



The Faculty of Medicine of Harvard University

Curriculum Vitae

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Name Can (Martin) Zhang, M.D., M.Sc, Ph.D.

Work Title Associate Professor in Neurology

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Place of Birth Heze, Shandong, China

Education

06/1999 M.D.	Clinical Medicine	Weifang Medical College, China
06/2002 M.Sc.	Immunology Mentor: Dr. Zai-lian Li	Department of Immunology, Weifang Medical College, China
10/2007 Ph.D.	Molecular Biology (with an emphasis in Neuroscience) Mentor: Dr. Aleister Saunders	Department of Bioscience and Biotechnology, Drexel University, U.S.

Postdoctoral Training

11/2007-06/2010	Research Fellow in Neurology Mentor: Dr. Rudolph Tanzi	Department of Neurology MGH and HMS, U.S.
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Faculty Academic Appointments

07/2010-09/2013	Instructor in Neurology	HMS
10/2013-02/2022	Assistant Professor in Neurology	HMS
02/2022-present	Associate Professor in Neurology	HMS

Appointments at Hospitals/Affiliated Institutions

07/2010-02/2022	Assistant in Neuroscience, Neurology Service	Department of Neurology, MGH
10/2013-02/2022	Assistant Investigator	Department of Neurology, MGH
02/2022-present	Associate Investigator	Department of Neurology, MGH
12/2018-present	Adjunct Faculty in Radiology	Department of Radiology, MGH
07/2019-present	Faculty Member	McCance Center for Brain Health, Mass General Neuroscience, MGH
02/2022-present	Associate in Neuroscience, Neurology Service	Department of Neurology, MGH

Other Professional Positions

08/1997-06/1998	Medical Clerkship	Laiyang Central Hospital, China
06/1998-06/1999	Medical Internship	Weifang Medical College Affiliated Hospital, China
09/1999-06/2002	Teaching Assistant	Department of Immunology, Weifang Medical College
08/2002-10/2007	Teaching Assistant	Department of Bioscience and Biotechnology, Drexel University
06/2016-05/2019	Consultant	AZTherapies
02/2021-01/2023	Scientific Advisory Board	Pluripotent Diagnostics Corp.

Major Administrative Leadership Positions

Local

11/2016-10/2017	Conference Organizer	The Mind and Body Conference of Tibetan Medicine, Boston
10/2017-present	Faculty Member Advisory Board	Chinese Scientists and Staff Association (CSSA), MGH
07/2019-present	Leader	Protein Biomarker Core Laboratory, McCance Center for Brain Health, MGH
03/2022-present	Participating Research Mentor	MGH Next-Gen PSTP Physician-Scientist Training Programs (R25) & MGH Next- Gen StARR Stimulating Access to Research in Residency Program (R38)

International

04/2011-03/2019	Visiting Professor	Weifang Medical College (non-voting)
11/2014-10/2018	Visiting Professor	Binzhou Medical College (non-voting)
09/2016-08/2020	Visiting Professor	Qingdao University Medical College and Qingdao Municipal Hospital (non-voting)
11/2017-10/2018	Conference Organizer	The Harvard Center Shanghai Conference on Brain Health, with an emphasis on Alzheimer's' disease, Shanghai (received a competitive travel award)
05/2022-present	Contributor	The WHO TPP Target Product Profile for dementia diagnostics; my role is providing expert opinion for recommending affordable dementia diagnostics

Committee Service

Local

02/2020-present	MGH ECOR Subcommittee	SRRP Subcommittee on Review of Research Proposals
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National

2018	Ph.D. Thesis committee	Mount Sinai School of Medicine, Committee for A. Browne
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International

10/2014-10/2019	Brain Disease Specialty Committee	World Federation of Chinese Medicine Societies (WFCMS)
02/2021-present	Scientific Advisor	Community of Biotechnology, Bangladesh

Professional Societies

11/1999-06/2002	Member	Society for Immunology-Shandong China
08/2003-10/2007	Member	The A. J. Drexel Institute of Basic and Applied Protein Science
10/2005-present	Member	Society for Neuroscience
08/2006-present	Member	American Society for Microbiology
04/2011-04/2014	Member	Anti-aging and Alzheimer's Committee, Chinese pharmacological Society

08/2014-08/2018	Member	Academic Society for Functional Foods and Bioactive Compounds
05/2018-04/2021	Member	IEEE, the Institute of Electrical and Electronics Engineers
05/2018-04/2021	Member	IEEE Engineering in Medicine and Biology Society, the Institute of Electrical and Electronics Engineers
12/2018-present	Member	Boston Biology and Biotechnology (BBB) Association, Boston Chapter of the Society of Chinese Bioscientists in America (SCBA)

Grant Review Activities

02/2019-present	Ad hoc Reviewer	Harvard Catalyst, The 2019 Harvard Clinical and Translational Science Center, on Microbiome in Human Disease pilot grant
05/2019-present	Ad hoc Reviewer	Neurology Department Transformative Scholar award
03/2020-present	Ad hoc grant Reviewer	Alzheimer's Association International Research Grant Program (IRGP)
03/2020-present	Ad hoc grant Reviewer	Cure Alzheimer's Fund (CAF) Research Grant Program
03/2020-present	Ad hoc grant Reviewer	NIH CMND (Cellular and Molecular Neurodegeneration) study section waiting list assigned by study section Scientific Review Officer, this study section reviews applications to study cellular and molecular aspects of neurodegeneration
03/2020	Ad hoc grant Reviewer	CZI (Chan Zuckerberg Initiative) Science Grants Program
06/2020	Ad hoc grant Reviewer	NIH ETTN-14 Emerging Technologies and Training in Neurosciences, Review for small business [SBIR and STTR] applications
12/2021	Ad hoc grant Reviewer	NIH Transformative Research Award Program for mail review
04/2022	Ad hoc grant Reviewer	NIH/NIA Career development for

established investigators and conference grants study section (AGCD-4); grant reviewer of the standing committee.

08/2022 Ad hoc grant Reviewer Florida Department of Health Ed and Ethel Moore Alzheimer's Disease Research Program 22-23

Editorial Activities

Peer Reviewer

01/2010-present	Ad hoc Reviewer	NeuroToxicology - Elsevier
05/2012-present	Ad hoc Reviewer	Plos One - The Public Library of Science
11/2014-present	Ad hoc Reviewer	Brain
11/2014-present	Ad hoc Reviewer	Molecules
06/2015-present	Ad hoc Reviewer	Journal of Neurochemistry
09/2015-present	Ad hoc Reviewer	Journal of Cellular and Molecular Medicine
10/2015-present	Ad hoc Reviewer	Oncogene - Nature
11/2015-present	Ad hoc Reviewer	International Journal of Molecular Sciences
06/2016-present	Ad hoc Reviewer	Journal of Alzheimer's disease
08/2017-present	Ad hoc Reviewer	Oncotarget
12/2017-present	Ad hoc Reviewer	Artificial Cells, Nanomedicine and Biotechnology - Taylor & Francis
04/2018-present	Ad hoc Reviewer	Acta Neuropathologica
05/2018-present	Ad hoc Reviewer	Age and Ageing
02/2019-present	Ad hoc Reviewer	Aging
02/2019-present	ad hoc Reviewer	Brain Behavior and Immunity
05/2019-present	Ad hoc Reviewer	ACS Chemical Neuroscience
11/2019-present	Ad hoc Reviewer	Current Alzheimer's Research
03/2020-present	Ad hoc Reviewer	Chemistry - A European Journal
03/2020-present	Ad hoc Reviewer	Molecular Genetics & Genomic Medicine

03/2020-present	Ad hoc Reviewer	Aging Cell
04/2020-present	Ad hoc Reviewer	Molecular Medicine Reports
05/2020-present	Ad hoc Reviewer	Neuropsychiatric Disease and Treatment
05/2020-present	Ad hoc Reviewer	Frontiers in Neuroscience
06/2020-present	Ad hoc Reviewer	Science China Life Sciences - Springer
07/2020-present	Ad hoc Reviewer	Phytomedicine - Elsevier
08/2020-present	Ad hoc Reviewer	iScience
10/2020-present	Ad hoc Reviewer	Molecular Psychiatry
05/2020-present	Ad hoc Reviewer	Frontiers in Aging Neuroscience
11/2020-present	Ad hoc Reviewer	Advanced Science
11/2020-present	Ad hoc Reviewer	Brain Research – Elsevier
12/2020-present	Ad hoc Reviewer	Scientific Reports
01/2021-present	Ad hoc Reviewer	Journal of Pain Research
03/2021-present	Ad hoc Reviewer	Alzheimer's Research & Therapy
04/2021-present	Ad hoc Reviewer	Molecular Neurobiology
05/2021-present	Ad hoc Reviewer	Current Drug Targets
06/2021-present	Ad hoc Reviewer	Gels – an MDPI Journal
06/2021-present	Ad hoc Reviewer	ACS Applied Materials & Interfaces
06/2021-present	Ad hoc Reviewer	Bioorganic Chemistry
09/2021-present	Ad hoc Reviewer	Advanced Healthcare Materials
10/2021-present	Ad hoc Reviewer	Translational Neurodegeneration
11/2021-present	Ad hoc Reviewer	Toxicology
01/2022-present	Ad hoc Reviewer	Journal of Pharmacology and Experimental Therapeutics
02/2022-present	Ad hoc Reviewer	Journal of Hazardous Materials
02/2022-present	Ad hoc Reviewer	Cellular and Molecular Life Science
03/2022-present	Ad hoc Reviewer	Journal of Neuroinflammation

