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.**

NAME: Veronica Galvan, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): VERONICAGALVAN

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
CAECE University, Buenos Aires, Argentina	MS	09/1994	Molecular Biology
University of Chicago	PhD	12/1999	Virology/Molecular Genetics and Cell Biology
Buck Institute for Research on Aging	Postdoctoral	12/2007	Neurobiology

A. Personal Statement

The focus of our research is on the molecular processes that lead to dementia in Alzheimer's disease (AD) and other neurological disorders of aging. I have generated mouse models of AD and used them to reveal mechanisms of neurodegeneration. Recently, my laboratory identified the mammalian-target of rapamycin (mTOR) as a central driver of disease in models of AD and vascular cognitive impairment, providing the first evidence for a molecular pathway that links aging to age-associated dementias. We identified the brain vasculature as a site of action of mTOR in AD pathogenesis, and recently singled out the cerebrovasculature as a novel target of tau toxicity in tauopathies, including but not limited to AD. Another focus of my group is the development of the common marmoset, a non-human primate (NHP), as a model of AD.

The goal of my laboratory is to advance our understanding of AD using rodent and NHP models. We strive to define how (a) mTOR activity and (b) pathogenic tau-induced cellular senescence mediates brain dysfunction in AD. To answer these questions, we use rodent and NHP primary culture-based models, *in vivo* optical and functional brain imaging, whole-tissue and single-cell proteomic and transcriptomic approaches, and neurobehavioral tools to measure the impact of experimental interventions on functional outcomes, and define the mechanisms involved. I expect that our work will close gaps in our understanding of AD and other tauopathies and determine how mTOR, pathogenic tau and cellular senescence can be targeted for therapeutic purposes, to fundamentally advance research in the neurodegeneration and geroscience fields.

Positions and Honors

Positions and Appointments

1994 - 1999	University of Chicago, Department of Molecular Genetics and Cell Biology, Committee on Virology (*Mentor: Bernard Roizman*)	Graduate Student
1999 - 2005	Buck Institute for Age Research (*Mentor: Dale Bredesen*)	Postdoctoral Fellow
2005 - 2008	Buck Institute for Age Research (*Mentor: Dale Bredesen*)	Staff Scientist
2009 – 2015	Department of Physiology and The Barshop Institute, University of Texas Health Science Center at San Antonio	Assistant Professor
2012 - present	Department of Biology, University of Texas at San Antonio	Adjunct Assistant Professor
2015 - 2018	US Department of Veterans Affairs	Research Health Scientist G13
2015 - present	Department of Cellular and Integrative Physiology and the Barshop Institute, University of Texas Health San Antonio	Associate Professor (Tenured)
2018 - present	US Department of Veterans Affairs	Research Health Scientist G14

Honors

1995 - 1997	Lucille Markey Scholarship in Molecular Medicine
2003	Scholar, National Institute on Aging Summer Institute on Aging Research
2003 - 2005	John D. French Alzheimer's Foundation Fellowship
2006	S.D. Bechtel Jr. Foundation Alzheimer's Award
2010	Ellison Medical Foundation New Scholar Award in Aging

