BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Hyman, Bradley	John B. Penney Jr. Professor of Neurology, Harvard Medical School
eRA COMMONS USER NAME BTHyman	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Northwestern University, Evanston, IL	B.A.	1977	Chemistry
University of Iowa, Iowa City, IA	Ph.D.	1982	Biochemistry
University of Iowa, Iowa City, IA	M.D.	1983	Medicine

A. Personal statement I am a neurologist and a physician scientist with a clinical practice and laboratory effort devoted to caring for and understanding patients with neurodegenerative diseases including Alzheimer's disease. I have participated in the MGH's Alzheimer's Disease Research Center since 1989 (and directed it since 2006). My laboratory focuses on translational studies, developing models of human neurodegenerative disease and comparing them to human neuropathology, often applying advanced imaging techniques including in vivo multiphoton microscopy, FRET imaging, and array tomography. Training of the next generation of scientists is also an important goal of the laboratory; I have trained over 50 fellows, 96% of whom remain in careers in science.

B. Present Positions and Honors:

Present Postions: John B Penney Jr Professor of Neurology, Harvard Medical School, Director, Mass Alzheimer Disease Res Center; Neurologist, Massachusetts General Hospital;

Past Positions: *Associate Prof Neurology*, Harvard Medical School (1993) *Assistant Prof Neurology*, Harvard Medical School (1989); *Medical internship* and *Neurology residency*, University of Iowa; *Fellowship* in Behavioral Neurology (1983); *Fellowship* in Neuropathology (1988) University of Iowa.

Honors: Alzheimer Assn Faculty Scholar Award; Metropolitan Life Award; Alzheimer Assn Pioneer Award, NIA MERIT Award. ISI top cited author in Neurosciences (Over 30,000 citations). ISI top cited author in Alzheimer disease (top 10 overall). H-index = 110. Member, NIH review panels 2001-2005; 2009, 2011- 12; Scientific American 2005 Technology Prize. Potamkin Prize, AHAF Centennial Award. Member, NIA panel for the clinical diagnosis of Alzheimer disease (2010); Co-chair, NIA panel for the neuropathological diagnosis of Alzheimer disease(2010). Elected member of American Academy of Physicians (2011); Alzheimer Assn Lifetime Achievement award (2012). Alzheimer Assn Lifetime Achievement award (2012). Am Assn of Neuropathologists Moore Award (2013). Member, NIA council (2013)

C. Publications: (selected from >600 papers and chapters)

1. Meyer-Luehmann M, Spires-Jones TL, Prada C, Garcia-Alloza M, de Calignon A, Rozkalne A, Koenigsknecht-Talboo J, Holtzman DM, Bacskai BJ, and Hyman BT. Rapid appearance and local toxicity of Aβ plaques in a mouse model of Alzheimer's disease. *Nature* 2008, 451:720-4. NIHMSID # 347731
2. Kuchibhotla KV, Goldman ST, Lattarulo CR, Wu H-Y, Hyman BT, and Bacskai BJ. (2008) Aβ plaques lead to aberrant regulation of calcium homeostasis *in vivo* resulting in structural and functional disruption of neuronal networks. *Neuron* Jul 31;59(2):214-25 PMCID: PMC2578820
3. Koffie RM, Meyer-Leuhmann M, Hashimoto T, Adams KW, Mielke ML, Garcia-Alloza M, Micheva KD, Smith SJ, Kim ML, Lee VM, Hyman BT and Spires-Jones TL. Oligomeric amyloid beta associates with

