CURRICULUM VITAE

ZHEN ZHAO

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PERSONAL INFORMATION:

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University of Southern California (USC)
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EDUCATION AND PROFESSIONAL APPOINTMENTS

EDUCATION:

Year	*Degree, Field, Institution, City*
2002-2009	Ph.D., Neuroscience, University of Southern California, Los Angeles, CA
1997-2001	B.S., Biological Sciences, Fudan University, Shanghai, China
1994-1997	Haiyan High School, Jiaxing, China

POST-GRADUATE TRAINING:

Year-Year	*Training Type, Field, Mentor, Department, Institution, City*
2012-2014	Post-doctoral training, Neurodegenerative diseases, Dr. Berislav Zlokovic, Department of Physiology and Biophysics, Zilkha Neurogenetic Institute, Keck School of Medicine, University of Southern California, Los Angeles, CA
2010-2012	Post-doctoral training, Microbiology and Immunology, Drs. Chengyu Liang, Department of Microbiology and Immunology, Norris Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA

ACADEMIC APPOINTMENTS:

Year-Year	*Appointment*	*Department, Institution, City, Country*
2017-present	Assistant Professor	Department of Physiology and Neuroscience, Keck School of Medicine, USC, Los Angeles, CA
2014-2017	Research Assistant Professor	Department of Physiology and Biophysics, Keck School of Medicine, USC, Los Angeles, CA

ADMINISTRATIVE APPOINTMENTS:

Year-Year	*Description*	*Institution, City, State, Country*
2023-present	Associate Director Neuromedicne PhD Program	Keck School of Medicine, USC, Los Angeles, CA
2020-present	Director, Cell Engineering & Regeneration Core	Keck School of Medicine, USC, Los Angeles, CA

HONORS, AWARDS:

Year	*Description*	*Awarding agency, address, city*
2023	Faculty Leadership Fellow	USC Center for excellence in teaching
2023	Investigator	IDSA Foundation
2020-2023	Top 1% Highly Cited Researchers in cross-field	Clarivate Analytics
2019	Investigator	BrightFocus Foundation
2016	Investigator	Whittier Foundation
2015	New Investigator	Alzheimer's Association
2002-2003	Provost's Scholarship	University of Southern California
1998-2001	People's Scholarship; Outstanding Students Leader; Excellent Graduate	Fudan University, Shanghai, China

TEACHING

DIDACTIC TEACHING:

University of Southern California

Year-Year	*Course Name*	*Units/Hrs*	*Role*
2021-Present	Medical Physiology II (INTD-573)	4 units	Lecturer
2019-2021	Micro-Seminar: Alzheimer's disease: challenges and opportunities	1 unit	Course director
2018-2023	Advanced Neuroscience (NEUR524)	4 units	Lecturer, course director in 2019
2004-2005	General Biology: Cell Biology and Physiology; Molecular Biology	4 units	Teaching Assistant

UNDERGRADUATE, GRADUATE AND MEDICAL STUDENT (OR OTHER) MENTORSHIP:

Year-Year	*Trainee Name*	*Trainee Type*	*Dissertation/Thesis/Project Title*
2023-Present	Yuan-Pu Chiu	Ph.D student	Understanding the vascular dysfunctions in MODEL-AD mouse models
2023-Present	Cristelle Hugo	Ph.D student	Understanding the vascular dysfunction in the MODEL-AD animal models.
2022-Present	Shangzhou Xia	Ph.D student	TMEM252-dependent microvascular dysfunction in mTBI and Alzheimer's disease
2022-Present	Jeff Deng	Undergraduate	The link between traumatic brain injury and dementia
2022-Present	Stephan Nishi	Undergraduate	The role GPR4 G-protein coupled receptor in brain vascular functions
2020-2022	Xinyan Liang	Ph.D student	The role of AD PLCG2risk gene in microglial dysregulation in TBI and Alzheimer's disease
2021-2022	Thanhtrang Trinh	Undergraduate	Microglia and Alzheimer's Disease Genetics with Coding Variant PLCG2
2021-2022	Adam Ludwig	Undergraduate	Modeling AD risk gene PLCG2 using iPSC-derived microglia
2019-2020	Haijian Wu	Medical student (Exchange)	Mer regulates microglia polarization and alleviates neuroinflammation following traumatic brain injury
2019-2020	Shupeng Dong	Ph.D student (Exchange)	The role Zika NS4A and 4B function in inhibiting neurogenesis and microcephaly
2020	Minwoo Tristen Kim	Undergraduate	Single cell RNAseq analysis of G-protein coupled receptor at the blood-brain barrier
2019-2021	Bangyan Zhang	Undergraduate	The molecular mechanism of PICALM dependent endosomal trafficking in AD
2018-2020	Brock Pluimer	Ph.D student	Genetic link between PICALM and AopE in Alzheimer's disease
2019	Narek Kltchian	Undergraduate	The role of AD ABI3 risk gene in microglial dysregulation in in Alzheimer's disease

2019	Darren Tsai	Undergraduate	Modeling traumatic brain injury in mice with controlled cortical impact
2016	Zhifei Luo*	Master student	Zika virus NS4A-NS4B inhibition of Akt-mTOR pathway contributes to deficient neurogenesis in human neural stem cells
2014-2015	Pan Kong*	Ph.D student	Role of PICALM in receptor mediated transport across the blood brain barrier
2014-2015	Sanket Rege*	Master student	A transgenic mouse model with overexpression of human RAGE
2013-2014	Gabriel Si*	Master student	Pericyte deficiency leads to white matter demyelination and axonal degeneration

GRADUATE STUDENT THESIS, EXAM AND DISSERTATION COMMITTEES:

Year-Year	*Trainee Name*	*Committee Type*	*Student Department*
2023-present	Cristelle Hugo	Ph.D Thesis	PIBBS
2023-present	Pao-Fen Ko	Master Thesis	BMM
2023-present	Kaixin Su	Ph.D Thesis	PIBBS
2023-present	Yuanpu Chiu	Ph.D Thesis	PIBBS
2022-present	Shangzhou Xia	Ph.D Thesis	NGP
2022-present	Allison Brookshier	Ph.D Thesis	PIBBS
2022-2023	Jennifer Huang	Ph.D Thesis	PIBBS
2022-present	Alexander Couto	Ph.D Thesis	NGP
2022-present	Anakha Ajayan	Ph.D Thesis	Neuroscience
2020-2022	Xinyan Liang	Ph.D Thesis	Neuroscience
2020-Present	Sheron Guo	Ph.D Thesis	Stem Cell
2020-Present	Jonathan Chang	Ph.D Thesis	Stem Cell
2019-2020	Qing Chang	Master Thesis	Biochemistry
2019-2023	Joshua Berlind	Ph.D Thesis	Stem Cell
2019-2020	Han Vu	Ph.D Thesis	Medical Biophysics
2019-2020	Brock Pluimer	Ph.D Thesis	Neuroscience
2018-2019	Qiuyang Chen	Master Thesis	Medical Physiology

POSTGRADUATE MENTORSHIP:

Year-Year	*Trainee Name*	*If past trainee, current position and location*
2023-Present	Yafei Qu	
2022-Present	Feixiang Chen	
2022-Present	Qinghai Liu	
2021-Present	Haowen Qiao	
2020-2021	Shu Zhang	Staff Scientist, City of Hope
2019-2021	Jianxiong Zeng	Investigator, Chinese Academy of Sciences
2019-2021	Xinying Guo	Investigator, Sun Yat-Sen University
2017-2020	Yingxi Wu	

SERVICE

UNIVERSITY SERVICES

2023-Present	Associate Director, Neuromedicne PhD Program
2019-2020	Member, Faculty Environment and Employment Committee (FEEC)
2019-Present	Director, Director, Cell Engineering & Regeneration Core at ZNI

PROFESSIONAL SOCIETY MEMBERSHIPS:

Year-Year	*Society*
2019-Present	The American Physiological Society
2016-Present	The Alzheimer's Association International Society (ISTAART)
2012-Present	Society for Neuroscience
2010-2011	American Cancer Society
2007-2009	Society for Neuroscience

RESEARCH AND SCHOLARSHIP

EDITORSHIPS AND EDITORIAL BOARDS:

Year-Year	*Position*	*Journal/Board Name*
2021-present	Associate Editor	Frontier in Aging Neuroscience
2019-Present	Reviewing Editor	Frontier in Aging Neuroscience
2014-Present	Editorial Board Member	Tends Journal of Sciences Research
2012-Present	Editorial Board Member	Journal of Organogenesis

MANUSCRIPT REVIEW:

Year-Year	*Journal*
2012-Present	*International Journal of Biomedical Science; Immunity & Ageing; Open Journal of Cell Biology; Modern Research in Inflammation; Journal of Behavioral and Brain Science; International Journal of Nanomedicine; Breast Cancer: Basic and Clinical Research; Advances in Aging Research; World Journal of Neuroscience; Development Growth and Differentiation; Clinical Medical Journals; Libertas Academica; Journal of Neuroscience; PLOS Pathogens; Cell Reports; Nature Communications; Molecular Neurodegeneration; Experimental Neurology; Ageing Research Reviews; Advanced Science, Med, etc.*

GRANT REVIEWS:

Year-Year	*Description*	*Awarding agency, City, State, Country*
2020-Present	Panelist	Alzheimer's Association (AARF-AARF-D program) American Association of University Women (AAUW)
2016-Present	Ad hoc reviewer	NIH/NIA (MDCN-M91, MDCN-P56, ZRG1 AN-Q, ZRG1 BP-P, ZRG1 AN-55, etc.) Alzheimer's Association Cure for Alzheimer's Fund American Association of University Women (AAUW) Austrian Science Fund (FWF) Auckland Medical Research Foundation UKRI (UK Research and Innovation) Swiss National Science Foundation (SNSF) American Institute of Biological Sciences (AIBS)

MAJOR AREAS OF RESEARCH INTEREST

Research Areas

1. Genetic risks in Alzheimer's disease
2. Neurovascular Unite and Blood brain barrier
3. Vascular cognitive impairment and dementia
4. The role of innate immunity in CNS diseases
5. Infectious etiology of neurodegeneration
6. Traumatic brain injury

GRANT SUPPORT (CURRENT):

Grant No.: RF1NS135617 (PI: Zhao) *Dates of Award: 09/01/23-8/31/28*
Agency: NIH/NINDS *Percent Effort: 10%*
Title: The role of ATP13A5 ATPase in determining blood-brain pericyte functions

Description: To delineate a molecular mechanism based on the ATP13A5 ATPase in brain pericytes that potentially drives the specialization and maintenance of the BBB in animal models.

Role: Principal Investigator

Grant No.: R01AG089640 (PI: Qi; MPI: Zhao) *Dates of Award: 08/15/24-8/14/29*
Agency: NIH/NIA *Percent Effort: 10%*
Title: ERAD-STING Crosstalk in Microglia: Unraveling the Pathogenesis of Alzheimer's Disease

Description: To study the chronic activation of STING-mediated innate immunity in the brain is a fundamental mechanism underlying neuroinflammation in AD pathogenesis, which is regulated by SEL1L-HRD1 ERAD.

Role: Principal Investigator (MPI)

Grant No.: R61NS137365 (PI: Shih; MPI: Zhao) *Dates of Award: 07/01/24-6/30/26*
Agency: NIH/NINDS *Percent Effort: 10%*
Title: Chemogenetic Mouse Models for Cerebral Hypoperfusion and VCID

Description: This R61/R33 project will develop a novel chemogenetic model for cerebral hypoperfusion that involves adjustable control of CNS capillary flow by engaging pericyte contractile dynamics.

Role: Principal Investigator (MPI)

Grant No.: R01AG089756 (PI: Tao; MPI: Zhao) *Dates of Award: 09/16/24-9/15/29*
Agency: NIH/NIA *Percent Effort: 10%*
Title: Understanding Neural Bases for Neuropsychiatric Impairments in Alzheimer's Disease Models

Description: This proposed research seeks to understand the
neural foundations of NPS-related behavioral abnormalities in mouse AD models. By combining a suite of cutting-edge approaches, we will integrate multimodality data from behavior assessments to spatial transcriptomics, anatomy, pathology, and neural function of the brain

Role: Principal Investigator (MPI)

Grant No. 23-1051406 (PI: Zhao) *Dates of Award: 8/01/2023-7/30/2026*
Agency: Alzheimer's Association *Percent Effort: 5%*
Title: Understanding the vascular dysfunctions in MODEL-AD mouse models

Description: The goal is to utilize the MODEL-AD AD Knowledge Portal and their new knockin animal models and provide an in-depth understanding of BBB and vascular changes during AD pathogenesis and progression in both EOAD and LOAD.
Role: Principal Investigator

Grant No.: R21AG085559 (PI: Zhao) *Dates*: 12/01/2024 - 11/30/2026
Agency: NIH/NIA *Percent Effort*: 5%

Title: Probing the heterogeneity of brain pericytes using new genetic tools

Description: To nvestigate the genetic and functional difference between BBB pericytes and non-BBB pericytes using our new genetic tools based on the Atp13a5 model, and understand their changes associated with aging and Alzheimer's disease.
Role: Principal Investigator

Grant No.: RF1NS122060 (PI: Zhao) *Dates of Award: 04/01/21-0/31/26*
Agency: NIH/NINDS *Percent Effort: 10%*
Title: A TIME252-dependent Microvascular Endophenotype in Alzheimer's Disease

Description: To understand a novel TMEM252-dependent mechanism of microvascular injury, which may also serve as a common molecular signature for microvascular injury and a common mechanism in aging and AD.

Role: Principal Investigator

Grant No.: R01AG070904 (PI: Feng) *Dates of Award: 06/01/2021 - 05/31/2026*
Agency: NIH/NIA *Percent Effort: 5%*
Title: Explore roles of HSV-1 in Alzheimer's disease using mouse models

Description: To delineate the role of deamidation in host defense and salvage NAD+ synthesis in neurons and in mice, and how aging and HSV-1 infection synergize to promote NAMPT deamidation and NAD+ depletion, thus fueling neurodegeneration in mice
Role: Co-investigator

Grant No.: R01NS110687 (PI: Zhao) *Dates of Award*: 05/01/2019-02/29/2025 (NCE)
Agency: NIH/NINDS *Percent Effort*: 20%

Title: Zika Virus Capsid Protein Mediated Blockage of host microRNA machinery

Description: To investigate capsid-dependent suppression of DICER function as a unique determinant of ZIKV immune evasion and pathogenesis, using different ZIKV strains and capsid variants in both human fetal NSCs and a mouse model of prenatal infection.
Role: Principal Investigator

Grant No.: R01AG061288 (PI: Zhao) *Dates of Award*: 04/15/2019-01/31/2025 (NCE)
Agency: NIH/NIA *Percent Effort*: 20%

Title: Pericyte-neuronal crosstalk in health and Alzheimer's disease

Description: To study the crosstalk between brain pericytes and neurons, particularly examining the influence of paracrine signaling of pericyte specific IGF2 on neuronal function and remodeling using both in vitro cell-based assays and hippocampal memory and behavior in transgenic murine models, as well as its influence on Tau hyperphosphorylation and pathology.
Role: Principal Investigator

Grant No.: R56AG082361 (PI: Zhao, MPI: Yuan) *Dates of Award: 09/01/23-8/31/25* (NCE)
Agency: NIH/NIA *Percent Effort: 10%*
Title: cGAS-STING mediated neuroinflammation in Alzheimer's disease

Description: To determine the role of cGAS-STING pathway in the pathogenesis of AD, and whether it serves a link between HSV-1 infection and increased risk for AD.

Role: Principal Investigator

Agency: IDSA Foundation (PI: Zhao) *Dates of Award: 03/01/23-4/15/25* (NCE)
Percent Effort: 5%
Title: cGAS-STING innate immune response modulates neuroinflammation in Alzheimer's disease

Description: To investigate whether chronic activation of innate immunity collectively triggered by β-amyloid and infections is a fundamental mechanism of neuroinflammation, and whether cGAS-STING pathway is a critical biological process in the development and progression of AD.