Memberships and Other Professional Activity

2003 .. 2010-present	Member, Society for Neuroscience, International Behavioral Neuroscience Society, American Aging Association, Gerontological Society of America
2010 – 2015	Co-leader, Nervous System Function Assessment lab, NIA San Antonio Nathan Shock Center of Excellence in the Basic Biology of Aging
2010 - present	Member, Internal Selection and Steering Committee, NIH T32 Training Program in the Biology of Aging
2011 - present	Member, National Scientific Advisory Council, American Federation for Aging Research
2012 – 2018	Member, Scientific Advisory Board, Rapa Holdings Inc. (currently Emtora Biosciences)
2013 – 2016	Research Chair, Board of Directors, Alzheimer's Association South Texas Chapter
2014 - 2017	Co-convener, Brain Interest Group (BIG), Gerontological Society of America
2015- present	Co-leader, Healthspan and Functional Assessment Core, NIH/NIA San Antonio Nathan Shock Center of Excellence in the Basic Biology of Aging
2015 - 2016	Member, Scientific Program Committee, 2016 International Conference on Aging and Disease, Stanford University
2016	Guest Editor, Special Issue, GeroScience, Journal of the American Aging Association
2016	Member, Committee to implement Chancellor-initiated University of Texas system "Moonshot" initiative to tackle Parkinson's disease
2015 - 2016	Member, Scientific Program Committee and Young Investigator Committee, BRAIN & BRAINPET 2017 ISCBFM International Symposium
2015	Organizer and Chair, 2016 International Conference on Aging and Disease Session III, "*Aging, metabolism and disease*"
2017	Co-Organizer, 2017 Barshop Symposium on Aging '*Sex Differences in Aging, Age- related Diseases and Interventions*'
2017-2018	Member, Program Committee, 48th Annual Meeting of the American Aging Association
2018	Member, Board of Directors of the American Aging Association
2018	Member, Executive Committee, American Aging Association
Oct 2018	President-Elect, American Aging Association (elected, effective 2021)
April 2019	Associate Director, Barshop Institute T32 Training Program on the Biology of Aging

Current Editorial Duties

2010 - present	Member, Editorial Board, *Aging and Disease*
2012 - 2019	Member, Editorial Board, *ISRN Geriatrics*
2013 – present	Member, Editorial Board, *Archives of Physiology*
2014- present	Review Editor, *Frontiers in Molecular Biosciences, Protein Folding and Degradation*
2016 - 2019	Associate Editor, *GeroScience*, Official Journal of the American Aging Association
2018 - present	Associate Editor, *Journal of Gerontology: Biological Sciences*
2019 – 2020	Deputy Editor, *GeroScience* (Journal of the American Aging Association)
2019 – 2020	Associate Editor, eLife, Aging, Geroscience and Longevity: A Special Issue
2020 – present	Co-Editor in Chief, *GeroScience* (Journal of the American Aging Association)

Review Panel Participation

2015 – 2018	Member, VA Neurobiology D Study Section (NURD), Veterans Administration
2016	Ad-Hoc Member, NIH/CSR Study Section ZRG1 MDCN-T
2016 - 2018	Ad-Hoc Member, NIH/CSR Cellular Mechanisms in Aging and Development (CMAD)
2018	Ad-Hoc Member, VA Neurobiology C (NURC) Study Section, Veterans Administration
2018	Member, NIH Special Emphasis Panel ZAG1 ZIJ-P A1
2018 – 2020	Member, Review Panel, American Federation for Aging Research (AFAR) Breakthroughs in Gerontology (BIG) Awards
2019	Ad-Hoc Member, NIH/CSR Chronic Dysfunction and Integrative Neurodegeneration (CDIN)

2020 Member, NIH RFA-NS-20-004 Neuroscience Special Emphasis Panel (SEP)
2020 Ad-Hoc Member, NIH/CSR NIA-B Study Section
2020 – 2026 Standing Member, NIH/CSR Cellular Mechanisms in Aging and Development (CMAD)

Intellectual Property

2007 US Patent 8329653 B2 "Compositions and methods for suppression of amyloid plaque formation associated with neurodegenerative disorders"
2008 US Patent application EP1744762 A2 "Transgenic Models of Alzheimer's Disease and Uses Thereof in the Treatment of a Variety of Neurodegenerative Diseases
2009 US Patent Application 13/128,800 "Inhibition of mammalian target of rapamycin"
2013 US Patent Application "Use of TOR inhibitors to maintain cerebrovascular health and/or restore cerebrovascular dysfunction"
2014 US Patent Application "The use of Inhibitors of mTOR to Improve Vascular Functions in APOE4 Carriers and Reduce Risk for Alzheimer's Disease and other Neurovascular Disorders"

