Investigator: A new investigator who is within 10 years of finishing research training.
First-time renewing; A former new or early-stage investigator's first renewal application when the investigator has no other NIH grant support.
ADRD: Research on Alzheimer's disease and on Alzheimer's-related Dementias

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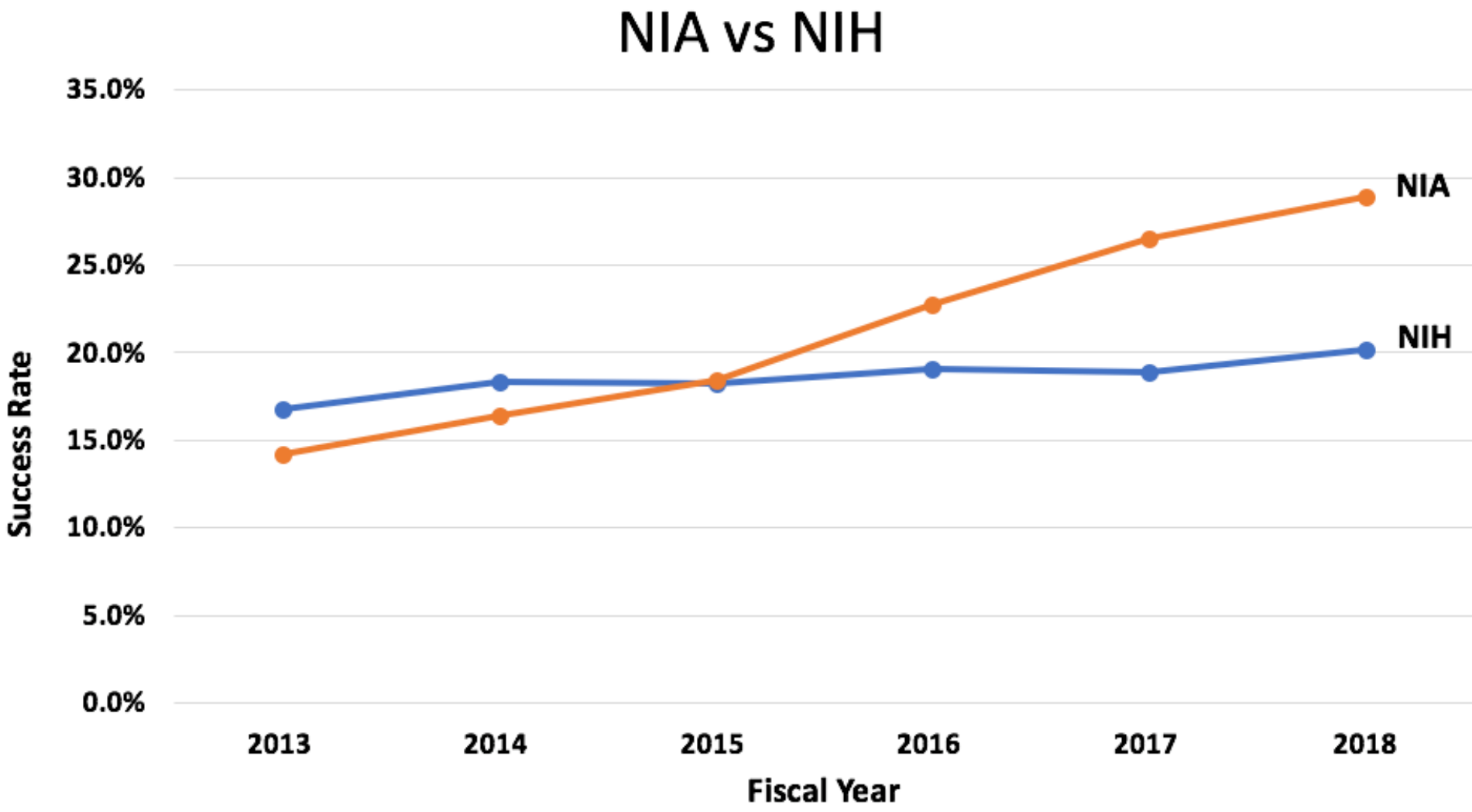
FY 2019 Pay Lines (PPG's, others)

NIA-reviewed Applications		
	General pay line	**AD/ADRD pay line**
Program projects (PO1)	20	38
Other NIA-reviewed research	20	38

FY 2019 Pay Lines (Training)

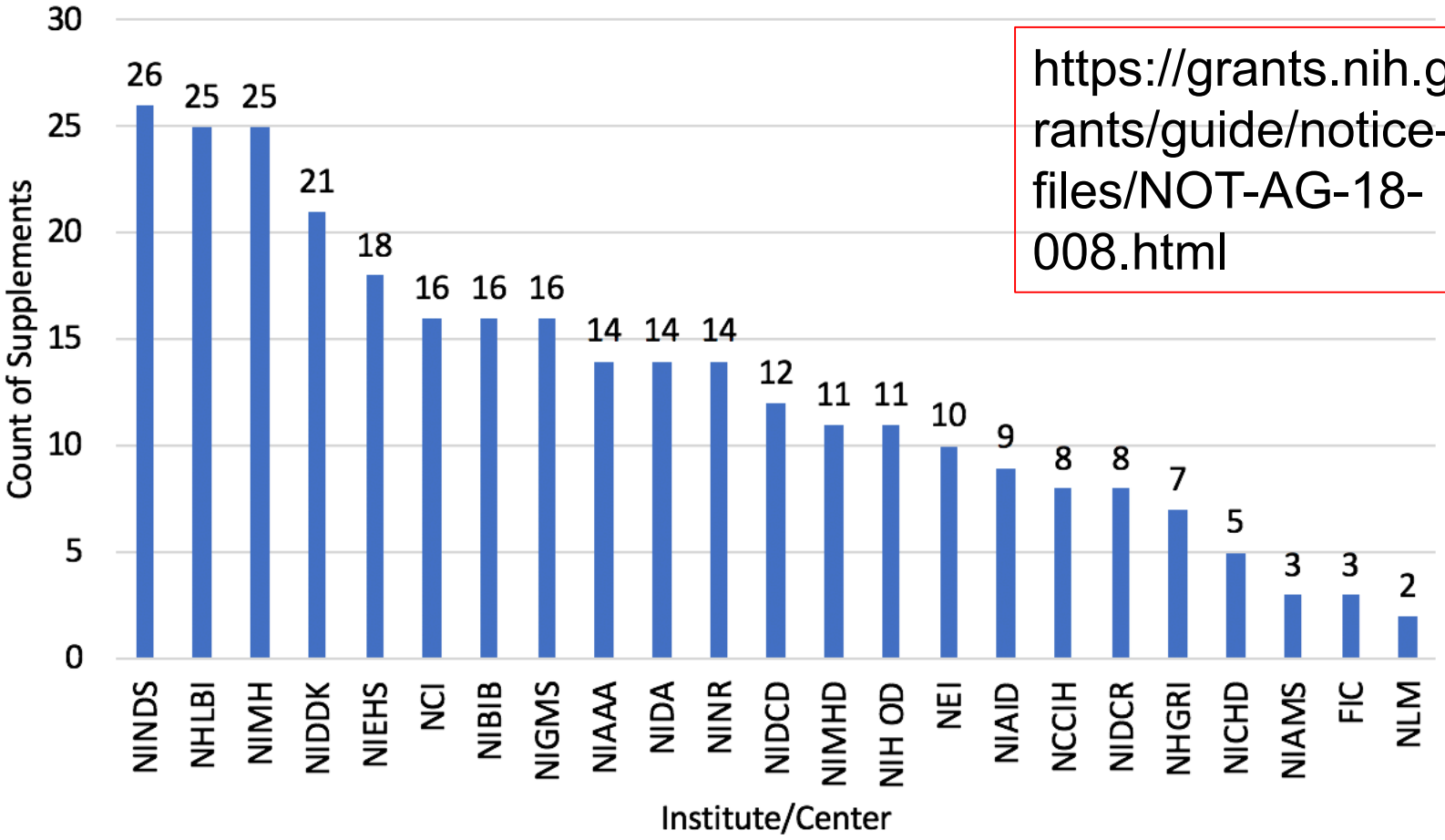
Training-related Applications		
	General pay line	AD/ADRD pay line
Training grants (T32, T35)	21	35
Career awards	21	28
Fellowships	28	32