Role: Principal Investigator

PREVIOUS RESEARCH SUPPORT

Grant No.: W81XWH2010424 (PI: Ichida and Zhao) *Dates of Award*: 03/01/2020 -06/28/2023
Agency: DoD/CDMRP *Percent Effort*: 5%
Title: Identification of Mechanotransduction Mechanisms Leading to Neuronal Injury in Cerebral Organoids

Description: The goal of our proposed study is to identify the cell autonomous mechanisms within neurons that lead to their degeneration after mechanical injury in both normal neurons and those derived from frontotemporal dementia patients that harbor FTD-causing genetic mutations.
Role: Co-Principal Investigator

Grant No.: A2019218S (PI: Zhao) *Dates of Award*: 07/01/2019-06/30/2023
Agency: BrightFocus Foundation *Percent Effort*: 10%

Title: Understanding the cerebrovascular link between traumatic brain injury and Alzheimer's disease

Description: To address this paucity of research, and investigate the cerebrovascular impairment induced by TBI and its impact on the susceptibility to Alzheimer's disease in animal models.

Role: Principal Investigator

Grant No.: 006312-00002 (PI: Zlokovic and Zhao) *Dates of Award*: 12/28/2015-12/27/19
Agency: Cure Alzheimer's Fund *Percent Effort*: 20%
Title: The role of PICALM mutations in Alzheimer's disease

Description: To determine the functions of new PICALM genetic mutations associated with Alzheimer's disease.

Role: Co-Principal Investigator

Grant No.: 00347-00001 (PI: Zhao) *Dates of Award*: 03/01/2017-06/30/2018
Agency: Whittier Foundation *Percent Effort*: 10%
Title: Combination Therapy with Human Neural Stem Cells and 3K3A-APC for Ischemic Stroke

Description: The goal is preclinical development of novel combination therapy with human neural stem cells (hNSCs) and an analog of activated protein C (3K3A-APC) as a later treatment for functional restoration in ischemic stroke.
Role: Principal Investigator

Grant No. NIRG-15-363387 (PI: Zhao) *Dates of Award*: 10/01/2015-9/30/2017
Agency: Alzheimer's Association *Percent Effort*: 20%

Title: PICALM-mediated autophagic Aß clearance and toxicity mitigation in pericyte

Description: The goal is to generate new insights into PICALM biology, particularly in regards to its roles in mediating autophagic clearance of Aβ species in pericytes.

Role: Principal Investigator

Grant No.: 5P50AG005142-32 (PI: Zhao) *Dates of Award*: 4/1/2016-3/31/2017
Agency: USC Alzheimer's disease Research Center *Percent Effort*: 10%
Title: Identification of active transcriptional regulatory elements for Alzheimer's vascular risk genes
Description:. The goal is to determine the transcriptional regulatory elements of vascular Alzheimer's risk genes.

Role: Principal Investigator

Grant No.: R03AG063287 (PI: Zhao) *Dates of Award*: 04/15/2019-01/31/2021
Agency: NIH/NIA *Percent Effort*: 10%
Title: Genetic interaction of PICALM and APOE in Alzheimer's disease
Description: To determine the genetic interaction between major LOAD-associated APOE and PICALM genes, and map the molecular and cellular mechanisms underpinning this functional interaction in neurodegeneration.
Role: Principal Investigator

Grant No.: R21AG066090 (PI: Zhao) *Dates of Award*: 04/15/2019-06/31/2023
Agency: NIH/NIA *Percent Effort*: 10%
Title: The molecular mechanism of PICALM-dependent endosomal trafficking
Description: To determine how PIMREG teams up with PICALM in controlling the intracellular trafficking and transcytosis of cargo vesicles cross the blood-brain barrier, which is essential for Aβ clearance.
Role: Principal Investigator

ISSUED AND PENDING PATENTS:

Zlokovic and Zhao. Generation of an inducible pericyte-specific cre mouse model. University of Southern California USC. File 15/681.150. US20180049411A1.

INVITED LECTURES, SYMPOSIA, KEYNOTE ADDRESSES

Year	***Type***	***Title, Location***
2023	*Tulane University Medical School*	*Microvascular Impairment in Alzheimer's Disease and Traumatic Brain Injury*
2023	*University of Michigan Medical School*	*Microvascular impairment in Alzheimer's disease and Traumatic brain injury*
2022	*MHG seminar Series Baylor College of Medicine*	*A Vascular Path to Neurodegeneration*
2022	*ASHG annual meeting 2022*	*Spatial transcriptomic profiling in 5xFAD mouse model with Stereo-seq*
2022	*21st University of California and Western US Neurotrauma Conference*	*A cerebrovascular link between TBI and Alzheimer's disease*
2022	*Loma Linda University Integrated Biomedical Science Seminar Series*	*A Vascular Path to dementia, Virtual Seminar via Zoom*
2020	*UCR Neuroscience Seminar Series*	*A Vascular Path to dementia, Virtual Seminar via Zoom*
2020	*RWD Seminar Series*	*A vascular path to neurodegeneration, Virtual Seminar via Zoom*
2020	*Nu Rho Psi - Guest Lecture Serie*	*A Vascular Path to dementia, Virtual Seminar via Zoom*
2019	*AFAR New Investigator in Alzheimer's Disease meeting*	*Genetic Interaction of PICALM and APOE in Alzheimer's Disease UCLA Luskin Conference Center, Los Angeles, California*
2019	*5th Leducq Transatlantic Network Meeting*	*Pericyte Loss Leads to Circulatory Failure and Pleiotrophin Depletion Causing Neuron Loss, Paris, France.*
2018	*5th Annual Zilkha Symposium on Alzheimer's disease*	*iPSC-out the causal linkage of AD-associated genetic variants, Los Angeles, CA.*
2017	*Cardiff University, UK Dementia Research institute*	*A Cerebrovasuclar Path to Neurodegeneration and dementia, Cardiff, UK*
2017	Alzheimer's Association International Conference 2017	The Role of PICALM and LRP1 in Transvaccular Aβ Clearance Across the Blood Brain Barrier, London, UK.

Year	*Type*	*Title, Location*
2017	*4th Annual meeting International Forum for Interdisciplinary Sciences*	*A Cerebrovasuclar Path to Neurodegeneration, Wuhan, China.*
2016	*Mini-symposium, Annual Meeting of the Society for Neuroscience*	*The Role of Endothelial PICALM on Brain Amyloid-β Homeostasis, San Diego, CA.*
2016	*USC ADRC Pilot Project Day*	*Whole genome Mapping of Active Transcriptional Regulatory Elements for Alzheimer's Vascular Risk Genes, Los Angeles, CA.*
2016	*Zilkha Neurogenetic Institute, USC*	*A Search for The Molecular Causes of Vascular Cognitive Impairment and Dementia, Los Angeles, CA.*
2016	*Cure Alzheimer's Fund Research Consortium Meeting*	*The role of human PICALM mutations in Alzheimer's disease, San Diego, CA.*
2015	*Mini-symposium, Annual Meeting of the Society for Neuroscience*	*Endothelial LRP1 controls cerebrovascular integrity and functions, Chicargo, IL.*
2014	*Mini-symposium, Annual Meeting of the Society for Neuroscience*	*Central role for PICALM in amyloid-β blood-brain barrier transcytosis and clearance, Washington, DC.*
2012	*Annual Retreat, Department of Microbiology and Immunology*	*Dual functions of UVRAG in maintaining genomic integrity, USC Keck School of Medicine, Los Angeles, CA*
2011	*Factor Meeting*	*UVRAG Maintains chromosome stability and centrosome integrity, USC Keck School of Medicine, Los Angeles, CA.*
2009	*Mini-symposium, Annual Meeting of the Society for Neuroscience*	*Regulate axon branching by the cyclic GMP pathway via inhibition of glycogen synthase kinase-3B during sensory axon development, Washington, DC.*

INVITED GRAND ROUNDS, CME LECTURES

Year	*Type*	*Title, Location*
2020	Infection & Immunity Research Lab Meeting	Probing Vascular-Neuronal Interaction in Health and Diseases Herman Ostrow School of Dentistry of USC, Los Angeles, CA
2019	Harbor UCLA Neurology Grand Rounds	BBB and vascular neuronal interactions Harbor UCLA Medical Center, Torrance, CA 90502

THESIS:

Year	*Degree*	*Institution*	*Title*
2009	*Ph.D. (Neuroscience)*	*University of Southern California*	*Regulation of axonal development by the cGMP signaling pathway*
2001	*B.S. (Biological Sciences)*	*Fudan University*	*The receptive field organization and orientation selectivity of neurons in the cat's lateral geniculate nucleus*

PUBLICATIONS:

See Google Scholar for complete list of publications:

https://scholar.google.com/citations?user=1IHEtogAAAAJ

(**Citations: 13889, h-index: 46, i10-index: 65**)

* to indicate mentees
$^{\Delta}$ to indicate co-first authors
** to indicate co-corresponding authors

REFEREED JOURNAL ARTICLES:

1. Guo X, Xia S, Ge T, Lin Y, Hu S, Wu H, Xie X, Zhang B, Zhang S, Zeng J, Chen JF, Montagne A, Gao F, Ma Q, **Zhao Z**. Atp13a5 Marker Reveals Pericyte Specification in The Mouse Central Nervous System. *Journal of Neuroscience* 2024, e0727242024; https://doi.org/10.1523/JNEUROSCI.0727-24.2024
2. Qiao H, Deng X, Qiu L, Qu Y, Chiu Y, Chen F, Xia S, Muenzel C, Ge T, Zhang Z, Song P, Bonnin A, **Zhao Z****, Yuan W******. SARS-CoV-2 induces blood-brain barrier and choroid plexus barrier impairments and vascular inflammation in mice. *Journal of medical virology* 2024. 96 (5), e29671
3. Lai JD, Berlind JE, Fricklas G, Lie C, Urenda J, Lam K, Sta Maria N, Jacobs R, Yu V, **Zhao Z**, Ichida JK. KCNJ2 inhibition mitigates mechanical injury in a human brain organoid model of traumatic brain injury. *Cell Stem* Cell. 2024 Apr 4;31(4):519-536.e8. doi: 10.1016/j.stem.2024.03.004.
4. Lin LL, Wang HH, Pederson B, Wei X, Torres M, Lu Y, Li ZJ, Liu X, Mao H, Wang H, Zhou LE, **Zhao Z**, Sun S, Ling Qi. SEL1L-HRD1 interaction is required to form a functional HRD1 ERAD complex. *Nat Commun.* 2024 Feb 16;15(1):1440. doi: 10.1038/s41467-024-45633-0.
5. Ma L, Wang F, Li Y, Wang J, Chang Q, Du Y, Sadan J, **Zhao Z**, Fan G, Yao B, Chen JF. Brain methylome remodeling selectively regulates neuronal activity genes linking to emotional behaviors in mice exposed to maternal immune activation. *Nat Commun.* 2023 Nov 29;14(1):7829. doi: 10.1038/s41467-023-43497-4.
6. Zheng J, Wu H, Wang X, Zhang G, Xu W, Xu S, Fang Y, Zhang A, Shao A, Chen S, **Zhao Z**, Zhang J, Yu J. Temporal dynamics of microglia-astrocyte interaction in neuroprotective glial scar formation after intracerebral hemorrhage. *J Pharm Anal.* 2023 Aug;13(8):862-879. doi: 10.1016/j.jpha.2023.02.007.
7. Shen G, Sanchez K, Hu S, Zhao Z, Zhang L, Ma Q. 3D doppler ultrasound imaging of cerebral blood flow for assessment of neonatal hypoxic-ischemic brain injury in mice. *PLoS One.* 2023 May 9;18(5):e0285434. doi: 10.1371/journal.pone.0285434.
8. Kisler K, Sagare AP, Lazic D, Bazzi S, Lawson E, Hsu CJ, Wang Y, Ramanathan A, Nelson AR, **Zhao Z**, Zlokovic BV. Anti-malaria drug artesunate prevents development of amyloid-β pathology in mice by upregulating PICALM at the blood-brain barrier. *Molecular Neurodegeneration.* 2023. 18 (1), 1-18
9. Qiao H, Chiu Y, Liang X, Xia S, Ayrapetyan M, Liu S, He C, Song R, Zeng J, Deng X, Yuan W, **Zhao Z**. Microglia innate immune response contributes the antiviral defense and blood-CSF barrier function in human choroid plexus organoids during HSV-1 infection. *Journal of Medical Virology.* 2023;95(2):e28472.
10. Xie X, Ma G, Li X, Zhao J, **Zhao Z****, Zeng J******. Activation of innate immune cGAS-STING pathway contributes to Alzheimer's pathogenesis in 5× FAD mice. *Nature Aging.* 2023, 3, 202–212.
11. Dong S, Xie X, Chen Y, Long G, Liang Q, **Zhao Z****, Zeng J******. Protocol for in utero injection to investigate Zika virus-related fetal microcephaly in mice. *STAR protocols*. 2022. 3 (1), 101057
12. Zhang S, Zeng J, Zhou Y, Gao R, Rice S, Guo X, Liu Y, Feng P, **Zhao Z**. Simultaneous Detection of Herpes Simplex Virus Type 1 Latent and Lytic Transcripts in Brain Tissue. *ASN Neuro.* 2022;14, 17590914211053505

13. Wu Y, Wu H, Zeng J, Pluimer B, Dong S, Xie X, Guo X, Ge T, Liang X, Feng S, Yan Y, Chen JF, Sta Maria N, Ma Q, Gomez-Pinilla F, **Zhao Z**. Mild traumatic brain injury induces microvascular injury and accelerates Alzheimer-like pathogenesis in mice. *Acta neuropathologica communications*. 2021; 9 (1), 1-14.

14. Wu H, Zheng J, Xu S, Fang Y, Wu Y, Zeng J, Shao A, Shi L, Lu J, Mei S, Wang X, Guo X, Wang Y, **Zhao Z**** Zhang J******. Mer regulates microglial/macrophage M1/M2 polarization and alleviates neuroinflammation following traumatic brain injury. *Journal of neuroinflammation*. 2021; 18 (1), 1-20.

15. Huuskonen MT, Wang Y, Nikolakopoulou AM, Montagne A, Dai Z, Lazic D, Sagare AP, **Zhao Z**, Fernandez JA, Griffin JH, Zlokovic BV. Protection of ischemic white matter and oligodendrocytes in mice by 3K3A-activated protein C. *Journal of Experimental Medicine* 2021. 219 (1), e20211372

16. Nikolakopoulou AM, Wang Y, Ma Q, Sagare AP, Montagne A, Huuskonen MT, Rege SV, Kisler K, Dai Z, Körbelin J, Herz J, **Zhao Z**,** Zlokovic BV******. Endothelial LRP1 protects against neurodegeneration by blocking cyclophilin A. *Journal of Experimental Medicine*. 2021; 218 (4)

17. Zhang H, Fan J, **Zhao Z**, Wang C, Wan LQ. Effects of Alzheimer's Disease-Related Proteins on the Chirality of Brain Endothelial Cells*. Cellular and Molecular Bioengineering*. 2021; 1-10

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3. **Zhao Z**. The Role of PICALM and LRP1 in Transvacular Abeta Clearance Across the Blood Brain Barrier. *Alzheimer's & Dementia*. 13(7): 180-181, 2017.
4. **Zhao Z**. PICALM Mediates Autophagic Aβ Clearance and Toxicity Mitigation in Pericytes. *Alzheimer's & Dementia*. 12(7): 1049, 2016.

5. **Zhao Z**. Annual Meeting of the Society for Neuroscience: 3K3A-APC and human neural progenitor cells for stroke repair in mice. San Diego, CA. November 2016.
6. **Zhao Z**. Annual Meeting of the Society for Neuroscience: Endothelial LRP1 Controls Cerebrovascular Integrity and Functions. Chicago, IL. October 2015.
7. **Zhao Z**. Annual Meeting of the Society for Neuroscience: Central role for PICALM in amyloid-β blood-brain barrier transcytosis and clearance. Washington, DC. November 2014.
8. **Zhao Z**. Annual Meeting of the Society for Neuroscience: An activated protein C analog stimulates neuronal production by human neural progenitor cells via a PAR1-PAR3-S1PR1-Akt pathway. San Diego, CA. November 2013.
9. **Zhao Z**. Annual Meeting of the Society for Neuroscience: Regulate axon branching by the cyclic GMP pathway via inhibition of glycogen synthase kinase-3B during sensory axon development. Washington, DC. November 2009.