C. Contributions to Science (selected from 70 total publications)

h-index=40 i10 index=60
Total citations: 5,714 (2,847 citations since 2015)

1. Molecular mechanisms of Alzheimer's disease (AD). A major focus of my laboratory is on the molecular processes that lead to dementia in AD, with an emphasis on those that link brain aging to AD pathogenesis. We have identified mTOR-dependent inhibition of autophagy in neurons and the deactivation of e*ndothelial* and *neuronal* nitric oxide (NO) synthases as critical mTOR-dependent molecular abnormalities that initiate AD-like disease in mouse models. Our work demonstrated that systemic attenuation of mTOR with rapamycin prevents and also *treats* established AD-like deficits in mice modeling the disease by decreasing net Aβ buildup in brain through the restoration of (a) proteostasis and (b) vascular integrity and function, enhancing Aβ clearance from brain. Because mTOR inhibitors such as rapamycin and rapalogs are FDA-approved, our studies have immediate translational implications for the treatment of AD, and potentially other dementias. A recent clinical trial in our institution demonstrated safety in healthy older adults treated with 1 mg/day rapamycin (Kraig et al 2018 *Exp Gerontol* PMID: 29408453). An application to fund a phase I-II trial in mild cognitive impairment and AD patients at the Biggs Institute in UT Health San Antonio will be submitted in Cycle I (Feb 5) of 2020.

a. Spilman P, Podlutskaya N, Hart MJ, Debnath J, Gorostiza O, Bredesen D, Richardson A, Strong R and **Galvan V** (2010) Rapamycin abolishes cognitive deficits and reduces Aβ levels in a mouse model of Alzheimer's disease. *PLoS One* 5:e9979. PMCID: PMC2848616 ***815 citations - F1000 Recomm***
b. Halloran JJ, Hussong S, Podlutskaya N, Burbank R, Austad S, Hart MJ, Fischer K and **Galvan V**. (2012) Long-term mTOR inhibition by rapamycin modulates cognitive and non-cognitive components of behavior in mice. *Neurosci*. 223:102-113. PMCID: PMC3454865 ***169 citations - F1000 Recomm***
c. Lin A, Halloran JJ, Burbank RR, Korde S, Zheng W, Hussong SA, Podlutskaya N, Strong R, Richardson A, Hart MJ, Fox PT, Lechleiter J, **Galvan V** (2013). Chronic rapamycin restores brain vascular density and function through NO synthase activation and improves memory in symptomatic mice modeling Alzheimer's disease. *J Cereb Blood Flow Metab*. 33:1412-21. PMCID: PMC3764385 ***137 citations***
d. Van Skike CE, Jahrling JB, Olson AB, Sayre NL, Hussong SA, Ungvari ZI, Lechleiter JD, **Galvan V**. (2017) Inhibition of mTOR protects the blood-brain barrier in models of Alzheimer's disease and vascular cognitive impairment. *Am J Physiol Heart Circ Physiol*. 314:H693. PMCID: PMC5966773 ***Article selected as American Physiological Society's APSselect 'Best Articles'***
e. Van Skike CE, Lin AL, Roberts Burbank R, Halloran JJ, Hernandez SF, Cuvillier J, Soto VY, Hussong SA, Javors MA, Hart MJ, Fischer KE, Austad SN, **Galvan V.** (2020) mTOR drives cerebrovascular, synaptic, and cognitive dysfunction in normative aging. *Aging Cell* e13057. PMC6974719

2. Vascular pathogenic tau in AD. We recently provided the first evidence for vascular pathogenic soluble tau aggregates in the etiology of brain microvascular dysfunction in Alzheimer's disease (AD) and 'pure' tauopathies. We showed that soluble extracellular tau aggregates accumulate in AD brain microvasculature and propagate to microvascular cells, including brain vascular endothelial and smooth muscle cells. Our ongoing studies seek to define (a) the impact of soluble tau aggregate propagation on the regulation of cerebral blood flow and neurovascular coupling; (b) molecular abnormalities triggered by transmission of soluble tau aggregates to brain vascular endothelium; and (c) the potential for removal of tau via immunotherapy to treat cerebrovascular dysfunction of AD.