RPG's success rates over time



Multi-IC Collaboration: AD/ADRD supplements

25 ICs and Offices participated in the FY18 notice for AD/ADRD supplements



https://grants.nih.gov/grants/guide/notice-files/NOT-AG-18-008.html

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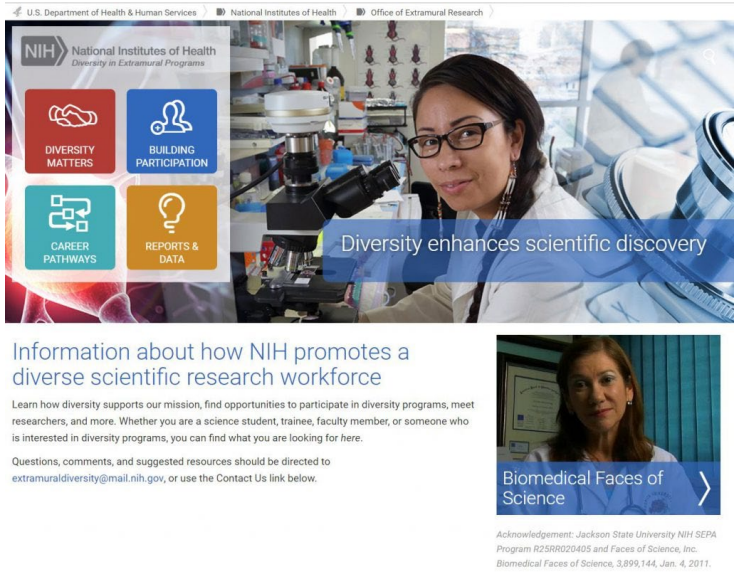
Recruitment to a Growing AD/ADRD Workforce

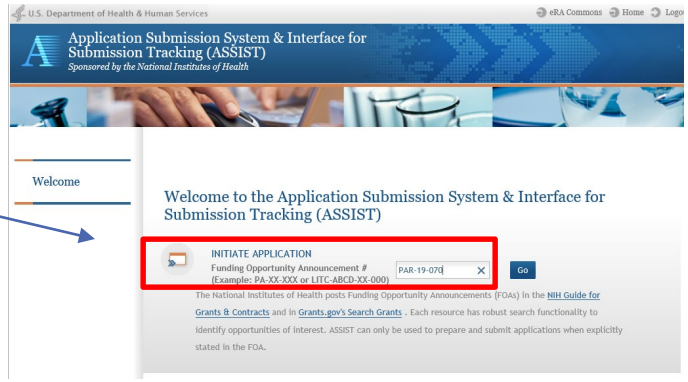
~1/4 of NIA's Alzheimer's and related dementias awardees from Fiscal Year 2015-2018 were either *new or early stage* investigators

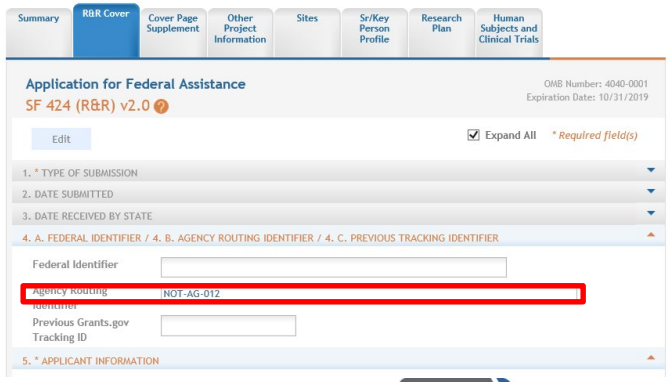
~1/3 of NIA's Alzheimer's and related dementias awardees were *new to the field*



New format for Alzheimer's Disease initiatives

- We changed how we advertise many initiatives!
- Parent FOAs (R01 and R21)
- Notices of Special Interest
- **PAR-19-070/PAR-19-071: Research on Current Topics in Alzheimer's Disease and Its Related Dementias (R01/R21 Clinical Trial Optional)**
- **Include the notice you are replying to in Field 4.b on the SF 424 Form!**





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PAR-19-070/PAR-19-071 examples of recently expired FOA's re-issued as NOSI

- **Include the notice you are replying to in Field 4.b on the SF 424 Form!**
- NOT-AG-18-053 : Major Opportunities for Research in Epidemiology of Alzheimer's Disease and Related Dementias and Cognitive Resilience (Formerly PAR-15-356). Dallas W. Anderson; dallas.anderson@nih.gov, Jonathan W. King; kingjo@nia.nih.gov