MEDIA AND TELEVISION APPEARANCES:

1. September 19, 2019. Alzheimer's Los Angeles Partners with BrightFocus Foundation to Fund New Alzheimer's Study. Brightfocus.org.
2. September 4, 2017. How is the blood brain barrier affected by Alzheimer's disease? VD Dementia.
3. September 4, 2017. Fresh faces and new ideas at the AAIC. VD Dementia.
4. September 4, 2017. Two sides to the story: clearance in Alzheimer's disease. VD Dementia.

Introduction

I received my Ph.D. in neuroscience from the University of Southern California (USC) in 2009, continued my journey at USC as a postdoctoral fellow in 2010, and was promoted to tenure-track assistant professor at in 2017. My scientific training and research expertise covers neurosciences and immunology, as I was mentored by several renowned mentors in these fields, particularly Dr Berislav Zlokovic on blood-brain barrier and neurodegenerative diseases. Currently, my main research objective is to explore the genetic, molecular and cellular mechanisms of neurodegeneration, understand the crosstalk between the cell types of the brain and explore new approaches to restore the functional crosstalk for the treatment of neurodegenerative diseases.

Summary of Accomplishments

In the last six year as a junior faculty member, I have accomplished: i) developing and maintaining a robust extramurally funded research program in the state-of-the-art Zilkha Neurogenetic Institute; ii) publishing research manuscripts in peer-reviewed high-profile journals (80 publications, >13000 citations, h-index: 46). iii) engaging in graduate and undergraduate education, and mentoring trainees at different levels from students to post-doctoral fellows; iv) contributing to the highly collaborative and innovative environment within the scientific community at USC. More importantly, my research team has brought unique expertise combining cutting-edge approaches in genetics, cellular and molecular biology. As principal investigator I successfully obtained federal grants with over 20 million funding in total cost, and over 1 million funds from five different private foundations. As a researcher, I have been listed among the top 1% Highly Cited Researchers in Cross-Field by Clarivate Analytics for 4 consecutive years between 2020-2023.

Research areas:

The blood-brain barrier (BBB) is central to the neurovascular unit function and integrity, and its dysfunction influences the pathogenesis and progression of many neurodegenerative diseases, including Alzheimer's disease. It has been known for nearly a century that vascular cells different between the brain and the peripheral, and they are even heterogeneous within the brain as several brain regions known as the circumventricular organs (CVOs) are not protected by the BBB. Recently, we have generated multiple new transgenic models based on single cell transcriptomics (NIH/NIA grant R01AG061288 and RF1NS135617), and now able to reliably separate BBB endothelial cells from the non-BBB endothelial cells using the *Zic3* and *Plvap* genetic markers, and BBB pericytes from non-BBB pericytes using the *Atp13a5* and *Pdgfrb* genetic markers, allowing us to achieve a better understanding of brain vascular biology and heterogeneity in the context of BBB functions, as well as their contributions to CNS disorders including TBI and AD.

Alzheimer's disease (AD) is the most common form of dementia in the elderly, manifesting amyloid plaque and neurofibrillary tangle formation, progressive neurodegeneration and cognitive decline. Over 95% of the AD patients are sporadic late-onset cases with unclear etiology, yet they are known to associated with over 30 genetic loci. With my previous experience working on *PICALM* as a major AD-associated gene, we investigated the genetic interactions between AD risk alleles, e.g., between *APOE* and *PICALM* (supported by NIH/NIA grants R21AG066090, R03AG0632875 and P50AG005142-32), and provided new insights to the AD risk genes in neuroimmune regulation and gender differences. More importantly, we recently reported that the cGAS-STING immune pathway is a critical molecular link between innate immunity and AD pathogenesis, and neuronal cells can sense the accumulation of cytosolic dsDNA in AD and signal microglia and astrocytes via this pathway.

Traumatic brain injury (TBI) is a leading cause of long-term disabilities and significantly increases the risk for Alzheimer's disease and dementia in later life. To investigate this link, I have built up a collaborative team include experts in bioinformatics, molecular and cell biology to understand the underlying causes of injury. We have provided new insights to the neuroimmune activation and microvascular injury in rodent models of TBI. More importantly, we have conducted single cell transcriptomic studies and identified new molecular signature of microvascular injury that is shared by traumatic brain injury and aging. More importantly, we identified a novel mechanism by which TMEM252 triggers ER stress in endothelial cells after TBI, and drives microvascular injury. This work is currently supported by NIH/NINDS grant RF1NS122060, and our findings will improve our understanding of vascular contributions to cognitive impairment and dementia (VCID), and may guide the development of new therapies targeting TMEM252.

Infectious disease of CNS is a leading cause of mortality and neurological impairment. It is linked to developmental disorders such as congenital Zika Syndrome, long-COVID, and neurodegenerative disease such as Alzheimer's disease. In fact, the viral origin of neurodegeneration has been long proposed; and viral infections induce cerebral dysfunctions known as sepsis-associated encephalophagy and can double the risk for dementia. My team recently demonstrated the specific impact of Zika infection on host's microRNA machinery and early neurodevelopment. We are now actively exploring the innate immune system and brain microglia as a converging point influenced by viral infection and the proteinopathies of Alzheimer's disease. Our findings reinforce the fundamental idea that dysregulation of the immune system is a main driving force of brain dysfunction and cognitive impairment.

Education and Services

As an assistant professor, I have been actively engaging in mentoring trainees at different levels from undergraduate students and technicians to graduate students and post-doctoral fellows, and very proud of their growth and development. Two postdoctoral fellows have successfully lunched their career as independent investigators and started their own research lab in China; four of the undergraduate students in the lab received the USC Provost's Undergrad Research Fellowships and three are now enrolled in medical schools; 5 technicians worked with us were accepted into top graduate programs at USC and other universities.

I actively participate in teaching for graduate and undergraduate courses. Besides regularly giving lectures for both Advanced Neuroscience (NEUR524) and medical Physiology (INTD-573), I also directed Advanced Neuroscience (NEUR524) in 2019, and a Micro-Seminar on Alzheimer's disease for undergraduates in 2019-2021. In addition, I also served on the Faculty Environment and Employment Committee (FEEC) in 2019-2020. Due to my active participation in teaching, I was nominated to be the KSOM CET Fellows in 2023.

In 2020, I started the Cell Engineering and Regeneration Core at ZNI to openly serve our research community. The main goal of the core is to develop unique cell-based research tools for tackling key questions of the nervous system. We provide effective support in cell culture and assays with multiple brain cell types for the studies of neurological and neurodegenerative diseases, and facilitate the multidisciplinary collaborations between genetics, biochemical cellular, system and physiological levels at ZNI. In the past 3 years, we worked with more than 10 labs, and successfully supported several NIH grants from USC, including RF1AG072442 (PI: Ulmer); R01NS126981 (PI: Bonnin), R01DC020887 (PI: Zhang); R21AG076232 (PI: Hong).

In 2022, I worked with Dr Li Zhang at ZNI to build a new Ph.D. program in Neuromedicine at USC. The goal of the program is to train next-generation investigators capable of participating and/or leading interdisciplinary research and development programs to address challenging questions regarding the neurological and neurodegenerative diseases. This program is now approved by the KOSM and graduate school, and starts to accept new students in Fall 2023. To successfully provide students with skill sets in conducting rigorous basic research and developing cutting-edge technologies, we also introduced two new courses: Foundation in Neuromedicine (NEUM 510), and Advanced Topics in Neuromedicine (NEUM 520). We hope this new program will fit with the University's goal to create a diverse and translational research workforce in neuroscience and neurotechnology research.

Impact and Recognition

As a junior investigator, I highly value innovation and always encourage my fellows to apply cutting-edge and multidisciplinary approaches to address scientific questions, and never to be confined to the status quo. In addition, I always put team science and open science as priorities. One example is the generation of new transgenic models for different cell types at the blood-brain barrier: our *Atp13a5* model alone has been transferred through USC Stevens Center for Innovation to over 50 labs internationally within just two years.