Castillo-Carranza DL, Nilson AN, Van Skike CE, Jahrling JB, Patel K, Gerson JE, Sengupta U, Abisambra J, Nelson P, Troncoso J, Ungvari Z, **Galvan V** and Kayed R (2017) Cerebral microvascular accumulation of tau oligomers in Alzheimer's disease and related tauopathies. *Aging Dis.* 8: 257-266. PMCID: 5440106. ***41 citations***

3. APP C-terminal proteolytic processing. Amyloid-ß, a peptide generated by proteolytic cleavage of the amyloid precursor protein (APP), is causally involved in Alzheimer's disease (AD). APP is a classic transmembrane protein with a short intracellular domain that serves as scaffold for signaling complexes and assembles with transcriptional complexes after its release by intramembranous cleavage of the APP precursor. My postdoctoral work provided the first *in vivo* evidence for a critical role of a novel proteolytic cleavage of APP at Asp664 in the etiology of synaptic and cognitive deficits of AD. These studies fundamentally changed our understanding of various APP preoteolytic products and their functional interplay, providing novel insights into mechanisms of AD neurodegeneration. New knowledge that was generated resulted in 2 patents and led to a clinical trial that started in 2014.

a. **Galvan V**, Gorostiza OF, Banwait S, Ataie M, Logvinova AV, Sitaraman S, Carlson E, Sagi SA, Chevallier N, Jin K, Greenberg DA, Bredesen DE. (2006) Reversal of Alzheimer's-like pathology and behavior in human APP transgenic mice by mutation of Asp664. *PNAS* 103:7130. PMCID: PMC1459029 ***259 citations - F1000 Recomm***

b. **Galvan V**, Chen S, Lu D, Koo EH and Bredesen DE. (2002) Caspase cleavage of members of the amyloid precursor family of proteins. *J Neurochem.* 82: 283-4. (No PMCID) ***116 citations***

c. Saganich MJ, Schroeder BE, **Galvan V**, Bredesen DE, Koo EH, Heinemann SF. (2006) Deficits in synaptic transmission and learning in APP transgenic mice require C-ter minal cleavage of APP. *J Neurosc*. 26:13428. PMCID: PMC6674728 ***121 citations***

d. Lourenco F, **Galvan V**, Corset V, Llambi F, Bredesen DE, and Mehlen P. (2009) Netrin-1 acts as an APP ligand and suppresses amyloid-ß production. *Cell Death Differ*. 16:655. PMCID: PMC2757418 ***89 citations–F1000 Recomm***

4. Biology of HSV-1 host-cell interactions. In my doctoral studies I discovered the pathways of activation and inactivation of programmed cell death triggered by contact of herpes simplex type 1 (HSV-1) virions with host cells. These studies provided the first evidence that HSV-1 activates several checkpoints of programmed cell death at the earliest time in infection and has evolved functions to block progression of all programmed death pathways triggered in infected cells. These studies opened up a new area of research in HSV-1-host cell interactions that led to important insights into the initial steps of both productive and latent infection by HSV-1 and prompted similar or divergent discoveries in other members of the Herpesvirus family. Data reported in Galvan and Roizman (1998) provided a foundation for additional subsequent high-impact studies and also contributed to the development and use of mutant HSV-1 vectors as oncolytic agents.