- NOT-AG-18-052: Capturing Complexity in the Molecular and Cellular Mechanisms Involved in the Etiology of Alzheimer's Disease / Deciphering the Glycosylation Code of Alzheimer's Disease (Formerly PAR-15-358), Austin Yang; yangj13@mail.nih.gov

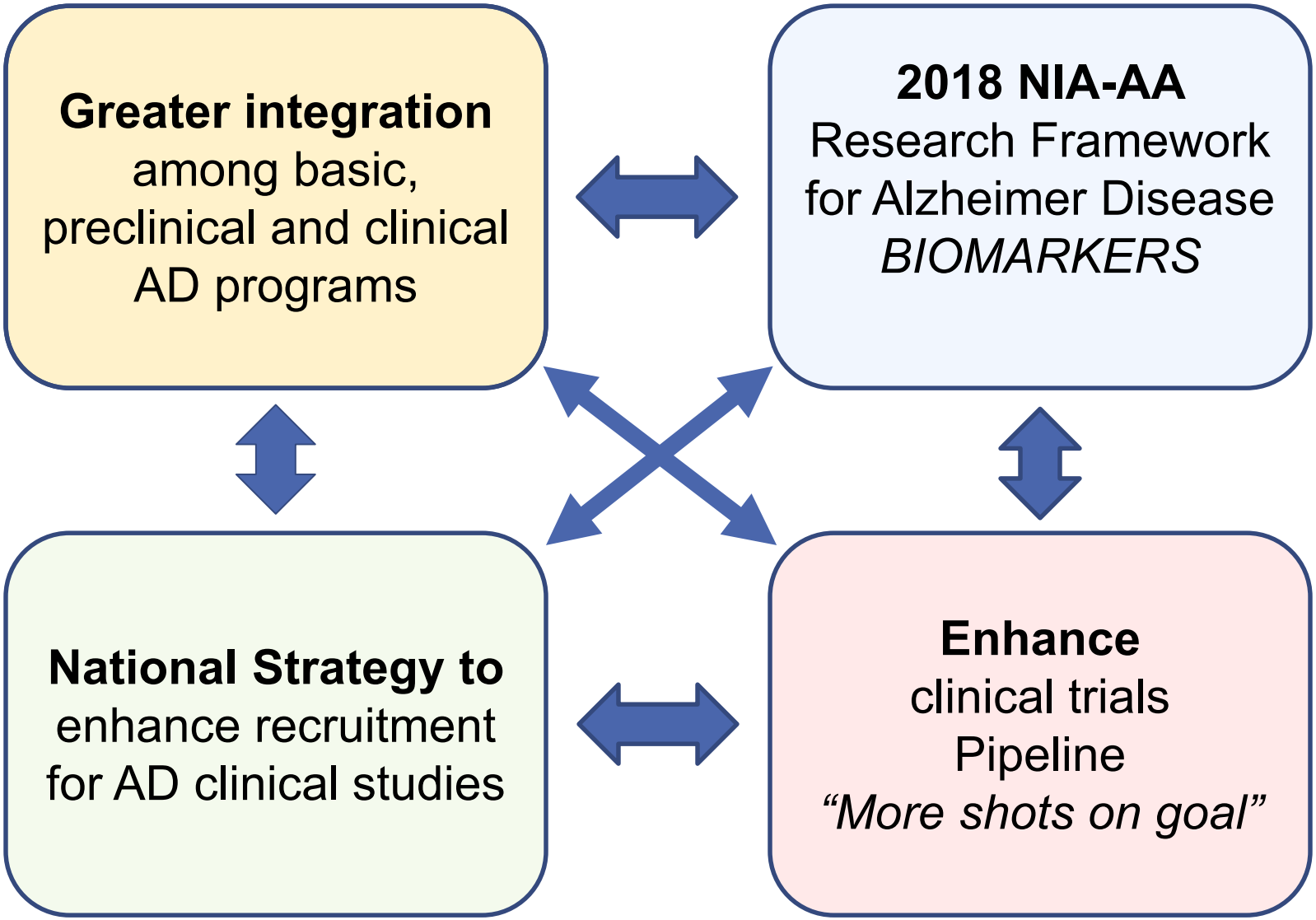
- NOT-AG-18-051: Understanding Alzheimer's Disease in the Context of the Aging Brain (Formerly PAR-15-357), Brad Wise; WiseB@mail.nih.gov

- NOT-AG-18-048: Common Mechanisms and Interactions Among Neurodegenerative Diseases (Formerly PAS-17-028), jhsiao@mail.nih.gov

- NOT-AG-18-048: Novel Approaches to Characterizing and Diagnosing Alzheimer's Disease and Related Dementias (Formerly PAR-15-359), John Hsiao; jhsiao@mail.nih.gov

- NOT-AG-18-047: Health Disparities and Alzheimer's Disease (Formerly PAR-15-349), Cerise Elliott; elliottce@mail.nih.gov

Some NIA-AD Research Priorities



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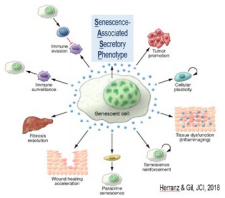
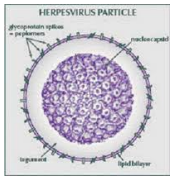
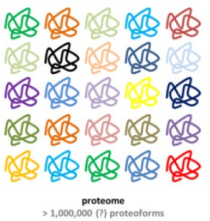
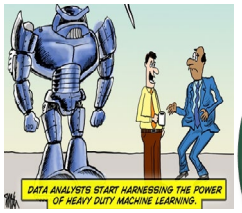
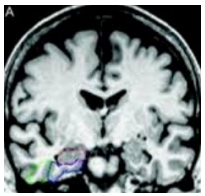
Alzheimer's Disease initiatives for FY2020

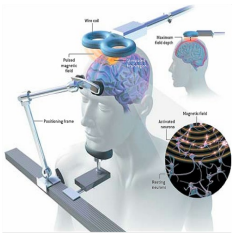












Basic/molecular mechanisms

- *Senescence CNS Aging and AD (DiBattista, Opanashuk)*
- *Oscillatory Gene Expression AD (Mackiewicz)*
- *Infectious Etiology of AD (Mackiewicz, Anderson)*
- *Regulation Proteome Dynamics in AD (Yang)*