My work on blood brain barrier, Alzheimer's disease, infection and immunity are highly cited, and I was listed as top 1% Highly Cited Researchers in 2020-2023. Based my expertise in neurodegenerative diseases, I have been invited to serving on the Review Committee for Alzheimer's Association and American Association of University Women (AAUW), and as associate editor for Frontier in Aging Neuroscience. In addition, I also regularly serve as ad hoc reviewer for NIH/NIA and other federal funds and foundations, as well as for >50 journals in cross-field for reviewing submitted manuscripts.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

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POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Fudan University, Shanghai, China	B.S	06/2001	Biological Sciences
University of Southern California, Los Angeles	Ph.D.	12/2009	Neuroscience
University of Southern California, Los Angeles	postdoctoral	09/2014	neurodegenerative diseases

A. Personal Statement

With a strong interest in CNS health and diseases, I obtained my Ph.D. training in neuroscience at USC on the topic of brain wiring and discovered that axon morphogenesis and bifurcation of sensory neurons are precisely controlled by cyclic guanosine monophosphate (cGMP) signaling. I was later trained with Dr. Zlokovic for a better understanding of the vascular contributions to neurodegenerative diseases, and later became Assistant Professor in the Department of Physiology and Neuroscience at USC to continue my journey as a neuroscientist. My research team is keen to understand the complex etiology of Alzheimer's disease and other neurodegenerative disorders, as well as explore the crosstalk between the components of the neurovascular unit in health and during pathogenesis and the interplay between genetic and environmental risk factors in Alzheimer's disease. Currently, I am Assistant Professor of Physiology and Neuroscience at Keck School of Medicine of USC, the Director of the Cell Engineering & Regeneration Core of Zilkha Neurogenetic Institute, and Associate Director of the Neuromedicine graduate program.

Ongoing and recently completed projects that I would like to highlight include:

RF1NS135617 (PI: Zhao)
09/19/2023-08/31/2026
The role of ATP13A5 ATPase in determining blood-brain pericyte functions

R01AG089640 (PI: Qi; MPI: Zhao)
08/15/24-8/14/29
ERAD-STING Crosstalk in Microglia: Unraveling the Pathogenesis of Alzheimer's Disease

R61NS137365 (PI: Shih; MPI: Zhao)
07/01/24-6/30/26
Chemogenetic Mouse Models for Cerebral Hypoperfusion and VCID

R01AG089756 (PI: Tao; MPI: Zhao)
09/16/24-9/15/29
Understanding Neural Bases for Neuropsychiatric Impairments in Alzheimer's Disease Models

R21AG085559 (PI: Zhao)

12/01/2024 - 11/30/2026
Probing the heterogeneity of brain pericytes using new genetic tools

RF1NS122060 (PI: Zhao)
04/01/2021-03/31/2026
A TIME252-dependent Microvascular Endophenotype in Alzheimer's Disease

B. Positions, Scientific Appointments, and Honors

Positions

2023-	Associate Director, Neuromedicine Graduate Program, Keck School of Medicine
2020-	Director, Cell Engineering & Regeneration Core, Keck School of Medicine
2017-	Assistant Professor, Department of Physiology & Neuroscience, Keck School of Medicine, University of Southern California
2017-	University of Southern California (NSCI 524: Advanced Overview of Neurosciences; INTD-573: Medical Physiology II; Microseminar in Alzheimer's disease)
2014-2017	Research Assistant Professor, Department of Physiology & Biophysics, University of Southern California
2012-2014	Research Associate, Laboratory of Berislav Zlokovic, M.D., Ph.D., University of Southern California
2010-2011	Research Associate, Laboratory of Chengyu Liang, Ph.D., University of Southern California
2005-2009	Graduate student, Laboratory of Le Ma, Ph.D., University of Southern California
2004-2005	Teaching Assistant in the Department of Biological Sciences at University of Southern California (BISC 120: General Biology; BISC220: Cell Biology and Physiology; BISC 320: Molecular Biology)
2003-2004	Graduate student, Laboratory of Emily Liman, Ph.D., University of Southern California
2001-2002	Research Assistant, Laboratory of Vision Science Center for Brain Science, Fudan University

Scientific Appointments

2019-present	Associate Editor, Frontiers in Aging Neuroscience
2012-present	Member of Editorial Board, Journal of Organogenesis
2019-present	International Society to Advance Alzheimer's Research and Treatment (ISTAART)
2012-present	Society for Neurosciences
2010-2011	American Cancer Society
2004-2009	Society for Neurosciences

Honors

2022-2023	Investigator	Infectious Diseases Society of America Foundation
2019-2021	Investigator	BrightFocus Foundation
2016	Investigator	Whittier Foundation
2015-2017	New investigator, Alzheimer's Association	
2002	Provost Fellowship, University of Southern California	
2001	Award for "Outstanding graduates in Shanghai"	
1998~2001	People's Scholarship, Fudan University	

C. Contribution to Science

1. The human brain consists of about 100 billion neurons and 100 trillion synaptic connections; therefore, a longstanding goal of almost every neuroscientist in the world is to understand how this enormous degree of neuronal connectivity is established precisely during development. As a graduate student, I studied an aspect of this "wiring" problem — the branching mechanism of axons, a fundamental step of establishing neuronal connectivity and plasticity. I not only reported first that natriuretic peptides hormones can act as neural trophic factors to promote axon outgrowth, branching and guidance, but also unveiled the molecular and signaling mechanisms underlying the bifurcation of sensory axons in the spinal cord. The findings solved a long-standing puzzle that sensory afferents from the dorsal root ganglions all bifurcate faithfully when reaching

the spinal cord, and laid down a solid ground for studying brain natriuretic peptide hormones as novel neural trophic factors. I am primary investigator or co-investigator on the following studies:

a. Zhao Z, Wang Z, Gu Y, Feil R, Hofmann F, Ma L. (2009) Regulate axon branching by the cyclic GMP pathway via inhibition of glycogen synthase kinase 3 in dorsal root ganglion sensory neurons. Journal of Neuroscience. 4;29(5):1350-60. PMCID: PMC2868143.

b. Zhao Z, Ma L. (2009) Regulation of axonal development by natriuretic peptide hormones. Proceedings of the National Academy of Sciences. 20;106(42):18016-21. PMCID: PMC2764873.

2. After graduation, I moved on to studying immunology, particularly autophagy — a cellular catabolic process that defends the cell against pathogens and recycles dysfunctional cellular components and one of the innate defensive mechanisms against exogenous pathogens in human cells. Between 2010 and 2012, I worked with Drs. Chengyu Liang and Jae Jung, and explored novel functions of autophagy in tumorigenesis and infectious disease. I also found that UVRAG, an autophagy protein, promotes the DNA damage repair in the nucleus and prevents incorrect cell division in the centrosomes, which directly explained why autophagy proteins are often potent tumor suppressor. I am primary investigator or co-investigator on the following studies:

a. Zhao Z, Oh S, Li D, Ni D, Pirooz SD, Lee JH, Yang S, Lee JY, Ghozalli I, Costanzo V, Stark JM, Liang C. (2012) A dual role for UVRAG in maintaining chromosomal stability independent of autophagy. Developmental Cell. 15;22(5):1001-16. PMCID: PMC3356442.

b. Zhao Z, Ni D, Ghozalli I, Pirooz SD, Ma B, Liang C. (2012) UVRAG: at the crossroad of autophagy and genomic stability. Autophagy. 8(9):1392-3. PMCID: PMC3442888.

c. Liang Q, Luo Z, Zeng J, Chen W, Foo S, Ge J, Wang S, Goldman SA, Zlokovic BV, Zhao Z**, Jung JU**. Zika Virus NS4A-NS4B inhibition of Akt-mTOR pathway contributes to deficient neurogenesis and dysregulated autophagy by human fetal neural stem cells. *Cell Stem Cells*. 2016 Nov 3;19(5):663-671. PMCID: PMC5144538 (**, co-corresponding authors)

1. Ischemic stroke is a major cause of morbidity and mortality in America, manifesting acute blockage of blood supply to the brain resulting often in an irreversible brain damage. Activated protein C (APC) and its analogs have been shown to be beneficial for stroke in rodents. I was primary investigator or co-investigator to show that APC agonist-based clinical therapeutics: i) exert neural and vascular protection with a substantially extended therapeutic window for stroke in rodents; ii) strongly potentiate the neurogenic activity of human NSCs; iii) are applicable for integration and neurogenic activity of transplanted human neural stem cells for stroke and CNS injuries as adjuvant with stem cell therapy. The findings contributed to development of new therapies for stroke.