03/2022-present	Ad hoc Reviewer	Journal of Medicinal Chemistry
05/2022-present	Ad hoc Reviewer	European Journal of Neurology
06/2022-present	Ad hoc Reviewer	Neurobiology of Aging
10/2022-present	Ad hoc Reviewer	ACS Omega
11/2022-present	Ad hoc Reviewer	CNS Neuroscience & Therapeutics
12/2022-present	Ad hoc Reviewer	Translational Psychiatry
01/2023-present	Ad hoc Reviewer	Ecotoxicology and Environmental Safety
01/2023-present	Ad hoc Reviewer	Molecular Pharmacology

Other Editorial Roles

01/2012-present	Associate editor	Discovery Medicine
10/2014-10/2017	Guest editor (special issue)	International Journal of Alzheimer's Disease
03/2015-03/2018	Editorial board member	Journal of Alzheimer's & Neurodegenerative Diseases
12/2019-12/2021	Associate editor	Journal of Alzheimer's Disease
05/2020-present	Guest editor	Frontiers in Neuroscience, Frontiers in Neurology and Frontiers in Psychiatry – Neurodegeneration
11/2020-02/2022	Guest editor	Frontiers in Aging Neuroscience – Neurodegeneration; Research topic “Progress of Translational Medicine in Alzheimer's Disease”
02/2021-02/2022	Review editor	Frontiers in Neuroscience – Neurodegeneration; Research topic “Mechanisms of Action in neurodegenerative Proteinopathies”
04/2022-present	Editor	Advanced Gut & Microbiome Research
10/2022-present	Guest editor	Frontiers in Molecular Bioscience; Research Topic “Molecular Pathology and Molecular Therapy of Major Chronic Disease”
10/2022-present	Editor	Bioengineering

Honors and Prizes

09/1994-06/1999	Fellowship for Academic Excellence, Weifang Medical College
09/1999-06/2002	Fellowship for Academic Excellence in Graduate studies, Weifang Medical College
11/2001	Research Award in Shandong Society for Immunology
04/2005	Honorable Mentions, Drexel University Research Day
04/2006	Dean's Award, Drexel University Research Day
04/2007	Honorable Mention, Drexel University Research Day
07/2009	Funds for Medical Discovery Fellow, MGH
04/2010	Massachusetts Alzheimer's Disease Research Center Fellow, MGH and Harvard University
04/2010	Ruth L. Kirschstein National Research Service Award
08/2010	Selected in the book; " <i>Weifang Medical College: Alumni with Exceptional Contribution</i> "
09/2011	NIH K99/R00 Pathway to Independence Award
02/2012	American Federation of Aging Research Young Investigator (Finalist)
02/2013	Ellison Medical Foundation New Scholar in Aging (MGH Nomination)
11/2013	Drexel University " <i>40 under 40</i> " selection; recognizes outstanding young alumni who are making a mark in their professions and community
09/2019	Mass General Neuroscience/McCance Center for Brain Health Scientific Projects to Accelerate Research and Collaboration (SPARC) award
07/2021	HMS Ruth and Maurice Freeman Award for Pain Neurology Research

[Report of Funded and Unfunded Projects](#)

Past funded projects

Year(s)	Role	Project title and description
07/2004-06/2006	Assistant	Search for Novel Alzheimer's disease candidate genes utilizing a novel luciferase assay NIH/NINDS (PI: A. Saunders), R21NS048227, Drexel University This study is focused on characterizing effects of Alzheimer's candidate genes by an AICD-based luciferase assay in cell-based studies.
07/2009-06/2010	PI	Functional studies of <i>ATXN1</i> using cell-based models Funds for Medical Discovery, MGH (\$61,000 total costs) The goal of the study is to analyze effects of Alzheimer's-related <i>ATXN1</i> on APP processing in cell-based models.

04/2010-03/2011	PI	<p>Characterization of a potential interaction between ATXN1 and BACE1 Harvard NeuroDiscovery Center and Massachusetts Alzheimer's Disease Research Center (MADRC) - 2010 Neurodegenerative Disease Pilot Study Grant Program (\$40,000 total costs) The study is focused on effects of <i>ATXN1</i> downregulation on BACE1 levels in cell-based models.</p>
04/2010-09/2011	PI	<p>Functional studies of <i>ATXN1</i> in APP processing and Alzheimer's disease pathogenesis Ruth L. Kirschstein National Research Service Award (<i>NRSA</i>); NIH T32AG000222 (\$60,000 total costs) The primary goal of this award is validation of <i>ATXN1</i> modulation on BACE1 levels in cell-based models.</p>
08/2011-07/2012	m-PI	<p>Identifying novel curcumin-like compounds in the treatment of Alzheimer's disease Cure Alzheimer's Fund (other PI: R. Tanzi; \$98,000 total costs) The goal of this study is to identify and characterize curcumin-like compounds using cell-based studies that display therapeutic potential of Alzheimer's disease.</p>
09/2011-07/2013	PI	<p>Characterization of <i>ATXN1</i> in APP processing and Alzheimer's disease pathogenesis NIH K99AG039482 NIH Pathway to Independence Award (\$250,000 total costs) The major goal of this study is elucidating the effects of <i>ATXN1</i> as a promising Alzheimer's gene on amyloid pathology using both cell and animal-based studies.</p>
12/2013-11/2016	PI	<p>Characterization of <i>ATXN1</i> in APP processing and Alzheimer's disease pathogenesis NIH R00AG039482 NIH Pathway to Independence Award (\$750,000 total costs) The major goal of this study is further analyzing the mechanisms by which <i>ATXN1</i> changes amyloid pathology using both cell and animal-based studies.</p>
10/2014-09/2015	m-PI	<p>Analysis of glucagon-like peptide (GLP)-1 receptor agonist exendin-4 for painful diabetic neuropathy HMS Ruth and Maurice Freeman Award for Pain Neurology Research (other PI: T. Cheng; \$20,000 total costs) The primary goal of this study is focused on characterizing the effects of the GLP-1 receptor agonist exendin-4 on painful diabetic neuropathy using both cell and animal-based models.</p>
10/2015-09/2017	m-PI	<p>Effects of tumor necrosis factor – alpha (TNF-α) signaling in painful prediabetic neuropathy HMS Ruth and Maurice Freeman Award for Pain Neurology Research (other PI: T. Cheng; \$20,000 total costs) The primary goal of this study is focused on mechanisms by which TNF-α affects painful prediabetic neuropathy using animal models.</p>
10/2015-09/2016	PI	<p>Characterizing a novel APP eta-processing pathway</p>

		<p>Cure Alzheimer's fund; (\$50,000 total costs) The primary goal of this study is to study a novel APP processing pathway by pharmacological modulation in Alzheimer's cell models.</p>
09/2015-04/2017	Co-I	<p>Near-infrared molecular imaging for monitoring therapy in Alzheimer's disease mouse models NIH R03AG050038 (PI: C. Ran) The object of this study is to develop novel near infrared molecular probes that can detect Alzheimer's amyloid neuropathology in transgenic animals.</p>
01/2016-01/2019	m-PI	<p>Identifying novel curcumin-like compounds in the treatment of Alzheimer's disease Cure Alzheimer's Fund (other PI: C. Ran; \$50,000 total costs) The main goal of this study is to analyze a library of novel curcumin-like Compounds for therapeutic potentials in Alzheimer's disease</p>
05/2016-04/2019	PI	<p>Characterization of effects of cromolyn on Alzheimer's neuropathology Cure Alzheimer's Fund (\$115,000 total costs) The object of this study is to characterize the mechanisms by which cromolyn attenuate Alzheimer's neuropathology using both Alzheimer's transgenic animals and microglial cell models.</p>
01/2017-01/2019	m-PI	<p>Characterizing novel γ-secretase modulators (GSMs) using systems level endophenotypes of hippocampal function MGH SPARK Fund, Department of Neurology (other PI: S. Gomperts; \$25,000 total costs) The main object of this study is to analyze effects of novel GSMs as promising therapeutics of Alzheimer's disease on hippocampal functions in transgenic animals.</p>
12/2013-11/2018	Co-I	<p>Characterization of Presenilin Biology (PI: R. Tanzi) NIH P01AG15379 (D. Selkoe); Program project, Project 2 The primary goal of this study is to investigate effects of pharmacological modulation of Alzheimer's presenilin underlying disease pathogenesis using cell and animal models.</p>
08/2018-07/2020	Co-I	<p>Near infrared fluorescence ocular imaging of soluble amyloid beta species NIH R21AG059134 (PI: C. Ran) The primary object of this study is to utilize curcumin-based probes to enable early detection of Aβ peptides in animal models.</p>
04/2019-01/2021	PI	<p>Molecular imaging of gamma-secretase for Alzheimer's Disease NIH R21AG062913 (\$460,635 total costs) The goal of this study is to develop gamma-secretase modulator-based PET probes to visualize gamma-secretase for Alzheimer's disease.</p>
04/2020-03/2021	Co-I	<p>AMPA-targeted PET imaging study of Alzheimer's disease NIH R01MH120197 (Liang) This grant is an R01 supplemental award with a goal to utilize subtype-selective AMPAR PET ligands in imaging studies of transgenic Alzheimer's disease mouse models.</p>