Resources

- *AD Genetic Cognitive Systems Analysis (Miller)*
- *Center for Genetics and Genomics AD (Miller)*
- *Increasing competitiveness of potential AD Centers (Silverberg, Elliott)*
- *Standardization AD imaging Biomarkers (Silverberg, Hsiao)*

Translation/ clinical trials

- *Non-Invasive Neurostimulation in AD (McLinden, Ryan)*

Training

- *Physician-Scientist Mentored Research in AD (Opanashuk)*
- *Stimulating Multidisciplinary Programs for AD (Elliott)*

NIH National Institute on Aging

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

NIA Program Director: Suzana Petanceska and Laurie Ryan

Generate

High-dimensional multi-omic data: ~2,500 human brains;~1000 blood samples

Integrate

Molecular profiling
Predictive Modeling
Experimental validation

6 Academic Teams
– NIA U01/R01grants –

www.synapse.org.ampad

Data
Network models
Code

AMP-AD Knowledge Portal

DATA SHARING

Sage BIONETWORKS Synapse

- P. De Jager, D. Bennett
- E. Schadt, B. Zhang, S. Gandy, J. Zhu, M. Ehrlich
- T. Golde, N.Price, N. Ertekin-Taner, S. Younkin,
- A. Levey, T. Montine, J. Troncoso, D. Geschwind
- R. Kaddurah-Daouk
- B. Yakner, L. Huei Tsai

AMP-AD Partners

NIH National Institute of Neurological Disorders and Stroke
FDA
abbvie
Biogen
gsk GlaxoSmithKline
Lilly
alzheimer's association
Alzheimer's Drug Discovery Foundation
US4against Alzheimer's
FNIH Foundation for the National Institutes of Health

NIH National Institute on Aging

Neuron 99, 1–19, July 11, 2018 © 2018 Elsevier Inc. 1

Neuron
Article

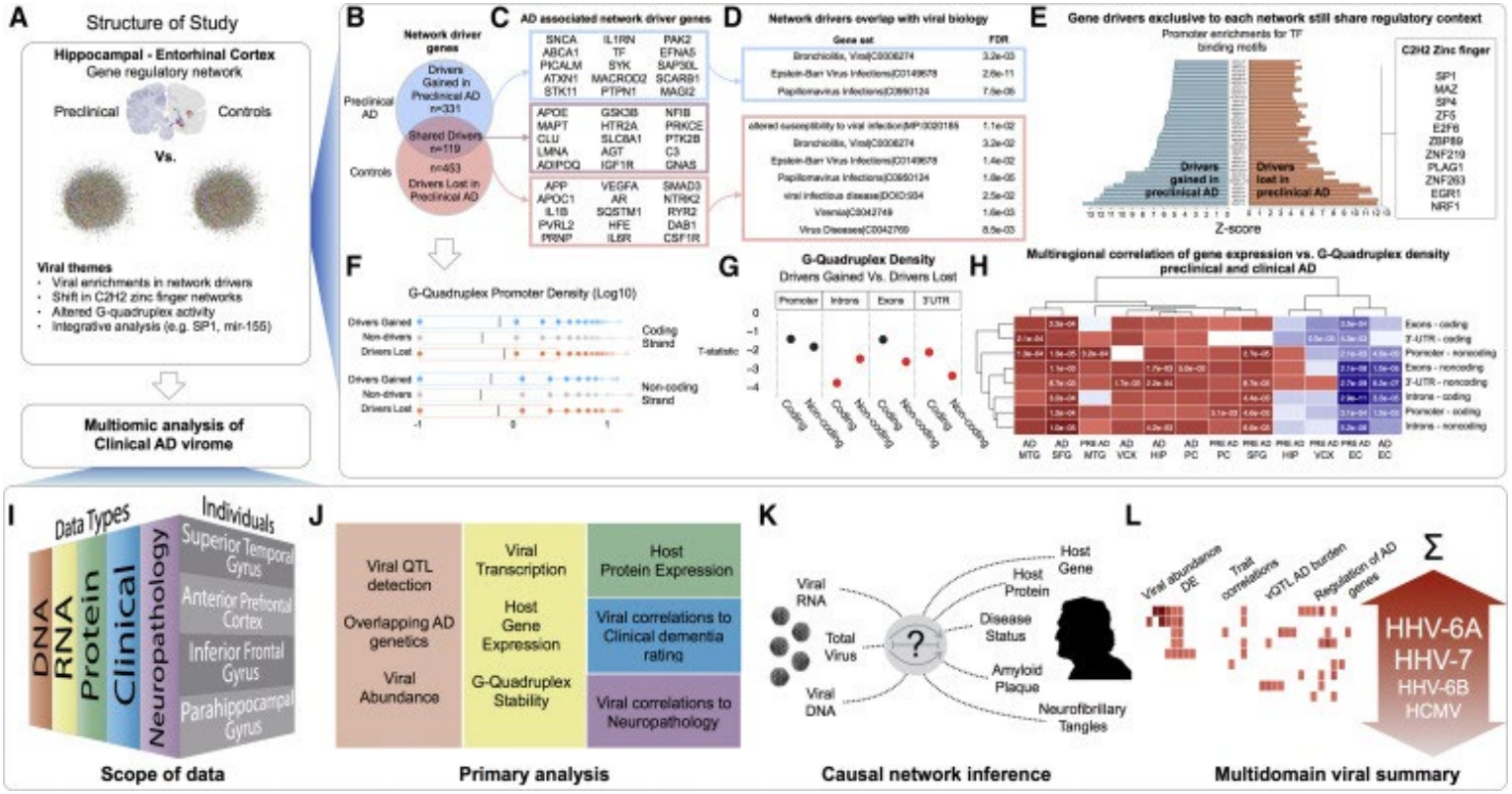
CellPress

Multiscale Analysis of Independent Alzheimer's Cohorts Finds Disruption of Molecular, Genetic, and Clinical Networks by Human Herpesvirus

Ben Readhead,[1,2,3,4,17] Jean-Vianney Haure-Mirande,[5,17] Cory C. Funk,[6] Matthew A. Richards,[6] Paul Shannon,[6] Vahram Haroutunian,[7,8] Mary Sano,[8,15] Winnie S. Liang,[9,10] Noam D. Beckmann,[1,2] Nathan D. Price,[6] Eric M. Reiman,[9,10,11,12] Eric E. Schadt,[1,2,13] Michelle E. Ehrlich,[1,2,5,14] Sam Gandy,[5,8,15,16,17] and Joel T. Dudley[1,2,3,4,17,18,*]

