

Alzheimer's Disease at UR

From Bench to Bedside,
From Molecules to Mind

M. Kerry O'Banion

Departments of Neuroscience & Neurology

A Brief History of AD Research at URMC

- T. Franklin Williams, MD: Medical Director, Monroe Community Hospital (1968-83); National Institute of Aging (NIA) Director (1983-91); Scientific Director, American Federation of Aging (1992-2002)
- Paul D. Coleman, PhD: Director, UR Alzheimer Disease Center (1990-2004); Editor-in-Chief, Neurobiology of Aging (1988-2015)
- Howard Federoff, MD, PhD (1995-2007): Director, Center on Aging and Developmental Biology—AD therapeutics and Early Diagnostic Markers
- Pierre Tariot, MD (1986-2006): Director, Memory Disorders Clinic—Involved in multiple national clinical trials
- Berislav Zlokovic, PhD (2001-2011): Director, Frank P. Smith Neurosurgical Labs—Multiple awards for work on neurovascular changes in AD



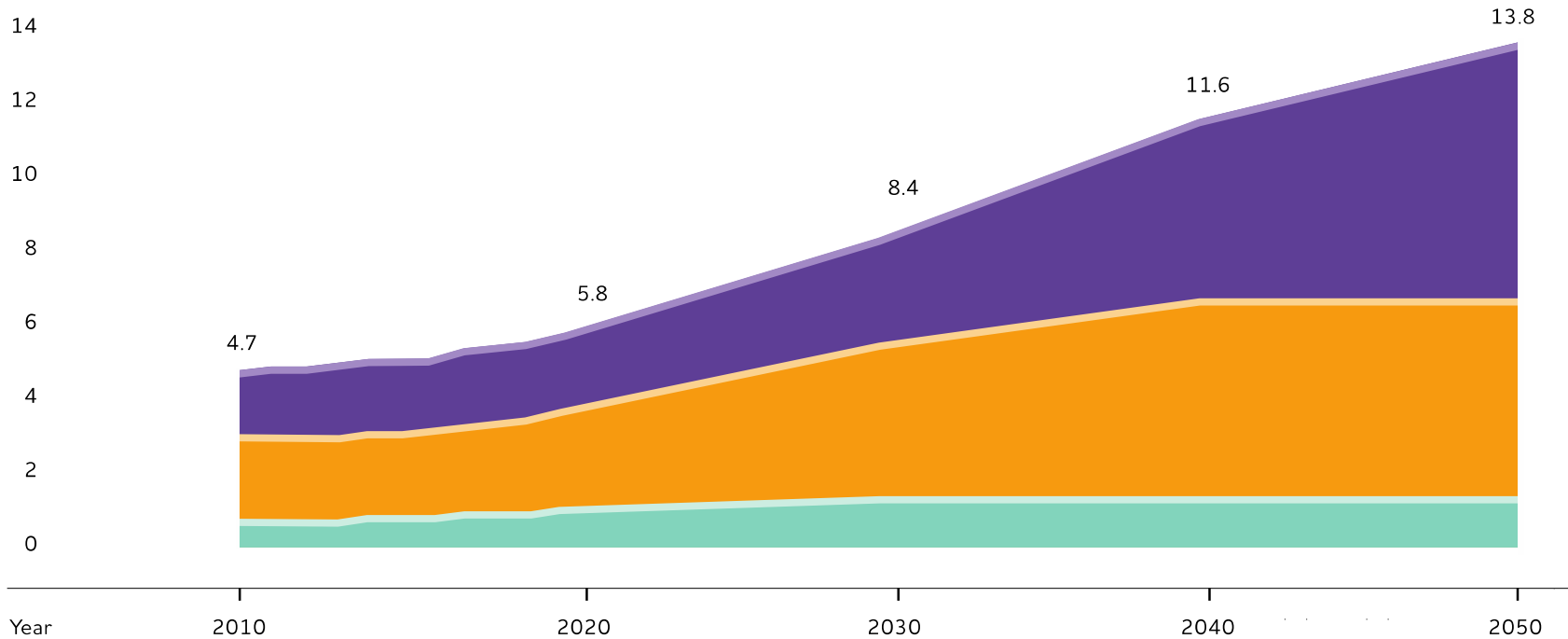
1. We haven't stopped aging

FIGURE 4

Projected Number of People Age 65 and Older (Total and by Age Group) in the U.S. Population with Alzheimer's Disease, 2010 to 2050