05/2019-04/2021*	PI	Regulation of human brown and beige adipocyte differentiation and function NIH R01DK077097; Subcontract PI of a supplementary grant for an R01 (prime PI: Y. Tseng) * no cost extension \$167,000 total costs The main objective is to identify and characterize therapeutic potential of cold exposure-related molecules in Alzheimer's disease.
09/2018-06/2021*	m-PI	Optogenetic modulation and physiological analysis of Alzheimer's disease NIH R56AG062208 (other PI: X. Ni; \$430,000 total cost) *no cost extension The goal of this project is to develop a new optogenetic system to modulate analyze pathological changes in Alzheimer's transgenic animals.
09/2019-08/2021	Co-I	PET tracer-guided prognosis and neuroprotective therapy for Alzheimer's disease NIH R03AG063290 (PI: H. Liang) The main goal is to develop a tracer to visualize Alzheimer's disease-related monoacylglycerol lipase (MAGL), the principle enzyme for metabolizing the cannabinoid ligand: 2-arachidonylglycerol (2-AG).
09/2019-02/2022	m-PI	Probing beta amyloid associated impairments of sleep physiology in Alzheimer's disease with novel gamma secretase modulators MGH McCance Center for Brain Health/Mass General Neuroscience Scientific Projects to Accelerate Research and Collaboration (SPARC) award (other PIs: S. Gomperts, W. Wang and B. Westover) \$30,000 total costs The goal is to identify and characterize sleep features through multi-model analyses in Alzheimer's animals.
03/2020-02/2022	Co-I	Imaging active plaques of Alzheimer's disease NIH R21AG065826 (PI: C. Ran) The goal is to use an amyloid plaque-binding probe enabling visualization of plaques in Alzheimer's disease transgenic animals.
07/2021-06/2022	m-PI	Modulation and detection of microglia-related RIPK1 and neuroinflammation in pain HMS Ruth and Maurice Freeman Award for Pain Neurology Research (other PI: S. Shen/C. Wang; \$50,000 total costs) The primary goal of this study is focused on pharmacological modulation and detection of RIPK1 using animal-based models.

Current funded projects

Year(s)	Role	Project title and description
01/2018-12/2023*	PI	Characterization of soluble GSMs in Alzheimer's disease pathology NIH R01AG055784 (\$2,129,725 total costs) The goal of this proposal is to explore the roles of novel gamma secretase modulators in Alzheimer's disease. * no cost extension
09/2019-08/2024	Co-I	Characterization of Presenilin Biology

NIH P01AG15379 Project 3 (PI: R. Tanzi);
 Program project (PI: D. Selkoe)
 The primary goal of this study is to analyze the pathophysiology of Alzheimer's presenilin using pharmacological agents and modulation of neurogenesis.

04/2020-03/2023	m-PI	Molecular imaging of RIPK1/necroptosis as a key biomarker in Alzheimer's disease NIH R61NS117197 (other PI: Dr. C. Wang; \$646, 632 total costs) The goal is to develop RIPK1/necroptosis imaging probes and explore their roles in Alzheimer's disease.
06/2021-05/2023*	PI	Molecular neuroimaging of RIPK1/necroptosis as putative biomarkers for Alzheimer's disease ADDF GC-201910-2019763 (\$230,000 total costs) * Renewal in progress. \$300,000 total cost. The primary objective of this study is to further characterize a new probe enabling visualization of RIPK1/necroptosis for Alzheimer's disease using preclinical models.
08/2021-07/2024	m-PI	Gut microbiota underlies the heterogeneity of aging brain's susceptibility to postoperative delirium NIH 1RF1AG070141-01A1 (other PI: S. Shen and C. Wang; \$1,739,007 total costs) The purpose of this grant is to dissect the biological underpinnings of the heterogeneity of aging brain's susceptibility to postoperative delirium, with a focus on gut microbiota and metabolites.
06/2022-05/2024	co-I	Investigation of sirtuin-1 expression in mice model of Alzheimer's disease over age NIH R03 (PI: C. Wang) The goal is to study the Sirtuin-1 expression changes in the brain of Alzheimer's disease animals over age.
09/2022-08/2026	m-PI	SCH: Machine Learning Enhanced Multimodal Sensor-on-a-chip for Minimally-invasive Early Detection of Alzheimer's Disease NSF (other PI: F. Ma) \$240,000 total costs The goal of this project is focused on identifying Alzheimer's biofluid biomarkers by deep learning-based multi-model method.
04/2022-03/2027	Subaward PI	Development of novel NLRP3 inflammasome inhibitors for Alzheimer's disease NIH U01 (PI: S. Zhang at VCU) \$774,744 total costs The goal of this project is focused on identifying and characterizing potential molecules that specifically and safely inhibit NLRP3 inflammasome, which may ultimately provide as potential therapeutics of Alzheimer's disease.
06/2022-05/2023	co-I	Molecular Magnetic Resonance Imaging of Inflammation: Administrative Supplement (PI: E. Gale)

NIH R01S1 (a supplement to our Parent R01)
 The goal is to apply reactive oxygen species specific MRI technology developed by the PI to visualize pathologic microglial activation in Alzheimer's disease pathogenesis.

07/2022-06/2024 m-PI Inhibiting RIPK1 with Necrostatin-1 for Safe and Effective Pain Treatment
 NIH R61; response to [NS21-029] - HEAL Initiative: Planning Studies for Initial Analgesic Development [Small Molecules and Biologics]
 \$295,000 total costs
 The project is to rigorously test our central hypothesis that inhibiting RIPK1 through Nec-1 is a safe and effective treatment for neuropathic pain, which may not only provide robust data on the efficacy and side effects of Nec-1, but also establish a multidisciplinary research team with extensive experience in translational pain research for the subsequent U19 Team Research phase.

Submitted projects

Year(s)	Role	Project title and description
01/2021-12/2023	m-PI	A Multimodal nanophotonic neural interface M. Keck Foundation; subcontract m-PI (other PI: X. Ni at Penn State University and S. Gomperts) \$1,200,000 total costs at MGH
09/2021-08/2026	m-PI	Mechanistic Study of Herbal Medicine for Treating Alzheimer's Disease NIH R01 (other PI: D. Lee) \$1,200,000 total costs
09/2021-08/2025	m-PI	Molecular Neuroimaging and Analysis of Sirtuin-1 in Alzheimer's disease NIH R01 (other PI: C. Wang) \$1,200,000 total costs
09/2021-08/2025	m-PI	Neuroimaging and analysis of infection-related gamma-secretase in Alzheimer's disease NIH R01 (other PI: C. Wang) \$2,400,000 total costs
04/2022-03/2027	PI	High-precision and multi-modal analysis of heterogeneity in Alzheimer's disease-associated proteinopathy NIH R01; PI of Subcontract (other PI: S. Huang at Penn State University and C. Ran) \$1,700,000 total costs at MGH
04/2022-08/2027	Subaward PI	Development of Natural Medicine for Treating Alzheimer's disease NIH U01 (PI: D. Lee at McLean) \$3,400,000 total costs
04/2022-08/2027	co-I	The impact of stress on cognitive aging and Alzheimer's disease research study NIH R01 (PI: P. Vannini at MGH)

04/2022-03/2027	m-PI	Developing SIRT1-based PET probes for brain imaging of Alzheimer's disease NIH R01 (PI: C. Wang) \$1,220,000 total costs
04/2022-03/2024	m-PI	Evaluating the effects of NR/NAD ⁺ supplementation on Alzheimer's disease animals NIH-R21 (other PI: C. Wang and SH. Choi)
04/2022-03/2027	PI	Repurposing a promising herbal medicine HLXL for Alzheimer's disease NIH R01 (other PI: R. Tanzi/D. Lee) \$3,637,065 total costs
10/2022-09/2027	m-PI	Developing HDAC11 inhibitors as potential therapeutics for Alzheimer's disease (PI: C. Wang) \$3,637,065 total costs
09/2022 - 08/2026	m-PI	New HDAC6-selective probes for neuroimaging NIH R01 (PI: C Wang) \$3,164,060 total costs
09/2022-08/2027	m-PI	Non-invasive Investigation of Gamma-secretase in Alzheimer's disease NIH R01 (PI: C. Wang) \$4,114,115 total costs
10/2022-09/2027	m-PI	Development of Chemiluminescence Imaging Probes for Amyloid beta in Animal Models NIH R01 (PI: C. Ran) \$4,162,455 total costs
12/2022-11/2027	m-PI	Isoform and domain selective bromodomain inhibitor for Alzheimer's research NIH R01 (PI: C. Wang) \$4,108,208 total costs Received 7% during scientific review in October 2022.
12/2022-11/2026	Co-I	Probing NLRP3 inflammasome in Alzheimer's disease NIH R01 (PI: S. Zhang at VCU) Co-PI of a subaward (other subaward PI: C. Wang) Received 1% during scientific review in October 2022.
04/2023-03/2025	m-PI	Probing neuroinflammation in Alzheimer's with NLRP3 PET radiotracers ADDF (other PI: S. Zhang at VCU and C. Wang at MGH) \$300,000 total cost at MGH
04/2023-03/2026	Consultant	Rapid biomarker discovery via quantum-enhanced Raman spectroscopy and interpretable machine learning PI: Dr. Shengxi Huang (Rice University) \$36,000 total costs
04/2023-03/2028	PI	Amelioration of Alzheimer's neuropathology by modulating TRN and improving sleep NIH R01 (other PI: S. Shen at MGH)