-RNA sequencing of 4 brain regions in 600 samples of postmortem brain (AD and Control) in early onset and AD progression, and then subsequent validation with another 900 RNA samples from three other cohorts indicating abundance of HHV-6A and HHV-7 nucleotides and pathways in AD

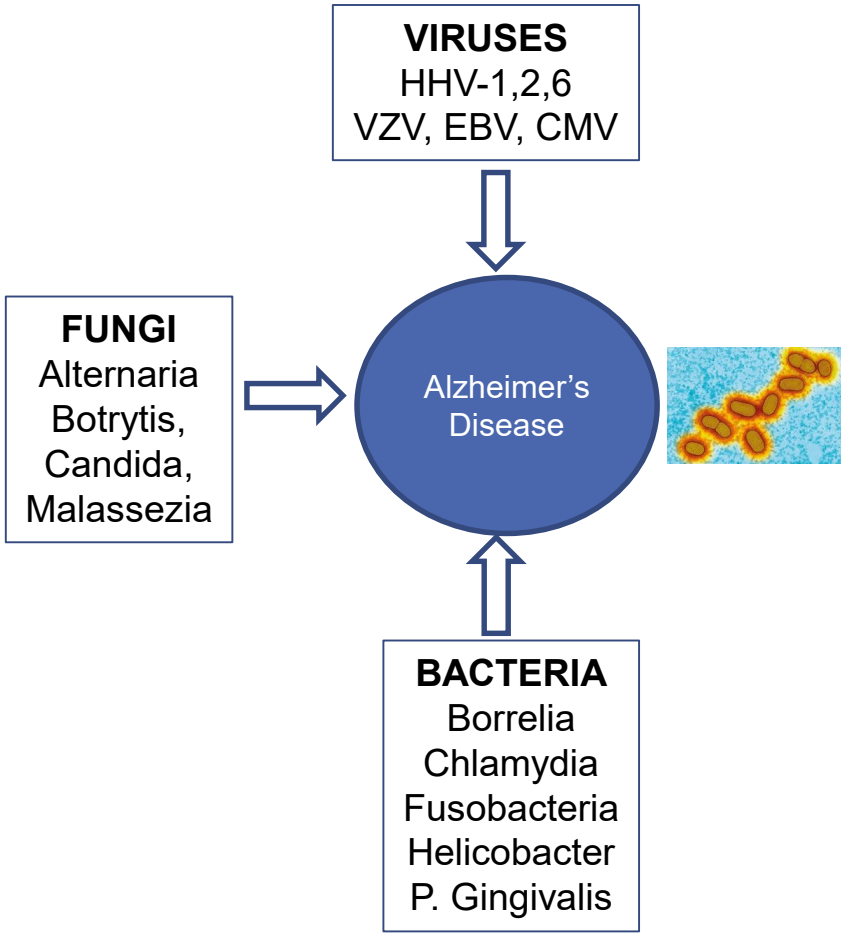
-Also regulatory relationship linking viral abundance and modulators of APP metabolism – APBB2, APPBP2, BIN1, BACE1, CLU, PICAL and PSEN1



PAR-19-070/PAR-19-071: Alzheimer's Disease
NOT-AG-19-012 : Infectious Etiology of Alzheimer's Disease (R01 only)

- **Include the notice you are replying to in Field 4.b on the SF 424 Form!**
- Mack Mackiewicz
  Miroslaw.Mackiewicz@nih.gov

1. Determine whether microbial pathogens represent a causal component of Alzheimer's disease (AD),
2. Establish mechanisms by which microbial pathogens impact neurodegenerative processes in AD,
3. Inform aspects of future translational studies in AD, including discovery of candidate therapeutics aimed at regulating pathogen-associated networks and molecules in AD.



Understanding AD in the context of Aging

HIV-1, HHV, other pathogens

Trauma, chemicals radiation, radicals, stress, metabolic, **viruses**

Aging

Proteinopathy

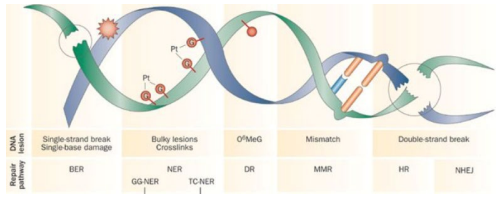
Proteostasis
Mitochondria
Inflammation
Endosomes
Growth Factors
Epigenetics
DNA damage
Senescent cells
Immune surveillance