a. Wang Y, Zhao Z, Chow N, Rajput PS, Griffin JH, Lyden PD, Zlokovic BV. Activated Protein C Analog Protects from Ischemic Stroke and Extends the Therapeutic Window of Tissue-Type Plasminogen Activator in Aged Female Mice and Hypertensive Rats. Stroke 2013;44, 3529–3536. PMCID: PMC3912991.

b. Wang Y*, Zhao Z*, Rege SV, Wang M, Si G, Zhou Y, Wang S, Griffin JH, Goldman SA, Zlokovic BV. (2016) 3K3A-APC stimulates post-ischemic neuronal repair by human neural progenitor cells in mice. Nature Medicine. 22(9):1050-5. PMCID: PMC5215920.

c. Zeng J, Wang Y, Luo Z, Chang LC, Yoo JS, Yan H, Choi Y, Xie X, Deverman BE, Gradinaru V, Gupton SL, Zlokovic BV, Zhao Z**, Jung JU**. (2019) TRIM9-Mediated Resolution of Neuroinflammation Confers Neuroprotection upon Ischemic Stroke in Mice. Cell Rep. 9;27(2):549-560

2. The blood-brain barrier (BBB) is the gate keeper of the CNS. Disruption of BBB is often associated with neurodegenerative diseases, such as Alzheimer's disease. Pericytes are vital integrators of multiple functions of the neurovascular unit and play important roles in maintaining the BBB integrity. I was primary investigator or co-investigator to show that pericyte degeneration and consequent BBB damage are: i) eminent features of Alzheimer's disease and *amyotrophic lateral sclerosis; ii) detrimental to neuronal functions and health; iii) exacerbating factors for pathogenesis and disease progression.*

a. Zhao, Z., and Zlokovic, B.V. (2014). Blood-brain barrier: a dual life of MFSD2A? Neuron 82, 728–730. PubMed PMID: PMC4114515.

b. Zhao, Z., Nelson, A.R., Betsholtz, C., Zlokovic, B.V., 2015. Establishment and Dysfunction of the Blood-Brain Barrier. Cell 163, 1064–1078. PMCID: PMC4655822.

c. Montagne A*, Zhao Z*, Zlokovic BV. Alzheimer's disease: A matter of blood-brain barrier dysfunction? *Journal of Experimental Medicine*. 2017, 6;214(11):3151-3169. (*, co-first authors)

d. Nikolakopoulou AM, Montagne A, Kisler K, Dai Z, Wang Y, Huuskonen MT, Sagare AP, Lazic D, Sweeney MD, Kong P, Wang M, Owens NC, Lawson EJ, Xie X, Zhao Z**, Zlokovic BV**. Pericyte loss leads to circulatory failure and pleiotrophin depletion causing neuron loss. Nature Neuroscience 22,1089-1098. PMCID: PMC6668719 (**, co-corresponding authors)

e. Guo X, Xia S, Ge T, Lin Y, Hu S, Wu H, Xie X, Zhang B, Zhang S, Zeng J, Chen JF, Montagne A, Gao F, Ma Q, Zhao Z. Atp13a5 Marker Reveals Pericyte Specification in the Mouse Central Nervous System. *Journal of Neuroscience*. 2024, 44 (43) e0727242024; https://doi.org/10.1523/JNEUROSCI.0727-24.2024

3. Traumatic brain injury (TBI) is a leading cause of long-term disabilities and significantly increases the risk for Alzheimer's disease and dementia in later life. To investigate this link, I have built up a collaborative team include experts in bioinformatics, molecular and cell biology to understand the underlying causes of injury. We have provided new insights to the neuroimmune activation and microvascular injury in rodent models of TBI. More importantly, we have conducted single cell transcriptomic studies and identified new molecular signature of microvascular injury that is shared by traumatic brain injury and aging. More importantly, we identified a novel mechanism by which TMEM252 triggers ER stress in endothelial cells after TBI, and drives microvascular injury:

    a. Wu Y, Wu H, Zeng J, Pluimer B, Dong S, Xie X, Guo X, Ge T, Liang X, Feng S, Yan Y, Chen JF, Sta Maria N, Ma Q, Gomez-Pinilla F, Zhao Z. Mild traumatic brain injury induces microvascular injury and accelerates Alzheimer-like pathogenesis in mice. *Acta Neuropathologica Communications*. 2021. 9 (1), 1-14
    b. Wu H, Zheng J, Xu S, Fang Y, Wu Y, Zeng J, Shao A, Shi L, Lu J, Mei S, Wang X, Guo X, Wang Y, Zhao Z**** Zhang J****. Mer regulates microglial/macrophage M1/M2 polarization and alleviates neuroinflammation following traumatic brain injury. *Journal of neuroinflammation*. 2021; 18 (1), 1-20
    c. Wu Y, Wu H, Guo X, Pluimer B, Zhao Z. Blood–Brain Barrier Dysfunction in Mild Traumatic Brain Injury: Evidence from Preclinical Murine Models. *Front Physiol*. 2020; 11: 1030. doi: 10.3389/fphys.2020.01030.
    d. Lai JD, Berlind JE, Fricklas G, Lie C, Urenda J, Lam K, Sta Maria N, Jacobs R, Yu V, Zhao Z, Ichida JK. KCNJ2 inhibition mitigates mechanical injury in a human brain organoid model of traumatic brain injury. *Cell Stem Cell*. 2024 Apr 4;31(4):519-536.e8. doi: 10.1016/j.stem.2024.03.004.

4. Alzheimer's disease (AD) is now one of leading causes of human death and represent one of the greatest pressures on our healthcare system. Currently, there no treatment available for AD, while the challenge remains to understand the role of genetic risk and the mechanisms of pathogenesis. I have been focusing on the cerebrovascular system and its role in flushing out toxic amyloid-β species from the brain. Recently, I discovered that PICALM, an AD risk gene, is also a key player in the transcytosis of Aβ by: i) mediating the internalization of Aβ receptor on the endothelial cell surface; ii) guiding Aβ trafficking through endocytic pathway for exocytosis of Aβ to the circulating blood. Therefore, reduced PICALM expression in brain endothelium accelerates disease progression in mice and correlates well with Aβ pathology and cognitive impairment in AD patients. These findings reinforce the fundamental idea that the cerebrovascular system maintains brain Aβ homeostasis. I am primary investigator on the following studies:

    a. Zhao Z, Sagare AP, Ma Q, Halliday MR, Kong P, Kisler K, Winkler EA, Ramanathan A, Kanekiyo T, Bu G, Owens NC, Rege SV, Si G, Ahuja A, Zhu D, Miller CA, Schneider JA, Maeda M, Maeda T, Sugawara T, Ichida JK and Zlokovic BV. (2015) Central role for PICALM in amyloid-β blood-brain barrier transcytosis and clearance. Nature Neuroscience 18, 978–987. PMCID: PMC4482781.
    b. Zhu D, Montagne A, Zhao Z. Alzheimer's pathogenic mechanisms and underlying sex difference. *Cellular and Molecular Life Sciences.* 2021. 78, 4907-4920

c. Xie X, Ma G, Li X, Zhao J, Zhao Z**, Zeng J**. Activation of innate immune cGAS-STING pathway contributes to Alzheimer's pathogenesis in 5× FAD mice. Nature Aging. 2023. 3, 202–212. (**, co-corresponding authors)

d. Kisler K, Sagare AP, Lazic D, Bazzi S, Lawson E, Hsu CJ, Wang Y, Ramanathan A, Nelson AR, Zhao Z, Zlokovic BV. Anti-malaria drug artesunate prevents development of amyloid-β pathology in mice by upregulating PICALM at the blood-brain barrier. *Molecular Neurodegeneration*. 2023. 18 (1), 1-18