\$3,719,705.00 total costs

07/2023-06/2025	Co-I	Epitope alteration for detecting auto-antibodies of beta-amyloid in serum NIH R21 (PI: C. Ran at MGH)
07/2023-06/2028	Co-I	Molecular Light for Phototherapy of Alzheimer s Disease NIH R01 (PI: C. Ran at MGH)
08/2023-07/2028	m-PI	Identifying early-stage and non-invasive biomarkers for Alzheimer's disease NSF LEAP (other PI: S. Huang at Rice University) \$400, 000 total costs at MGH

Current Unfunded Projects

Year(s)	Role	Project title and description
03/2018-	PI	Characterization of epigenetic modulators in Alzheimer's disease A study to characterize molecules targeting HDACs and BRD4 with Dr. C. Wang at MGH and Dr. R. Tanzi at MGH
07/2018-	PI	Analysis of biomaterials in Alzheimer's models A collaborative study comprised of an international group of experts from Dr. K. Liu at the Chinese Academy of Science CAS, Dr. A. Herrmann at University of Groningen and Dr. R. Tanzi at MGH
08/2018-	Co-I	Synthesis and development of molecules that regulate GSK3 β in Alzheimer's disease A study in collaboration with Dr. C. Wang at MGH and Dr. Q. Li at University of Hawaii
10/2018-	Co-I	A research consortium for Alzheimers' etiology and prevention, focused on: 1) biomarker analysis in Alzheimer's disease and other aging-related neurological disorders, 2) disease modification through tea drinking; and 3) choral singing. A study in collaboration with Dr. L. Feng at National University of Singapore NUS, C. Li at Shanghai Jiaotong University and J. Yu at Fudan University
04/2019-	m-PI	The impact of gut microbiota in chronic pain-induced Alzheimer' disease progression A study in collaboration with Dr. S. Shen and Dr. C. Wang, both of whom are from MGH.
07/2020-	m-PI	Bioprinting of a human cell-based model for pathophysiological analysis of Alzheimer's disease A study in collaboration with Dr. Y. Zhang at BWH and S. Choi
08/2020-	m-PI	Molecular neuroimaging of mitophagy in pathophysiology of aging and across Alzheimer's Disease continuum A study in collaboration with Dr. C. Wang at MGH and Dr. E. Fang at the University of Oslo
10/2020-	Co-I	Characterization of UBQLN1 proteins in Alzheimer's disease in cell and animal models

A study in collaboration with Dr. A. Saunders and Dr. D. Marenda at Drexel University

07/2021- m-PI Characterization and modulation of brain connectomics of Alzheimer's disease
A study in collaboration with Dr. C. Wang at MGH

Report of Local Teaching and Training

Teaching of Students in Courses

Year(s)	Course Title; Type of students/audience	Location; Level of effort
09/1999-06/2002	<i>Immunology</i> 40 medical and dental students	Weifang Medical College 4 hrs/wk for 12 wks
09/2002-10/2007	<i>Biology</i> (Bio 101, 102, 104, 105); 16 undergraduate students in bioscience and non-bioscience concentrations; Lectured lab for each quarter of the school year	Drexel University 6-hrs/wk for 12 wks
09/2003-11/2003	<i>Human Physiology</i> (Bio202) 18 undergraduate students concentrated on bioscience	Drexel University 6 hrs/wk for 12 wks
12/2003-03/2004	<i>Biochemistry I</i> (Bio 306) 10 graduate and 10 undergraduate students majored in bioscience	Drexel University 6 hrs/wk for 12 wks
04/2004-06/2004	<i>Data Analysis in Bioscience</i> (Bio 441) 10 graduate and 10 undergraduate students majored in bioscience	Drexel University 6 hrs/wk for 12 wks
09/2004-11/2004	<i>Microbiology</i> (Bio 221) 18 undergraduate students in concentrated in bioscience	Drexel University 6 hrs/wk for 12 wks

Research Supervisory and Training Responsibilities

Year(s)	Type of responsibility/Location	Level of effort
2001-2002	Supervision of research as a Research Assistant for graduate and undergraduate students at Department of Immunology, Weifang Medical College. Responsible for providing hands-on support on individual research projects on molecular immunology	10 hrs/wk; daily mentorship for 12 months
2003-2007	Supervision of research as a Research Assistant for undergraduate students on molecular aspects of Alzheimer's disease in Dr. Aleister Saunders' laboratory at Department of Bioscience and Biotechnology of Drexel University. Responsible for managing project initiation, experimentation,	10 hrs/wk; daily mentorship for 4 and a half years

research progress, data analysis and presentation on individual research projects.

2007-present	Supervision and mentorship of research for trainees, project collaborators, and colleagues at MGH and HMS. Responsible for management of multiple projects within the larger Genetics and Aging Research Unit of the Department of Neurology at MGH.	10 hrs/wk; daily mentorship for over 13 yrs
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Formally Supervised Trainees and Faculty

Year(s)	Name and degrees/Current position; trainee's accomplishments from the training (career stage, mentoring role, accomplishments)
2001-2002	Dr. Xingtian Liu, M.D.; Professor, Tai'an Medical University, China Career stage: Graduate student. Mentoring role: M.Sc thesis co-supervisor. Accomplishments: received a research award in the Shandong Society for Immunology.
2004-2006	Dr. Shyam Patel, M.D./Ph.D.; Assistant Professor at UMass Medical School Career stage: undergraduate research. Mentoring role: research co-supervisor. Accomplishments: trainee conducted research on cell and molecular studies on Alzheimer's cells which led to a research paper publication, followed by training in an M.D./Ph.D. program at the University of Medicine and Dentistry of New Jersey.
2006-2007	Dr. Srihari Sundararajan, M.D.; Physician at the University Radiology, NJ Imaging Center Career stage: undergraduate research. Mentoring role: research co-supervisor. Accomplishments: conducted research on cell and molecular biology of AD before trainee's education in an M.D. program at the SUNY Downstate Medical Center.
2007-2008	Dr. Jason DiVito, D.O./MBA; Physician at Memorial University Medical Center Career stage: Research Technician. Mentoring role: research supervisor Accomplishments: conducted studies on Alzheimer's cell-based studies which led to a presentation titled "Genetic and functional analysis of NT_ZNF" at the seminar series of the Genetics and Aging Research Unit of MGH, and two research paper publications, before acceptance into the graduate school at the Edward Via Virginia College of Osteopathic Medicine.
2008	Jesse Stevenson, B.Sc.; Mechanical Engineer, DCS Corp Career stage: Research Intern. Mentoring role: research supervisor Accomplishments: conducted research on cell and molecular biology of Alzheimer's disease, resulting in a published research paper
2008-2009	Dr. Andy Browne, Ph.D.; Computational Biologist, Bristol Myers Squibb Career stage: Research Technician. Mentoring role: research supervisor Accomplishments: conducted research on cell-based studies of Alzheimer's disease, which led to four published research papers, before trainee's Ph.D. education in Neuroscience at the Mount Sinai School of Medicine.
2010-2011	Dr. Kenneth M. MaKay, M.D.; Ophthalmologist, Mass Eye and Ear

Career stage: Research Technician. Mentoring role: research supervisor
Accomplishments: conducted research focused on studies of cell and molecular biology in Alzheimer's disease; presented a poster in February 2011, titled "Curcumin significantly decreases A β levels by modulating the processing of APP in the secretory pathway" in the Annual Retreat of Department of Neurology of MGH; followed by acceptance into the M.D. program in School of Medicine at the University of Pennsylvania.