Abeta
Tau
Synuclein
TDP43
Others

Synapse damage

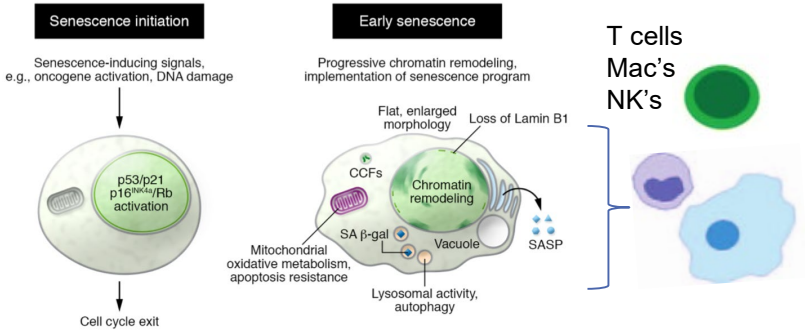
Neurodegeneration

DNA damage



Transposable elements

senescence/immune surveillance



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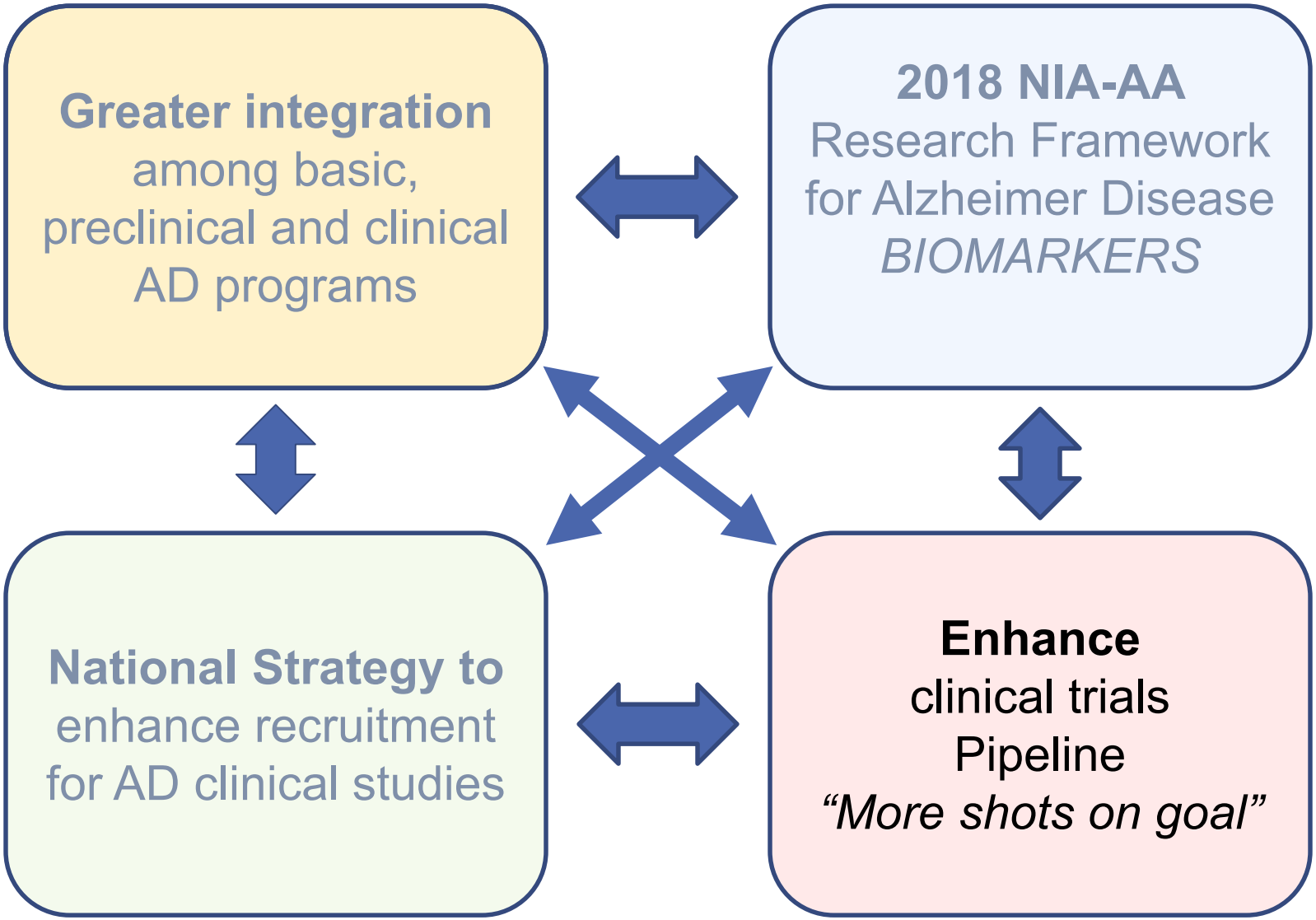
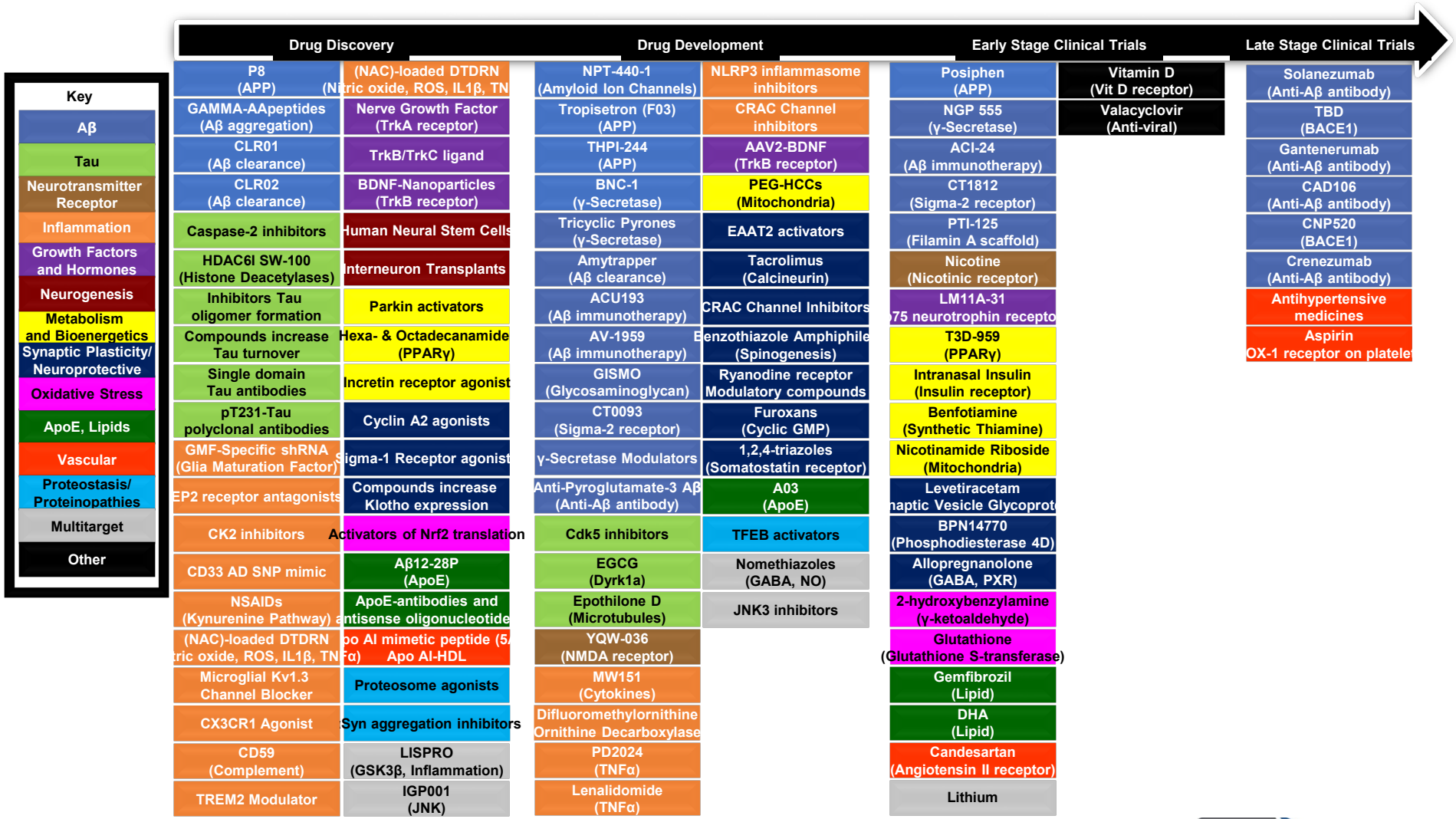
Some NIA-AD Research Priorities