5. Viral infection is a leading cause of mortality and neurological impairment. It is linked to developmental disorders such as congenital Zika Syndrome, and neurodegenerative disease such as Alzheimer's disease. In fact, the viral origin of neurodegeneration has been long proposed; and viral infections induce cerebral dysfunctions known as sepsis-associated encephalophagy and can double the risk for dementia. My team has recently demonstrated the physiological impact of ZIKV-host interaction during fetal infection and neurodevelopment. We are now actively studying the innate immune system and brain microglia in the pathogenesis of Alzheimer's disease. These findings reinforce the fundamental idea that dysregulation of the brain's immune response is a main driving force of neurovascular dysfunction and cognitive impairment in AD. I am primary investigator on the following studies:

    a. Zeng J, Dong S, Luo Z, Xie X, Fu B, Li P, Liu C, Yang X, Chen Y, Wang X, Liu Z, Wu J, Yan Y, Wang F, Chen JF, Zhang J, Long G, Goldman SA, Li S, Zhao Z**, Liang Q**. The Zika Virus Capsid Disrupts Corticogenesis by Suppressing Dicer Activity and miRNA Biogenesis. 2020. *Cell Stem Cell* 27 (4), 618-632. e9 (**, co-corresponding authors).
    b. Zeng J, Luo Z, Xie X, Liang X, Yan Y, Liang Q, Zhao Z. Functional mapping of AGO-associated zika virus-derived small interfering RNAs in neural stem cells. 2021. *Frontiers in cellular and infection microbiology* 11, 628887
    c. Qiao H, Chiu Y, Liang X, Xia S, Ayrapetyan M, Liu S, He C, Song R, Zeng J, Deng X, Yuan W, Zhao Z. Microglia innate immune response contributes the antiviral defense and blood-CSF barrier function in human choroid plexus organoids during HSV-1 infection. *J Med Virol.* 2023 95(2):e28472

    d. Qiao H, Deng X, Qiu L, Qu Y, Chiu Y, Chen F, Xia S, Muenzel C, Ge T, Zhang Z, Song P, Bonnin A, Zhao Z**, Yuan W**. SARS‐CoV‐2 induces blood‐brain barrier and choroid plexus barrier impairments and vascular inflammation in mice. *Journal of medical virology* 2024. 96 (5), e29671

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/12Km9twAcZk5p/bibliography/public/

USC University of Southern California

ZILKHA NEUROGENETIC INSTITUTE

August 11, 2025

Dear Search Committee,

I am very pleased to apply for the open rank faculty position in Biomedical and Health Informatics Bioengineering at the Center for Biomedical Informatics and Genomics of Tulane University School of Medicine.My current research focuses on the genetic underpinning and cellular specialization of the cerebrovascular system and blood-brain barrier, as well as the vascular contributions to CNS diseases, such as brain injuries, dementia and infection. My group applies genetic, molecular and cellular bioengineering, functional biomaterials, stem cell and regenerative medicine approaches, and extensively collaborate with experts in neural engineering and biomedical imaging, to address the overarching questions in neuroscience and neurodegenerative diseases.

Research and Publications: My scientific training and research expertise cover blood-brain barrier and neurodegenerative diseases. Currently, my main research objective is to explore the genetic, molecular and cellular mechanisms of neurodegeneration associated with amyloid proteinopathies, understand the crosstalk between the different cell types of the brain, and explore new technologies and approaches for the treatment of neurodegenerative diseases. In the last six year as an assistant professor, I have developed and maintained a robust extramurally funded research program in the fast-growing department of Physiology and Biophysics, and contributed to the highly collaborative and innovative environment at USC. My research team published over 80 research articles and reviews in high-profile journals, which received 13878 citations, and a h-index of 46.

Funding: As a junior investigator, I highly value innovation and always encourage my fellows to apply interdisciplinary approaches and address key scientific questions, while never be confined to the status quo. My research team has brought unique expertise combining cutting-edge approaches in genetics, cellular and molecular biology, and successfully obtained over 20 million NIH funding in total, as well as over 1 million funds from five different private foundations. Based on BRIMR analysis of NIH funding: I ranked #8 in Physiology in 2021 with total of $3,149,301 annual funding, and #6 in Physiology in 2023 with total of $4,111,642 annual funding.

Impact and Recognition: My work on blood brain barrier, Alzheimer's disease, infection and immunity are highly cited, and I was listed among the top 1% Highly Cited Researchers in Cross-Field by Clarivate Analytics for 4 consecutive years between 2020-2023. Based my expertise in neurodegenerative diseases, I have been invited to serving on the Review Committee for Alzheimer's Association and American Association of University Women (AAUW), and regularly serve as ad hoc reviewer for NIH/NIA and other federal funds and foundations.

Enclosed are the list of my main research areas, services and fundings (past, current and pending). Should you have any question, please feel free to contact me at any time.

Sincerely yours,

Keck School of Medicine of the University of Southern California
1501 San Pablo Street, ZNI 101, Los Angeles, California 90089-2821 ● Tel: 323 442 2144 ● Email: zni@usc.edu

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List of Fundings

	Funding source	Project title	Total cost	Role
2015-2019	Alzheimer's Association	PICALM-mediated autophagic Aß clearance and toxicity mitigation in pericyte	$100,000	PI
2015-2019	Cure Alzheimer's Fund	The role of PICALM mutations in Alzheimer's disease	$600,000	MPI
2017-2018	USC ADRC Pilot grant (5P50AG005142-32)	Identification of active transcriptional regulatory elements for Alzheimer's vascular risk genes	$30,000	PI
2017-2018	Whittier Foundation	Combination Therapy with Human Neural Stem Cells and 3K3A-APC for Ischemic Stroke	$50,000	PI
2019-2022	NIH/NIA (R03AG063287)	Genetic interaction of PICALM and APOE in Alzheimer's disease	$330,000	PI
2019-2023	NIH/NIA (R21AG066090)	The molecular mechanism of PICALM-dependent endosomal trafficking	$453,750	PI
2019-2023	BrightFocus Foundation	Understanding the cerebrovascular link between traumatic brain injury and Alzheimer's disease	$300,000	PI
2020-2023	DoD/CDMRP	Identification of Mechanotransduction Mechanisms Leading to Neuronal Injury in Cerebral Organoids	$825,000	MPI
2019-2025 (NCE)	NIH/NIA (R01AG061288)	Pericyte-neuronal crosstalk in health and Alzheimer's disease	$2,062,500	PI
2019-2025 (NCE)	NIH/NINDS (R01NS110687)	Zika Virus Capsid Protein Mediated Blockage of host microRNA machinery	$2,170,165	PI
2021-2026	NIH/NINDS (RF1NS122060)	A TIME252-dependent Microvascular Endophenotype in Alzheimer's Disease	$3,837,946	PI
2021-2026	NIH/NIA (R01AG070904)	Explore roles of HSV-1 in Alzheimer's disease using mouse models	$4,125,000	Co-I
2022-2027	NIH/NIDCD (R01DC020887)	Cell-type basis for auditory processing in the inferior colliculus	$2,942,920	Co-I
2022-2025 (NCE)	IDSA Foundation	cGAS-STING innate immune response modulates neuroinflammation in Alzheimer's disease	$300,000	PI
2022-2025	Alzheimer's Association ALZ Discovery Program	Understanding the vascular dysfunctions in MODEL-AD mouse models	$250,000	PI

2023-2025 (NCE)	NIH/NIA (R56AG082361)	cGAS-STING mediated neuroinflammation in Alzheimer's disease	$826,222	PI
2023-2026	NIH/NINDS (RF1NS135617)	The role of ATP13A5 ATPase in determining blood-brain pericyte functions	$2,438,887	PI
2024-2026	NIH/NIA (R21AG085559)	Probing the heterogeneity of brain pericytes using new genetic tools	$453,750	PI
2024-2029	NIH/NIA (R61/R33 NS137365)	Chemogenetic Mouse Models for Cerebral Hypoperfusion and VCID	3,309,485	MPI
2024-2029	NIH/NIA (R01AG089756)	Understanding Neural Bases for Neuropsychiatric Impairments in Alzheimer's Disease Models	3,584,595	MPI
2024-2029	NIH/NIA (R01AG089640)	ERAD-STING Crosstalk in Microglia: Unraveling the Pathogenesis of Alzheimer's Disease	4,159,360	MPI