- 2010-2011 Dr. Raj Hooli, Ph.D.; Geneticist, Eli Lilly, and Company
Career stage: Research Technician and Ph.D. student at Drexel University.
Mentoring role: research co-supervisor. Accomplishments: conducted a Ph.D. thesis research on cell biology studies of Alzheimer's genes, resulting in a published manuscript.
- 2009-2012 Dr. Daniel Child, M.D./Ph.D.; Physician at the University of Washington
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: conducted investigations on the biology of Alzheimer's cell models, which led to a poster presentation on February 2012, titled: "Curcumin and curcumin-like derivatives: mechanisms of action in the therapeutics of Alzheimer's disease", at the Massachusetts ADRC and Boston University 25th Annual Poster Symposium, as well as two published manuscripts, followed by acceptance into the M.D./Ph.D. program at the University of Pennsylvania.
- 2011-2012 Dr. Dipal V. Savla, M.D.; Fremont Center Pediatric Urgent Care
Career stage: undergraduate research. Mentoring role: research co-supervisor.
Accomplishments: conducted research for her undergraduate research, focused on cell and molecular biology of Alzheimer's disease, followed by acceptance into the M.D. program at the Mount Sinai School of Medicine.
- 2012-2013 Dr. Sean Miller, Ph.D.; President and CEO at Pluripotent Diagnostics
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: conducted research on the cell and molecular biology of Alzheimer's disease, which led to 4 research paper publications, including two in *Science*; a poster presentation titled "Characterization of novel gamma-secretase modulators in processing of the amyloid-beta precursor protein and in the therapeutics of Alzheimer's disease" at the 2013 MGH MIND Symposium; received a Fulbright Scholarship for his graduate school research, followed by acceptance into a Ph.D. program in Neuroscience at the Johns Hopkins University.
- 2011-2013 Scott Schulte, Software Engineer at Raytheon
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: conducted research on Alzheimer's cell and molecular studies, presented a talk titled "Decreasing amyloidogenesis in the secretory pathway through the inhibition of Golgi brefeldin A resistant guanine nucleotide exchange factor 1" at the seminar series of the Genetics and Aging Research Unit of MGH, with the work leading to a manuscript under submission.
- 2012-2016 Joe Wade, M.Sc.; Analyst at Health Dialog
Career stage: Research Intern and Research Technician. Mentoring role: research supervisor. Accomplishments: conducted research as an intern for two summers (2012-13), then as a Research Technician for two years (2014-2016), before trainee's master's education at Boston University; published two research manuscripts with another one in submission; presented a poster titled

“Characterization of novel gamma-secretase modulators as potential therapeutics of Alzheimer's disease” at the 2014 MGH Scientific Advisory Committee.

- 2013-2014 Justin Klee, President and Founder of Amylyx Pharmaceuticals Inc.,
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: conducted research on cell and molecular studies on Alzheimer's cell models, which led to a published article.
- 2014-2015 Dr. Frank Raven, Ph.D.; Postdoc, University of Michigan
Career stage: M.Sc. thesis student. Mentoring role: research supervisor.
Accomplishments: performed his master's thesis research on cell-based studies of Alzheimer's disease, fulfilling the requirement for the Maastricht University in the Netherlands and resulting in two research paper publications.
- 2015 Dr. Luke Liu, M.D.; Physician of Hematology and Oncology, University of Pittsburg
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: performed studies on cell biology of Alzheimer's disease, before match into a medical residency program
- 2015 Dr. Zhiguo Sheng, Ph.D.; Associate Professor, the Chinese Academy of Sciences
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: performed studies using cell models of Alzheimer's disease
- 2015-2016 Liam Cheng, M.D. student
Career stage: research intern. Mentoring role: research co-supervisor.
Accomplishments: performed studies and developed research techniques in imaging for the cell biology of Alzheimer's disease, before acceptance into the M.D. program.
- 2015-2016 Cathleen Huang, M.D. student
Career stage: research intern. Mentoring role: research supervisor.
Accomplishments: conducted research on cell models of Alzheimer's disease and developed research expertise in molecular biology before acceptance into the M.D. program.
- 2016 Pablo Soto, M.D. student
Career stage: research intern. Mentoring role: research supervisor.
Accomplishments: conducted research on Alzheimer's disease using cell models before acceptance into the M.D. program.
- 2016-2018 Nolan Shen, M.D. student,
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: performed studies on cell and molecular biology of Alzheimer's disease, presented a poster titled “Development of gamma-secretase modulators as potential therapeutics of Alzheimer's disease” at the poster session of the MGH Scientific Advisory Committee, Annual Meeting, with the work resulting in 5 research paper publications, before acceptance into the M.D. program.
- 2016-2017 Dr. Yu Wan, M.D., Ph.D.; Associate Professor of Neurology, Qingdao Municipal Hospital and Qingdao Ocean University
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: performed studies for her postdoc research on cell and molecular biology of Alzheimer's disease, presented a talk titled “Characterizing

the potential roles of curcumin like compounds in Alzheimer's disease" at the seminar series of the Genetics and Aging Research Unit of MGH, with the work resulting in 4 research paper publications.

- 2017 Kenneth Shinozuka, Founder, CEO at SensaRx, LLC.
Career stage: research intern during the undergraduate study at the Harvard College. Mentoring role: research supervisor.
Accomplishments: performed research on curcumin-related cell and molecular studies on Alzheimer's cell models, which resulted in a research paper publication.
- 2017 Linda Lee, M.D. student
Career stage: research intern. Mentoring role: research supervisor.
Accomplishments: performed research on cell-based studies of Alzheimer's disease, before acceptance into the M.D. program.
- 2018 Dr. Juanjuan Su, Ph.D.; Biophysicist at The Chinese Academy of Sciences
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: performed studies on biomedical material-based investigation on Alzheimer's disease, resulting in a research paper publication.
- 2018-2019 Dr. Yang Feng, Ph.D.; Biochemist, The Chinese Academy of Science
Career stage: Ph.D. thesis student. Mentoring role: research supervisor.
Accomplishments: performed studies on the effects of new biomedical materials on Alzheimer's model cells, presented a talk titled "Developing and characterizing novel biomaterials for Alzheimer's disease" at the seminar series of the Genetics and Aging Research Unit of MGH, with the work resulting in a research paper publication.
- 2018-2021 Dr. Yingxia Liang, M.D., Ph.D.; Professor at Weifang Medical Univ.
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: performed postdoctoral research, with a focus on cell and animal-based studies of Alzheimer's disease, which led to 8 published research papers and 2 manuscripts in preparation.
- 2018-2021 Sherri Zhen; Research Associate at Boston Univ.
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: performed studies on molecular and cellular biology of Alzheimer's disease, with the work resulting in a published research paper and 2 research papers in preparation
- 2019-2021 Siyi Zhang; Faculty at the China Medical University
Career stage: Ph.D. thesis student; Mentoring role: research supervisor.
Accomplishments: performed research on cell-based studies of Alzheimer's disease, presented a talk titled "Epigenetic regulation through BRD4 for Alzheimer's disease" at the seminar series of the Genetics and Aging Research Unit of MGH, with the work resulting in a published research paper and the other one in preparation.
- 2020-2022 Dr. Dan Lei, M.D., Ph.D.; Physician Scientist at XiangYa Hospital
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: performed postdoc research on cell-based studies of Alzheimer's disease; presented a talk titled "RIPK1-related neuroinflammation in

Alzheimer's disease " at the seminar series of the Genetics and Aging Research Unit of MGH, with the work resulting in a research paper in preparation.

- 2019-present Dr. Yulong Xu, Ph.D.; Instructor at MGH and HMS
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor (co-mentored with Dr. C. Wang).
Accomplishments: performed postdoc research on developing neuroimaging probes for Alzheimer's disease, including a new probe for gamma-secretase, won a "poster prize" at the 2019 Mass General Neuroscience 2nd annual symposium poster presentation, with the work resulting in 3 research papers in publication and the other one in preparation.
- 2021-present Ashley Comm; Research Technician at MGH
Career stage: Research Technician. Mentoring role: research supervisor.
Accomplishments: engaged in assistance of bench-based experiments and analytic studies in understanding and treating Alzheimer's disease
- 2021-present Dr. Prasenjit Mondal, Ph.D.; Postdoctoral Fellow at MGH and HMS
Career stage: Postdoc Research Fellow. Mentoring role: research supervisor.
Accomplishments: recently started in Dr. Zhang's group and performed postdoc research with the focus on evaluating the effects of promising therapeutics of Alzheimer's disease that target γ -secretase on preclinical disease models.
- 2021-2022 Claire Suen, Harvard College
Research intern during the undergraduate study at the Harvard College.
Mentoring role: research supervisor.
Accomplishments: performed research on cell and molecular studies on Alzheimer's cell models, which resulted in a research presentation anticipated by the end of internship.
- 2021 Ethan Wong, Boston Univ.
Research intern during the undergraduate study.
Mentoring role: research supervisor.
Accomplishments: performed research on cell and molecular studies on Alzheimer's cell models.
- 2022 Shreya Parikh, Boston Univ.
Research intern during the undergraduate study.
Mentoring role: research supervisor.
Accomplishments: developed expertise by training for research on cell and molecular studies on Alzheimer's cell models.
- 2022 Anya Chen, Belmont High School
Research summer intern
Mentoring role: research supervisor.
Accomplishments: developed research expertise knowledge and interest by literature reading, presentation, and hands on experience for research on cell and molecular studies on Alzheimer's disease