NIH National Institute on Aging

NIA-AD clinical trials pipeline toward 2025

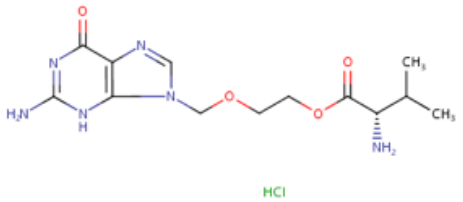
NIA Program Directors: Laurie Ryan, Zane Martin, Larry Refolo



NIH National Institute on Aging

Valacyclovir clinical trial in AD

PI: Devanand, Davangere P
Institution: Columbia University/ New York State Psychiatric Institute



Rationale: Infections from herpes virus including HSV1 (oral herpes) and HSV2 (genital herpes) have been implicated in etiology for AD.

Anti-HSV drugs reduce Aβ and p-tau accumulation in infected mouse brains.

Study Design (groups, doses): Oral Valacyclovir at 2 g to 4 g per day, randomized, double-blind, 18-month Phase II, will involve **130 mild AD patients (65 valacyclovir, 65 placebo)** who test positive for herpes simplex virus-1 (HSV1) or HSV2

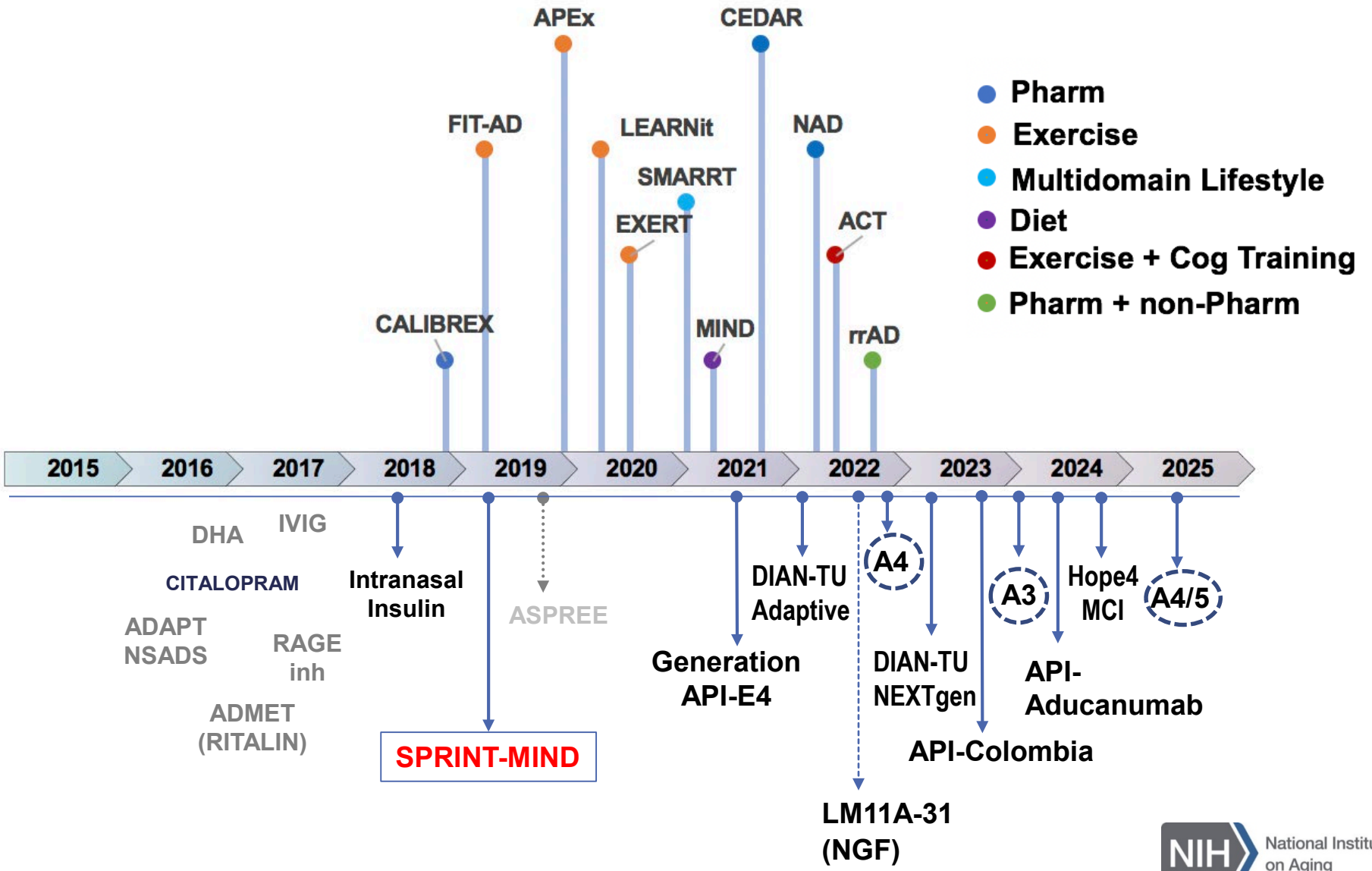
Outcome measures include:

- Change in Alzheimer's Disease Assessment Scale - Cognition (ADAS-COG11, modified version) scores from baseline to 78 weeks
- Pet amyloid scan with 18F-Florbetapir and with 18F-MK-6240[Time Frame: Week 0, Week 78]
- Change in Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL)

Study duration: 78 weeks study
Study start date to estimated end date: Feb 2018 – Aug 2022

NIH National Institute on Aging

Status of NIA-AD Phase II/III clinical trials toward 2025



NIH National Institute on Aging

Improving data sharing efforts

BIG DATA

OPEN SCIENCE

DATA

DATA HARMONIZATION AND ACCESS

PATHWAY AND TARGET IDENTIFICATION

DIAGNOSTICS AND THERAPEUTICS

New! ADBB FY2020

MULTIPLE SHOTS ON GOAL
PRECISION/PERSONALIZED MEDICINE

NIH National Institute on Aging

Save the Date!