Millions of people with Alzheimer's

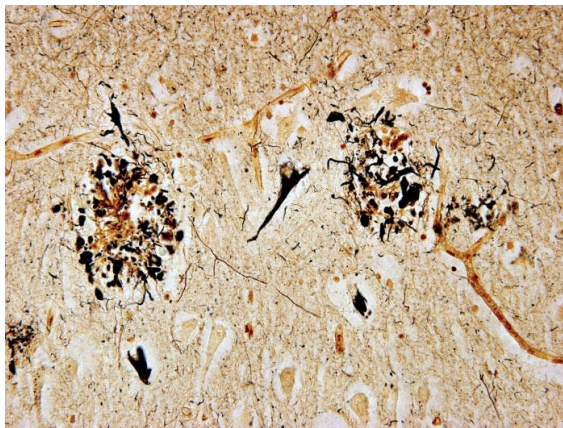
■ Ages 65-74 ■ Ages 75-84 ■ Ages 85+



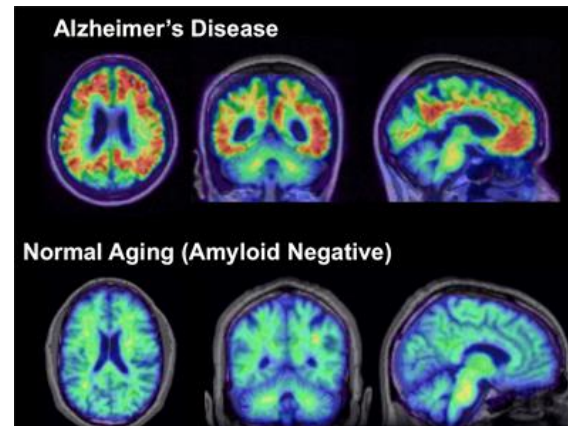
Alzheimer's Association: 2016 Alzheimer's Disease Facts and Figures

2. We haven't cured Alzheimer's

- Despite 15 years of clinical trials aimed at amyloid-beta, the clearest “cause” of Alzheimer's, we have not identified a cure
- We know much more about genes and other risk factors for the disease: *There are many more targets to go after*
- With neuroimaging we can now track AD progression: *Early diagnosis and therapeutic efficacy*



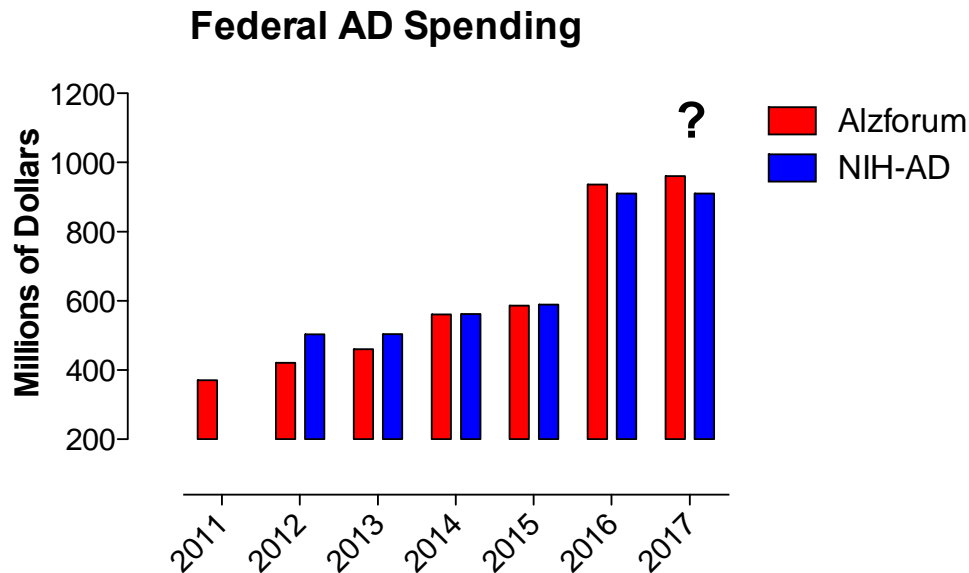
Perl, 2010



<http://sph.berkeley.edu>

3. Funding for AD research is rising

- Dec 2010: National Alzheimer’s Project Act (NAPA) signed into Law
- In 2014, Alzheimer’s Accountability Act created path for a Bypass Budget, first enacted in 2016