Local Invited Teaching and Presentations

Year(s)	Title of presentation or name of course/ Type of presentation/role(s); Location (Note if presentations were sponsored by outside entities; note if presentations were the result of selected abstracts) <i>No presentations below were sponsored by 3rd parties/outside entities.</i>
07/2007	An AICD based functional assay to discover novel APP processing regulators; a talk at the Genetics and Aging Research Unit at MGH
05/2008	Genetic and functional analysis of a novel genetic variant underlying the pathogenesis of Alzheimer's disease; a talk at the Genetics and Aging Research Unit at MGH
10/2009	Genetic variants identified in Alzheimer's disease genome-wide association studies: functional roles on APP processing and disease pathogenesis; a talk at the Genetics and Aging Research Unit at MGH
08/2010	Functional characterization of APP processing modulators - insights into Alzheimer's disease pathogenesis and therapeutics; a talk at the seminar series of MIND at MGH
10/2014	The amyloid- β hypothesis and the road to clinical therapies for Alzheimer's disease; a talk at the Genetics and Aging Research Unit at MGH
12/2014	The amyloid- β hypothesis and the roadmap to clinical therapies for Alzheimer's disease; a talk at the MassGeneral Institute for Neurodegenerative Disease (MIND) seminar series at MGH
10/2017	Curcumin analogs for the potentials of Alzheimer's disease; a talk at the Mind-body conference and Tibetan Medicine at the Joseph Martin Conference Center of HMS
04/2018	Elucidating and attenuating Alzheimer's pathology for prevention and treatment of disease; a talk at the Genetics and Aging Research Unit at MGH
11/2018	Translating Alzheimer's disease molecular mechanisms into effective therapeutics; a talk at the seminar series of the MassGeneral Institute for Neurodegenerative Disease (MIND) at MGH
10/2018	Systems approach of Alzheimer's disease: translating molecular mechanisms into useful therapeutics, a talk at the Conference on the Forefront of Complementary and Integrative Medicine, Joseph Martin Conference Center at HMS
05/2019	A multi-domain cognitive training program for prevention and intervention of dementia toward healthy aging; a talk at the Martino's Center for Biomedical Imaging at MGH
09/2019	Probing β -amyloid associated impairments of sleep physiology in Alzheimer's disease using novel γ -secretase modulators; a talk for the MGH SPARC Award at the 2 nd annual MGH Neuroscience symposium
10/2019	Identifying new molecular mechanisms of Alzheimer's disease - insight for understanding pathogenesis and intervention of disease; a talk at the Martino's Center for Biomedical Imaging at MGH

05/2020	Zooming in on abeta generation and clearance mechanisms for developing and characterizing Alzheimer's interventions; a talk at the seminar series of the MassGeneral Institute for Neurodegenerative Disease (MIND) at MGH
05/2020	Therapeutic Development for Alzheimer's Disease - from disease pathogenesis to translational approaches; a talk at the Department of Medicine, Brigham and Women's Hospital
09/2020	Probing A β -associated impairments of sleep physiology in Alzheimer's disease with novel γ -secretase modulators; a talk at the McCance Center for Brain Health, MGH
09/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk for the Science Showcase, Faculty of Arts and Sciences, Harvard University
12/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk for the Science Showcase, Faculty of Arts and Sciences, Harvard University
04/2021	Modulation of γ -secretase for Alzheimer's disease and A β -associated sleep impairments; MGH McCance Center for Brain Health
04/2021	Modulation of γ -secretase for Alzheimer's disease and A β -associated sleep impairments; SPARC Award Talk to the MGH Neuroscience Leadership Council
04/2021	Modulation of γ -secretase for Alzheimer's disease intervention: imaging opportunities and beyond; MGH Martino's Center, Clinical Research Program
07/2021	Modulation of γ -secretase for Alzheimer's disease; a talk for MGH MIND Symposium for Innovative Molecular, Physiological and Therapeutic Approaches to Neurodegenerative Disease
10/2021	Modulation and detection of microglia-related RIPK1 and neuroinflammation in pain; a talk for MGH Neurology Research Retreat
04/2022	Translational Medicine of Alzheimer's disease; a talk at the MGH_Martinos Spring 2022 Clinical Research Skill Enhancement Public Program Lecture 6
09/2022	Prevention and treatment of Alzheimer's disease through A β 42-reducing γ -secretase modulators and exercise: Insights on Translational Medicine, MGH Martinos Synapse program for research development.
10/2022	Prevention and treatment of Alzheimer's disease through γ -Secretase modulators, MGH Neuroscience Leadership Council
01/2023	Alzheimer's disease: molecular pathogenesis and imaging biomarker discovery, MGH Martinos Synapse program for research development, sponsored by the American Chinese Medical Exchange Society (ACMES)
Year(s)	Title of presentation or name of course/Type of presentation/role(s); Location <i>No presentations below were sponsored by 3rd parties/outside entities.</i>

07/2015	Molecular mechanisms and translational medicine on Alzheimer's disease – insights into its prevention and therapeutics; 2015 Multicultural Coalition on Aging Elders' Conference on Alzheimer's Disease at Tufts University; an invited talk in Chinese at a workshop through MADRC and Greater Boston Chinese Golden Age Center.
10/2017	Curcumin analogs for the potentials of Alzheimer's disease; a talk for the Hong Kong Youth Life Science Academy during their visit to Boston
03/2018	Elucidating, attenuating, and detecting Alzheimer's pathology for prevention and treatment of disease; a talk at the Mass Medical International in Boston
06/2018	An updated view for translating molecular mechanisms underlying Alzheimer's disease into effective therapeutics; a talk at the Translational Strategies in CNS meeting in Boston by the World Preclinical Congress of the Cambridge Healthtech Institute
09/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the Discovery-On-Target (DOT) meeting in Boston organized by the Cambridge Innovation Institution
06/2021	Alzheimer's disease – etiology and management; a talk for The Greater Boston Chinese Cultural Association (GBCCA)

National Invited Presentations

Year(s)	Title of presentation or name of course/Type of presentation/role(s); Location
	<i>No presentations below were sponsored by 3rd parties/outside entities.</i>
07/2007	Identifying novel modulators of APP processing in Alzheimer's disease; a talk at the Department of Molecular Biology, School of Osteopathic Medicine at University of Medicine and Dentistry of New Jersey
07/2007	An AICD based functional assay to discover novel APP processing regulators; a talk at the Department of Neurology, Mount Sinai School of Medicine
11/2010	Functional characterization of <i>ATXN1</i> in β -secretase processing of APP; a talk at the Mini-symposia, Society for Neuroscience, 38 th conference, San Diego (a selected abstract for the talk)
11/2013	Development of a successful research career; a talk as a guest speaker at the Drexel University Graduate Student Seminar
06/2018	Novel insights for translating molecular mechanisms underlying Alzheimer's disease into effective therapeutics; a talk at the Translational Strategies in CNS meeting by the World Preclinical Congress
06/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the Department of Molecular Biosciences and Bioengineering, University of Hawai'i at Mānoa
07/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the College of Pharmacy, University of Minnesota

07/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the Center for Craniofacial Molecular Biology; University of South California
08/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the Department of Neuroscience, Mayo Clinic
09/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the School of Pharmacy, Virginia Commonwealth University
10/2020	Alzheimer's disease – pathogenesis and therapeutic intervention; a talk at the Department of Biology, Drexel University
10/2021	Modulation of γ -secretase for Alzheimer's disease; an invited talk at the Barrow Neurological Institute

International Invited Presentations

Year(s)	Title of presentation or name of course/Type of presentation/role(s); Location
	<i>No presentations below were sponsored by 3rd parties/outside entities.</i>
04/2011	Characterization of novel APP processing modulators – insights into the underlying mechanisms of Alzheimer's disease and relevant therapeutic strategies; a talk at the School of Basic Medicine, Binzhou Medical College, YanTai, China
04/2011	Characterization of novel APP processing modulators for Alzheimer's disease; a talk at the Graduate School, Weifang Medical College, Weifang, China
04/2011	Characterization of curcumin in processing of APP; a talk at the 2011 Conference on Alzheimer's disease and related neurodegenerative disorders, Jinan, China
04/2011	Characterization of novel APP processing modulators; a talk at the Department of Biochemistry, Beijing Institute of Basic Medical Sciences, Academy of Military Medical Sciences, Beijing, China
04/2012	Characterization of novel APP metabolism modulators - insights into the pathogenesis and therapeutics of Alzheimer's disease; a talk at the Institute of Brain Science, National Yang-Ming University, Taiwan
04/2012	Characterization of novel APP metabolism modulators - insights into the pathogenesis and therapeutics of Alzheimer's disease; a talk at the Department of Neurology, Taipei Medical University Shuang-Ho Hospital, Taiwan
05/2012	Natural products that modulate APP metabolism; a talk at the Institute of Microbiology and Biochemistry, National Taiwan University, Taiwan
05/2012	Characterization of genes encoding APP metabolism modulators - insights into the pathogenesis and therapeutics of Alzheimer's disease; a talk at the Department of Public Health, National Taiwan University, Taiwan
04/2014	From bench to bedside: molecular translational medicine focused on amyloid hypothesis to treat Alzheimer's disease; a talk at the Department of Neurology, Shandong Provincial Hospital, Jinan, China