AD/ADRD Care and Services Summit (II)

March 24-25, 2020

Natcher Conference Center

Bethesda, MD

NIH National Institute on Aging

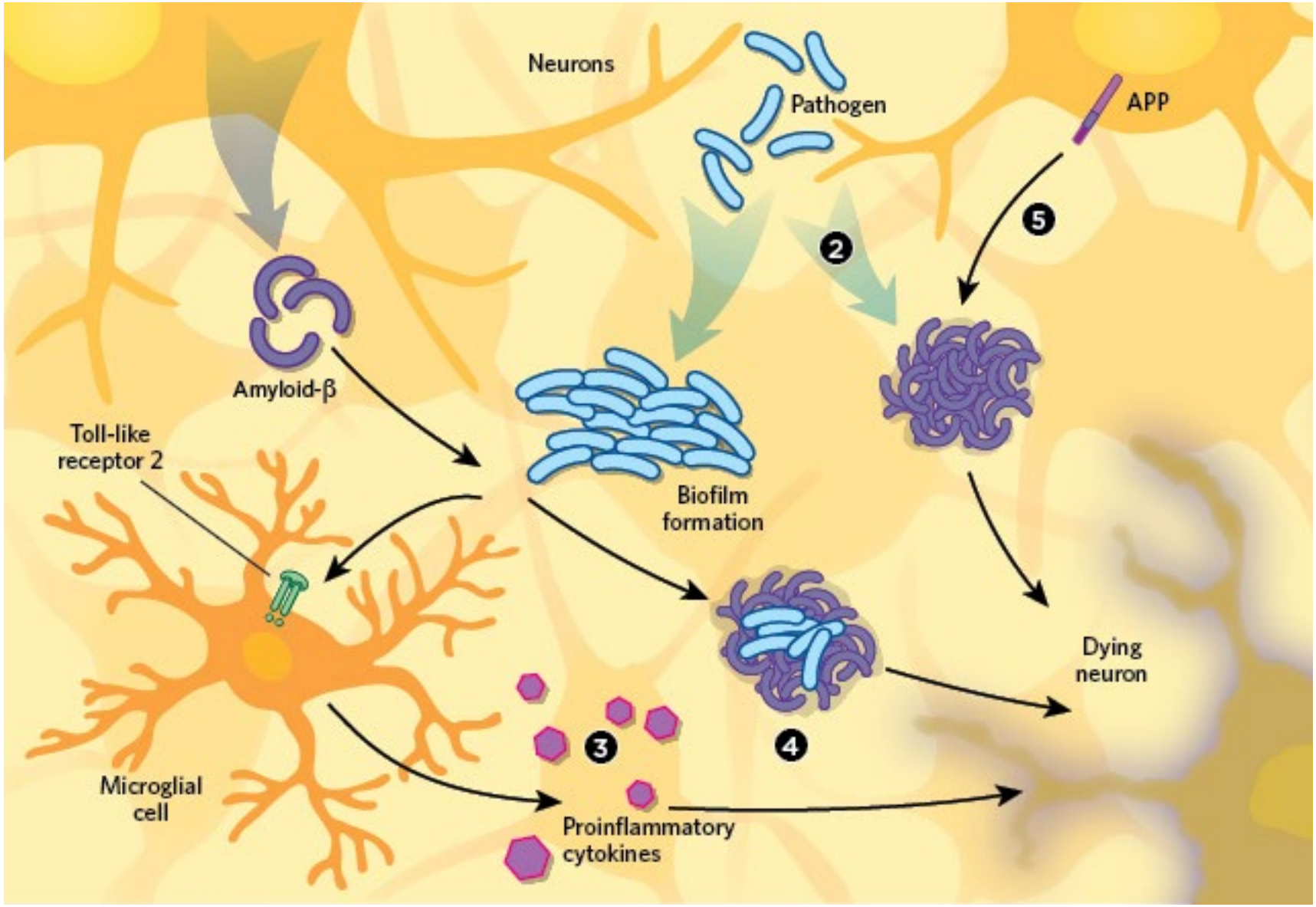
NIH National Institute on Aging

Concept Approvals:
https://www.nia.nih.gov/approved-concepts

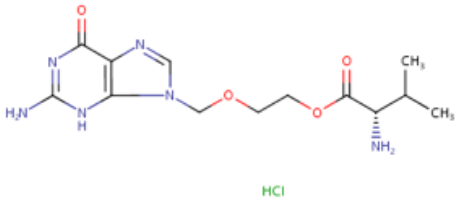
General FOAs:
https://www.nia.nih.gov/research/funding

Alzheimer's Disease and Related Dementias FOAs:
http://www.nia.nih.gov/AD-FOAs

Follow our "Inside NIA" blog:
https://www.nia.nih.gov/research/blog



Valacyclovir clinical trial in AD



PI: Devanand, Davangere P
Institution: Columbia University/ New York State Psychiatric Institute

Rationale: Infections from herpes virus including HSV1 (oral herpes) and HSV2 (genital herpes) have been implicated in etiology for AD.
- HSV1 and HSV2 DNA are present in amyloid plaques. HSVs are reported to trigger amyloid aggregation, and an HSV1 reactivation is associated with tau hyperphosphorylation. Anti-HSV drugs reduce Aβ and p-tau accumulation in infected mouse brains.

- Clinically, after the initial oral infection, herpes simplex virus-1 (HSV1) becomes latent in the trigeminal ganglion and recurrent reactivation may produce neuronal damage and AD pathology. Clinical studies show cognitive impairment in HSV seropositive patients, and antiviral drugs show strong efficacy against HSV.

Study Design (groups, doses): Oral Valacyclovir at 2 g to 4 g per day, randomized, double-blind, 18-month Phase II, will involve **130 mild AD patients (65 valacyclovir, 65 placebo)** who test positive for herpes simplex virus-1 (HSV1) or HSV2

Outcome measures include:
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NIH National Institute on Aging