postsynaptic densities and correlates with excitatory synapse loss near senile plaques. *Proc Natl Acad Sci* 2009 Mar 10;106(10):4012-7. PMCID: PMC2656196
4. Kuchibhotla KV, Lattarulo CR, Hyman BT, and Bacskai BJ. Synchronous Hyperactivity and Intercellular Calcium Waves in Astrocytes in Alzheimer Mice. *Science* 2009 Feb 27;323(5918):1211-5 PMCID: PMC2884172
5. de Calignon A, Fox LM, Pitstick R, Carlson GA, Bacskai B, Spires-Jones TL, Hyman BT. Casapse activation precedes and leads to tangles. *Nature* 2010 Apr 22;464(7292):1201-4 PMCID: PMC3091360
6. Hyman BT, Phelps CH, Beach TG, Bigio EH, Cairns NJ, Carrillo MC, Dickson DW, Duyckaerts C, Frosch MP, Masliah E, Mirra SS, Nelson PT, Schneider JA, Thal DR, Thies B, Trojanowski JQ, Vinters HV, Montine TJ. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimers Dement. 2012 Jan;8(1):1-13 . PMCID: PMC3266529
7. Koffie, R. M., Hashimoto, T., Tai, H. C., Kay, K. R., Serrano-Pozo, A., Joyner, D., Hou, S., Kopeikina, K. J., Frosch, M. P., Lee, V. M., Holtzman, D. M., Hyman, B. T. and Spires-Jones, T. L. (2012). "Apolipoprotein E4 effects in Alzheimer's disease are mediated by synaptotoxic oligomeric amyloid-beta." *Brain* 135(Pt 7): 2155-68. PMCID: PMC3381721
8. de Calignon A,, Polydoro M, Suárez-Calvet M, William C, Adamowicz DH, Kopeikina KJ, Pitstick R, Sahara N, Ashe KH, Carlson GA, Spires-Jones TL, Hyman BT . Propagation of tau pathology in a model of early Alzheimer's disease *Neuron* 2012 73:685-97 PMCID: PMC3292759
9. Rudinskiy, N., Hawkes, J. M., Betensky, R. A., Eguchi, M., Yamaguchi, S., Spires-Jones, T. L. and Hyman, B.T. 2012. "Orchestrated experience-driven Arc responses are disrupted in a mouse model of Alzheimer's disease." *Nat Neurosci*. 2012 Oct;15(10):1422-9 PMCID: PMC3458168
10. Polydoro M, de Calignon A, Suárez-Calvet M, Sanchez L, Kay KR, Nicholls SB, Roe AD, Pitstick R, Carlson GA, Gómez-Isla T, Spires-Jones TL, Hyman BT. Reversal of Neurofibrillary Tangles and Tau-Associated Phenotype in the rTgTauEC Model of Early Alzheimer's Disease. *J Neurosci*. 2013 Aug 14;33(33):13300-11. PMID: 23946388 PMCID: PMC3742920
11. Pooler AM, Polydoro M, Wegmann SK, Pitstick R, Kay KR, Sanchez L, Carlson GA, Gomez-Isla T, Albers MW, Spires-Jones TL, Hyman BT. Tau - amyloid interactions in the rTgTauEC model of early Alzheimer's disease suggest amyloid induced disruption of axonal projections and exacerbated axonal pathology. *J Comp Neurol.* 2013 Jul 10. doi: 10.1002/cne.23411.
12. Polydoro M, Dzhala VI, Pooler AM, Nicholls SB, McKinney AP, Sanchez L, Pitstick R, Carlson GA, Staley KJ, Spires-Jones TL, Hyman BT. Soluble pathological tau in the entorhinal cortex leads to presynaptic deficits in an early Alzheimer's disease model. *Acta Neuropathol*. 2013 Nov 24. [Epub ahead of print] PMID:24271788 PMCID
13. Kim T, Vidal GS, Djurisic M, William CM, Birnbaum ME, Garcia KC, Hyman BT, Shatz CJ. Human LilrB2 is a β-amyloid receptor and its murine homolog PirB regulates synaptic plasticity in an Alzheimer's model. *Science.* 2013 Sep 20;341(6152):1399-404. doi: 10.1126 NIHMSID #533614
14. Hudry E, Dashkoff J, Roe AD, Takeda S, Koffie RM, Hashimoto T, Scheel M, Spires-Jones T, Arbel-Ornath M, Betensky R, Davidson BL, Hyman BT. Gene transfer of human APOE isoforms results in differential modulation of amyloid deposition and neurotoxicity in mouse brain. *Sci Transl Med.* 2013 Nov 20;5(212):212ra161. doi: 10.1126/scitranslmed.3007000. PMID: 24259049 PMC in process
15. Kuchibhotla KV, Wegmann S, Kopeikina KJ, Hawkes J, Rudinsky N, Andermann ML, Spires-Jones TL, Bacskai BJ, Hyman BT. Neurofibrillary tangle-bearing neurons are functionally integrated into cortical circuits*. Proc Natl Acad Sci* 2014 Jan 7;111(1):510-4 PMID:24368848

D. Research Support.

Ongoing Research Support:

5 P50 AG005134-30 Hyman (PI) 05/01/09-03/31/14
NIH/NIA
Massachusetts Alzheimer's Disease Research Center
The specific goals are: To propose and support new research in neuroscience directed toward uncovering the etiology and pathogenetic mechanisms of AD and related dementias; to enhance collaborative dementia

research funded outside of the ADRC; and to catalyze education, training and information transfer related to AD and related dementias. Role: PI