- 04/2014 An integrative view of mechanisms underlying the pathology of Alzheimer's disease and their potentials in clinical application; a talk at the Department of Neurology, Capital Medical University at Xuanwu Hospital, Beijing, China
- 11/2014 The amyloid- β hypothesis and the road to clinical therapies for Alzheimer's disease; a talk at the Department of Biochemistry, Binzhou Medical College, Yantai, China
- 11/2014 The amyloid- β hypothesis and the road to clinical therapies for Alzheimer's disease; a talk at the Department of Neurology, Qingdao Municipal Hospital /Qingdao Ocean University, Qingdao, China
- 11/2014 The amyloid- β hypothesis and the road to clinical therapies for Alzheimer's disease; a talk at the School of Medicine, National University of Singapore, Singapore
- 11/2014 The amyloid- β hypothesis and the road to clinical therapies for Alzheimer's disease; a talk at the Department of Neurology, Shuanghe Hospital and the Taipei Medical University, Taiwan
- 08/2016 Translating mechanisms underlying Alzheimer's disease into effective therapeutics; a talk at the Institute for Biomedical Sciences, Weifang Medical College, Weifang, China
- 08/2016 Perspectives of research on Alzheimer's disease for future physician scientists; a talk at the Graduate School at Weifang Medical College, Weifang, China
- 09/2016 Translating mechanisms underlying Alzheimer's disease into effective therapeutics; a talk at the Research Summit in celebration of 100th anniversary of Qingdao Municipal Hospital/Qingdao Ocean University, Qingdao, China
- 09/2016 Translating mechanisms underlying Alzheimer's disease into effective therapeutics; a talk at the Institute of Biomedical Sciences, BinZhou Medical College, Yantai, China
- 05/2017 Developing small molecule-based therapeutics for Alzheimer's disease; a talk at the Chinese Medical Association 5th Alzheimer disease conference in Beijing, China
- 07/2017 Developing small molecule-based therapeutics for Alzheimer's disease; a talk at the Department of Neurology, Taipei Medical University, Taipei, Taiwan
- 07/2017 Characterizing mechanisms underlying Alzheimer's disease and translating into potential therapeutics; a talk at the Life and Science Institute, Qinghua University, XinZhu, Taiwan
- 10/2018 Translating molecular mechanisms into useful therapeutics of Alzheimer's disease; a talk at the Harvard Center Shanghai conference on brain health, with an emphasis on Alzheimer's' disease, Shanghai, China (a presentation with a selected abstract)
- 10/2018 Translating molecular mechanisms into useful therapeutics of Alzheimer's disease; a talk at the Graduate School, Weifang Medical College, Weifang, China

10/2018	Translating molecular mechanisms into useful therapeutics of Alzheimer's disease; a talk at the Department of Neurology, Qingdao Municipal Hospital and Qingdao Ocean University, Qingdao, China
07/2019	Translating Alzheimer's disease molecular mechanisms into effective therapeutics; a talk at the School of Medicine, Weifang Medical University, Weifang, China
07/2019	From Alzheimer's disease molecular mechanisms to effective therapeutics; a talk at the Department of Biochemistry, Binzhou Medical University, Yantai, China
07/2019	Translating Alzheimer's disease molecular mechanisms into effective therapeutics; a talk at the School of Medicine, National University of Singapore, Singapore
07/2019	Translating Alzheimer's disease molecular mechanisms into effective therapeutics; a talk at the Department of Neurology, Hua Shan Hospital and Fudan University, Shanghai, China
07/2019	Translating Alzheimer's disease molecular mechanisms into effective therapeutics; Shanghai Mental Health Center, Shanghai Jiao Tong University, Shanghai, China
08/2020	Alzheimer's disease – pathogenic mechanisms and therapeutic intervention; a talk at the UK Dementia Research Institute, Imperial College London, UK
09/2020	Alzheimer's disease – pathogenesis and therapeutic intervention; a talk at the Department of Psychiatry, University of Oxford, UK
10/2020	Alzheimer's disease – pathogenesis and therapeutic intervention; a talk at the Department of Public Health and Caring Sciences, Uppsala University, Sweden
10/2020	Alzheimer's disease – pathogenesis and therapeutic intervention; a talk at the Department of Biochemistry, Binzhou Medical University, Yantai, China
02/2021	Alzheimer's disease – progress in translational medicine; a talk at the International Biotech Symposium 2021, Bangladesh
08/2021	Modulation of γ -secretase for Alzheimer's disease; an invited talk at the 2nd Huashan Hospital, Cognition & Brain Disorders International Conference, Fudan University, Shanghai, China
08/2021	Modulation of γ -secretase for Alzheimer's disease; an invited talk at the International Neuroscience and Neurological Conference, Jinan, Shandong, China

Report of Education of Patients and Service to the Community

Years	Organizations/institutions and role
Spring 2003-06	Drexel University: Served as a coordinator in the Alternative Spring Break sponsored by the Drexel University, for activities in fund-raising, community work and research showcase during community services at Shiprock, NM (2003, 2004 and 2006) and Immokalee, FL (2005)
08/2003-07/2004	Drexel University: Served as the Vice President for the Chinese Students and Scholars Association (CSSA) of Drexel University

- 2010 Timilty Middle School at Roxbury: Served as Project Judge for scientific poster session organized by the MGH Outreach Program for Community Health Improvement
- 2013-present MGH: Served as project manager and provided service for the research community through the MesoScale Discovery MSD system for protein analysis, and supported projects on identifying and characterizing biomarkers underlying diseases for departments and institutions (and number of projects) listed below:
- 1) Department of Neurology at MGH (8 projects)
 - 2) Department of Radiology at MGH (3 projects)
 - 3) Department of Surgery at MGH (1 project)
 - 4) SBTI consortium, or the Self-directed biological transformation initiative from a collaborative group for biomarkers of research consortium including several institutions (1 project)
 - 5) Departments of Neurobiology and Neurology, Center for Molecular Neurobiology at the University of Chicago (4 projects)
 - 6) Department of Neurology at Tufts University (1 project)
 - 7) Department of Obstetrics, Gynecology, and Reproductive Biology, and Vincent Center for Reproductive Biology at MGH (1 project)
 - 8) Department of Neurology, Mayo Clinic (1 project)
 - 9) School of Pharmacy, Virginia Commonwealth University (1 project)
- 2018 Served as a faculty member and guest host for the MGH and HMS visit of Dr. Y. Huang from the Tianqiao and Chrissy Chen Institute (TCCI) of Shanghai.
- 2019 Served as a faculty member and guest host for the MGH visit of colleagues from the Shanghai Institute of Visual Art (SIVA).
- 2019 Served as a faculty member and seminar host at the MIND seminar for Drs. Daniel Trombly and Christopher Dowdy from the Biocytogen for a talk on animal model development by genetic engineering and maintenance
- 2021 Served as a faculty member and seminar cohost at MIND for Dr. Liu Shi from the Oxford Univ. for a talk on biomarkers of Alzheimer's' disease

Report of Technological and Other Scientific Innovations

Patent, if any, pending or awarded /If described in print/on web, provide citation. Describe the influence or potential influence of the innovation on research or clinical care, including how the material is used locally (at HMS), regionally, nationally or internationally; if developed as a member of a committee, describe your contribution (1-2 sentences)

1. "Receptor-interacting serine/threonine-protein kinase 1 imaging probes" Wang C, **Zhang C**, Tanzi RE and Lan Y. Partners invention disclosure submitted in Feb 2020 (MGH Invention #:

2020-230). In the disclosure, we have done preclinical imaging studies in animal and we are working on further development, expecting to have IND and IRB ready in 2022 for the first-in-human imaging study of RIPK1. It is anticipated to be a useful tool for research and clinical application to detect neuroinflammation. Now it is developed at MGH and once validated, it will be available for broader applications to regional, national, and international levels. I contributed to conceptualization and experimental design.

2. "Brain Penetrant SIRT1 Positron Emission Tomography Ligands" Wang C, Xu Y, **Zhang C**, and Tanzi RE. Partners Invention Disclosure (ID) submitted in April 2020 (MGH Invention #: 2020-359). In this disclosure, we provided evidence showing SIRT1 molecular imaging in Alzheimer's animal brains and nonhuman primate brains with high specificity. Currently, we are working on further development, with the goal for the first-in-human imaging study. It is anticipated to be a useful tool for research and clinical application to detect aging-related neurodegenerative disorders. Now it is developed at MGH and once successfully validated, it will be available for broader applications to regional, national, and international levels. I contributed to conceptualization and experimental design.
3. "Depletion of Microglia by Pexidartinib Ameliorates Pain-related Behavioral Impairments in a Pain Mouse Model". **Zhang C**, Yang L, Gomm A, Tanzi RE, Wang C, and Shen S. Partners Invention Disclosure (ID) submitted in May 2022 (MGH Invention #: 2022-360). In this disclosure, we provided evidence showing a potential pain medicine in a pain model. Currently, we are working on further development, with the goal for a human trial for pain management. Now it is further developed at MGH and once successfully validated, it will be available for broader applications to regional, national, and international levels. I am Lead Inventor (Licensing Manager: David Silva) and contributed to conceptualization and experimental design.
4. "Histone Deacetylases Inhibitors". Wang C, **Zhang C**, and Tanzi RT. Partners Invention Disclosure submitted in December 2022 (MGH Invention #: 2022-270). In this disclosure, we provided evidence showing molecules for potential application in AD. Currently, we are working on further development, with the goal for a human trial. Once it is further developed and successfully validated, it will be available for broader applications to regional, national, and international levels. I contributed to conceptualization and experimental design.