https://report.nih.gov/categorical_spending.aspx

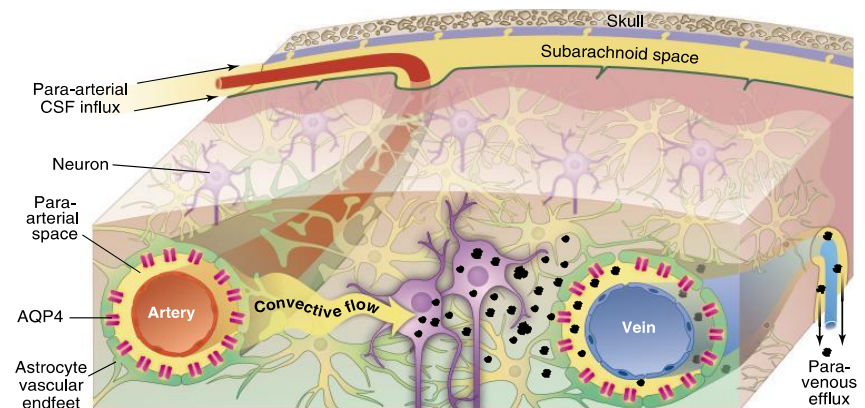
<http://www.alzforum.org/news/community-news/proposed-2016-budget-boosts-alzheimers-funding-60-percent>

Current AD Research at URMIC

- Gail V. W. Johnson, PhD, Anesthesiology
 - Understanding mechanisms involved in clearing tau from the cell
 - Grants from BrightFocus Foundation and NINDS
- M. Kerry O'Banion, MD, PhD, Neuroscience
 - Modulating innate immunity to target amyloid beta and tau
 - Effects of radiation on AD pathogenesis
 - Grants from NIA and NASA
- Alison Elder, PhD, Environmental Medicine
 - Effects of environmental particulates on AD pathogenesis
 - Grant from NIEHS (Multi-PI with O'Banion)
- Houhui Xia, PhD, Pharmacology & Physiology
 - Role and regulation of protein phosphatase-1 in synaptic transmission and memory formation
 - Grants from NIMH and NSF

Current AD Research at URMCM

- Rashid Deane, PhD, Neurosurgery
 - Brain clearance mechanisms for tau and ApoE
 - Grants from NIA and NINDS
- Maiken Nedergaard, MD, DMSc, Neurosurgery, Center for Translational Neuromedicine
 - Glymphatic contribution to amyloid and tau accumulation in AD
 - Glymphatic contribution to small vessel brain disease
 - Grants from NIA, NINDS, Cure Alzheimer's Fund, and Foundation Leducq



Go with the flow. Convective glymphatic fluxes of CSF and ISF propel the waste products of neuron metabolism into the para-venous space, from which they are directed into lymphatic vessels and ultimately return to the general circulation for clearance by the kidney and liver.

Current AD Research at UPMC

- Charles Duffy, MD, PhD, Neurology
 - Visuospatial disorientation in aging and AD
 - Founder and CEO of Cerebral Assessment Systems, developer of Cognivue®
 - Grant from NEI
- Feng Vankee Lin, PhD, RN, School of Nursing
 - Early markers of Alzheimer's disease and "Supernormal Aging"
 - Neuroplasticity training for cognitive aging
 - Grants from Alzheimer's Association, NIA, and NINR
- Anton Porsteinsson, MD, Psychiatry, Director of the Alzheimer's Disease Care, Research and Education Program (AD-CARE)
 - Part of national trial networks including ADCS, ATRI, ADNI, DOD-ADNI and GAP-NET
 - Major participant in clinical trials targeting amyloid-beta, beta-secretase, agitation, apathy and memory loss in AD patients

Opportunities

- Current URMC Investigators are involved in a wide range of preclinical, translational and patient-oriented/clinical research projects
- NIA recently released 17 new AD RFAs and PAs; anticipate continued increases in funds committed to AD research
- How can we enhance AD research at URMC?
 - Gather investigators to consider common areas for collaboration
 - Focus on developing a PO1 grant
 - Engage/Join Rochester Aging Research Center
 - Other suggestions?