5 R01 AG026249-06A1 Hyman (PI) 09/15/10-08/31/15
NIH / NIA
Anatomical Changes in Tau Transgenic Models
The project will study the mechanisms of tau induced neuronal death using transgenic models. Role: PI

1P01 AG036694-01 Sperling (PI) 07/15/10-06/30/15
NIH/NIA (Sub to BWH)
Project 3: Molecular markers from the transition of normal aging to early Alzheimer's disease
This project will provide dynamic molecular and neurophysiological (i.e., functional) biomarkers to complement the detailed cognitive/imaging profiles emerging from Projects 1, 2 and 4 during the transition from normal aging to very early AD. Role: project PI

1R01AG041507-01 Hyman (PI) 04/01/11-03/31/16
NIH/NIA
Calcineurin-mediated neurodegeneration in Alzheimer Disease
The coordinated efforts of senior scientists will share resources and expertise to identify mechanisms shared between Alzheimer and epilepsy. Identifying the molecular pathways for these and other age-related neurological disorders will allow development of new therapeutics. Role: PI

AHAF Grant 2011086 Hyman (PI) 07/01/11-06/30/14
American Health Assistance Foundation
Modeling the interaction of tau and Ab in Alzheimer's Disease
We plan to develop, characterize and utilize a novel transgenic mouse model, developed in the Hyman laboratory, that will allow us to lest new ideas and hypotheses about the earliest phases of Alzheimer's disease (AD), and to lest ideas about the causes of progression in AD, specifically the interaction of tau and Abeta at the earliest phase of the disease. Role: PI

1 R01 AG040530-01 Haigis (PI) 07/01/11-06/30/14
NIH
In vivo systems biology of neurodegenerative diseases
Our study aims to utilize emerging technologies and computational modeling to characterize the molecular and cellular changes that occur in the brain during the onset and progression of tau-related neurodegenerative disease. Our ultimate goal is to identify new therapeutic opportunities to protect neurons from the ravaging effects of the pro-death stimuli that underlie neurodegeneration. Role: Consult on neuropathology and provide tissue

5U01AG016976-13 Kukull (PI) 07/01/09-06/30/14
NIH/NIA (Sub to Univ. of Washington)
National Alzheimer's Coordinating Center (NACC)
NACC collects and stores research data from Alzheimer's Disease Centers as mandated by NIA. Alzheimer's Coordinating Centers are required to submit designated limited research data to NACC for inclusion in their database. These data consist of, but are not limited to, a Minimum Data Set, a new and expanded Uniform Data Set, neuropathologic data, ancillary survey data, and meta data describing individual ADC characteristics. Role: Director of the Mass ADRC – site PI

Neotope Biosciences Limited Hyman (PI) 08/01/12-07/31/14
Testing therapeutic intervention to prevent the spread of tau pathology in rTgTauEC mice
Major Goals: examine an intervention to impact tau pathobiology in an animal model. Role: PI

5U01AG016976-14 Kukull (PI) 07/01/12-06/30/14
NIH/NIA (Sub to Univ. of Washington/ NACC)
Special Project: Optimization of Neuropathologic Assessment of Alzheimers Disease
The impact of this project on the field of AD research will be broad because minimizing variation in the neuropathologic assessment of AD will fuel progress in others areas of AD research that use neuropathologic assessments as the current gold standard, including genomics, neuroimaging, biomarkers, and cognitive and behavioral research. Role: Director of the Mass ADRC

Completed Research Support:

5 R01 AG008487-20 Hyman (PI) 09/01/06-08/31/12
NIH/NIA
Neurologic Alterations in Alzheimer's Disease
This project will study the anatomy of the pathological change in Alzheimer disease and transgenic mice using new quantitative anatomical tools and multiphoton microscopy. Role: PI

ZEN-09-132524 Hyman (PI) 10/01/09-09/31/12
Alzheimer's Association
Untangling tangles in AD
This project will either confirm the importance of targeting fibrillar tau or support a paradigm shift in which soluble misfolded tau species are viewed as the primary neurotoxic agent, raising the possibility that disaggregation of NGT would increase toxicity. Role: PI

CART Award Hyman (PI) 07/01/11-06/30/12
Coins for Alzheimer's Research Trust
Nanotechnology solutions for Alzheimer problems
We hypothosize that new nanotechnology can provide reagents that may provide access across this barrier, with the potential to both substantially advance biomedical research, improve the ability of neuroimaging agents to report on their targets, and potentially even improve therapeutic access. The combination of nanotechnology with multiphoton microscopy could lead to the direct study of new targets in the central nervous system, and could improve drug access to the brain leading to the potential for truly revolutionary changes. Role: PI