[Report of Scholarship](#)

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Publications that are not peer-reviewed in print or other media (Commentaries, Book Chapters and Monographs, and Conference Consensus)

84. **Zhang C**, Li Z, and Feng Y. Clinical immunology and immunodeficiency diseases, Oct 2001(10) 41-89 (a book chapter in a textbook for medical students) (*Book Chapter*)
85. **Zhang, C**. Identifying genes that encode APP metabolism modulators – Hunting for Alzheimer's disease genes. 2010 (a monograph published by LAP Lambert Academic Publishing AG & Co. KG) (*Monograph*)

86. Yu JT, **Zhang C**. Pathogenesis and therapeutic strategies in Alzheimer's disease: From Brain to Periphery. **Neurotox Res**. 2016 Feb;29(2):197-200. PMID: 26597964 (*Commentary*)
87. Frautschy S, Schubert D, Maher P, Ran C, Moore A, Bacskai BJ, Koronyo M, Koronyo Y, Martins R, **Zhang C**, Tanzi RE, Cole G and Heger M. Some chemists stumped by positive curcumin trials. **Nature** 2017. (*Correspondence*).
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89. **Zhang C**, Lu Y, Feng L, Li C, Barako T, Liu K, Zhou Q, Cheng S, Pan A, Xue L, Zhang S, Lee D, Li Q, Li L, Yu JT, Sisodia S, and Ran C, Proceedings of the Harvard-Shanghai conference on brain health - a special meeting for understanding and intervention of Alzheimer's disease. **Journal of Advances in Health** 2019; 1 (1)1-8 (*Conference Consensus*)
90. **Zhang C**. Microbial involvement in Alzheimer's disease, an invited book chapter for the book titled: **Microbiome and Brain Health**. 2020 (*Book Chapter*)

Thesis

91. **Zhang, C**. Inhibition of hepatitis B virus expression via antisense X gene transported by lactosaminated L-lysine in HepG2.2.15 cells. Weifang Medical College, China, 2002 (*M.Sc. thesis*)
92. **Zhang, C**. Identifying genes that encode APP metabolism modulators on chromosome 9q22., Drexel University, USA, 2007 (*Ph.D. thesis*)

Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings (during the last three years)

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| 07/2019 | Primary age-related tauopathy: biological definition and longitudinal clinical outcome; a poster presented at the Alzheimer's Association International Conference (AAIC) |
| 09/2019 | Probing β -amyloid associated impairments of sleep physiology in Alzheimer's disease using novel γ -secretase modulators; a poster presented at the MGH 2 nd annual neuroscience symposium |
| 09/2019 | A herbal medicine decreases Alzheimer's pathology in a human 3-D neural culture and enhances microglial amyloid- β clearance; a poster at the 2 nd annual MGH neuroscience symposium |
| 10/2019 | A herbal medicine decreases Alzheimer's pathology in a human 3-D neural culture and enhances microglial amyloid- β clearance; a poster presented at the MGH Neurology annual retreat |
| 11/2019 | A herbal medicine decreases Alzheimer's pathology by upregulating microglial amyloid- β clearance both in vitro and in vivo; a poster presented at the MADRC's Growdon Symposium |
| 05/2022 | Regulation of Epigenetic BET Proteins on Alzheimer's Disease in Preclinical Models, a poster selected for presentation at the 2022 AAIC conference, San Diego |

- 05/2022 Novel HDAC11 Inhibitors for Alzheimer's Disease Treatment in Preclinical Models, a poster selected for presentation at the 2022 AAIC conference, San Diego
- 05/2022 Regulation of Amyloidosis and Neuroinflammation by the Gut Microbiome, a poster for which I am a co-author selected for presentation at the 2022 AAIC conference, San Diego
- 06/2022 Targeting neuroinflammation in X-linked dystonia parkinsonism; an abstract submitted for presentation to SFN
- 01/2023 Molecular imaging of NAD⁺-dependent deacetylase SIRT1 in the brain, an abstract submitted to the Society of Nuclear Medicine and Molecular Imaging SNMMI annual meeting, Chicago
- 03/2023 Targeting inflammation as a therapeutic strategy for X-linked dystonia parkinsonism; an abstract presented at the MGH SAC meeting.

Narrative Report

A dedicated biomedical investigator with extensive research experience and particularly a neuroscientist with a track record of proven success in the basic, preclinical and clinical research, I am leading a translational neuroscience program focusing on mechanistic insights and biomarker discovery, with a goal committed to discovering novel and promising molecules to not only better understand the etiology of major clinical disorders, including Alzheimer's disease and pain, but also advance drug development enabling disease intervention in clinic.

For my research career, I have been focused on the studies using RNAi in combination with other biomedical technologies. Notably, after receiving my medical training, I have spent the past 2 decades dedicated on biomedical research, focusing on Alzheimer's disease (AD) and pain. My main research accomplishment is the establishment of a translational neuroscience program that led to drug discovery in three key direction. **1)** I characterized promising molecules by mechanistic studies may help advance them from preclinical to clinical testing, e.g. the γ -secretase modulators (GSMs). Through a mechanism in ameliorating AD-related neuropathology and reducing $A\beta_{(42:40)}$ ratios, our GSMs have been developed and characterized over the past years, which has resulted in the identification of a lead compound that is the focus for an Investigational New Drug (IND) application of an AD trial anticipated in 2023. In support of the GSM studies, I led a multidisciplinary team at MGH and reported, for the first time, a GSM-based molecular imaging probe for γ -secretase. It has validated target engagement and has provided a useful tool to detect γ -secretase in brains of animals and potentially humans. In addition to the GSM-based $A\beta$ reduction strategy, I am performing other lines of studies, including curcumin and its analogs and the herbal medicine HLXL, both of which modulate neuroinflammation to reduce AD neuropathology in preclinical models. Presently, I am studying preclinical stage molecules with clinical potentials, including inhibitors of NLRP3, RIPK1, HDAC6 and HDAC11. **2)** I investigated FDA-approved non-AD drugs, including bexarotene and cromolyn, repurposed for AD using preclinical models with a goal to support them as FDA-approved non-AD drugs toward clinical trials of AD. **3)** I led the discovery of PLX-3397, an FDA-approved medicine for cancer and a CSF-1R inhibitor, which may ameliorate pain in an animals model, with a patent prepared supporting a potential clinical trial using PLX-3397 in pain.

Moreover, I led and advised on dozens of research projects studying the complex etiology of AD, focusing on characterizing AD-related pathogenesis and $A\beta$ metabolism, with the studies covering over multiple aspects which included genetics, biomaterial engineering, as well as plasma and brain biomarker discovery. For AD genetics, I developed a high-throughput assay to identify AD candidate genes and reported the loss-of-function mechanism of an AD candidate gene, *ataxin-1*, using AD cell models. For biomaterials, I utilized an extracellular matrix-related protein, elastin, and reported novel mechanisms by which elastin increases $A\beta$ levels in AD models. For plasma biomarker in AD, I reported that plasma IL-12/IFN- γ axis predicts cognitive trajectories in cognitively unimpaired older

adults. For biomarkers in AD brains, I reported a new SIRT1 probe for detecting SIRT1 in animal brains. To further understand common mechanisms in aging, I reported that neuroinflammatory responses and gut microbiota are common and key players for AD pathology and pain-related neuropathy. Collectively, my findings have elucidated molecular mechanisms of AD, broadened the understanding of disease etiology and advanced the drug development of AD.

I have published over 80 articles, including 65 research papers, 20 of which are 1st and last-authored papers, in addition to 15 reviews or non-peer-reviewed articles. For funding, I have been continuously applying for and receiving federal and private funding with over \$6 million total cost funded grants and over \$10 million total cost pending grants, with my role as a PI/m-PI. I currently have 8 active grants, 5 as a PI/m-PI, and 3 as a co-investigator. I have 3 grants that have been well reviewed at study sections, including an R01 and an U01 both of which are within funding lines. For talks, I have given 71 invited lectures, which include 25 local, 11 national and 35 international lectures.

In addition to my research findings as my main expertise of excellence, my other supporting activities include establishing a multiplex protein analysis system that has enhanced research projects in collaboration inside and outside of MGH/HMS. For mentorship, I have trained and inspired undergraduate or summer intern students who became full-time MGH technologists before moving onto graduate schools for M.D. and/or Ph.D. education, as well as Postdoc Fellows who became physician scientists or investigators. Many of my trainees have received M.D. and/or Ph.D. degrees and are becoming assets in their positions who are providing service for patients or investigating human pathophysiology or improving drug development.

In summary, my research program has substantially advanced the field's understanding of the pathogenesis of AD and has advanced the potential of successful therapeutic development. In addition, I have established myself as a recognized authority in my field, a local academic resource, and an important asset to the community.