a. **Galvan V** and Roizman B. (1998) Herpes simplex virus 1 induces and blocks apoptosis at multiple steps during infection and protects cells from exogenous inducers in a cell-type-dependent manner. *Proc. Natl. Acad. Sci. USA* 95:3931-36. PMCID:PMC19940 ***269 citations***

b. **Galvan V**, Brandimarti R and Roizman B. (1999) Herpes simplex virus 1 blocks caspase-3-independent and caspase-dependent pathways to cell death. *J Virol.* 73:3219-26. PMCID:PMC104085. ***104 citations***

c. Zou G, **Galvan V**, Campadelli-Fiume G and Roizman B. (2000) Glycoprotein D or J delivered in trans blocks apoptosis in SK-N-SH cells induced by a herpes simplex virus 1 mutant lacking intact genes expressing both glycoproteins. *J Virol.* 74:11782-91.PMCID:PMC112461 ***181 citations***

d. **Galvan V**, Brandimarti R, Munger J and Roizman B. (2000) Bcl-2 blocks a caspase-dependent pathway of apoptosis activated by HSV-1 infection in HEp-2 cells. *J Virol.* 74:1931-38. PMCID:PMC111671.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1jkK1ehNbwzQp/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing

1R01 RF1 AG068283-01 Galvan, Van Remmen (MPI) 09/15/20 – 09/14/24
NIH/NIA
Tau-induced astrocyte senescence in Alzheimer's disease
The goal of this project is to define the involvement of tau-induced astrocyte senescence in AD and advance the knowledge of how pathogenic tau and senescence can be targeted therapeutically.
Role: PI/MPI

5I01BX002211-06 Galvan (PI) 10/01/19 – 09/30/23
VA Research and Development Merit Award
Pathogenic Tau Promotes Brain Vascular Dysfunction in Alzheimer's Disease
The major goal of this project is to define mechanisms of pathogenic tau-induced brain vascular dysfunction in AD and determine the potential for tau immunotherapy in AD and other tauopathies**.**
Role: PI

1R01AG057964 Perez, Galvan (MPI) 09/15/17 – 06/30/22
Brain cellular senescence as a driver of Alzheimer's disease
The goal of this project is to determine the role of brain cellular senescence in Alzheimer's disease.
Role: PI/MPI

Alzheimer's Association Part of the Cloud – Gates Award Seshadri (PI) 09/01/2020 - 08/31/22
Phase 2 Clinical Trial of Rapamycin for Alzheimer's Disease
The aim of this double-blinded placebo-controlled trial is to examine the safety, tolerability, and feasibility of one-year oral rapamycin treatment in individuals with amnestic mild cognitive impairment and Alzheimer's disease.
Role: Co-Investigator

2P30 AG013319-21 Strong (PI) 09/01/20 – 08/31/25
NIH/NIA SA Nathan Shock Center of Excellence in the Biology of Aging
This project supports the San Antonio Nathan Shock Center whose goal is to provide services to enable research in the biology of aging and in age-associated diseases.
Role: Core Co-Leader

T32 AG021890 Training Grant on the Biology of Aging 05/01/19 - 04/30/24
Musi, Nicolas (PI)
Galvan, Veronica (MPI)
Hornsby, Peter (MPI)
Role: Associate Director

1R01O9AG064078-01 Ran (PI) 08/01/19 – 04/30/24
Membrane lipid peroxidation in pathogenesis of Alzheimer's disease
The goal of this study is to understand the role of membrane lipid peroxidation in neurodegeneration of AD and define efficacy of Glutathione peroxidase 4 (Gpx4) as a target in AD.
Role: Co-Investigator

R41AG062163-01 Lechleiter (PI) 09/01/18 – 05/31/21
NIH/NIA
Astrocyte activation by small-molecule ADORA3 agonists: a novel therapy for Alzheimer's disease
The goal of this project is to define the efficacy of small molecule ADORA3 agonists as therapies for Alzheimer's disease using mouse models.
Role: Co-Investigator

Owens Foundation Award-08 12/01/20 - 11/31/21
William & Ella Owens Medical Research Foundation
Cerebrovascular tau in Alzheimer's disease
The goal of this project is to define the functional impact of pathogenic tau accumulation in brain vasculature in AD and other tauopathies.

Robert L. Bailey and daughter Lisa K. Bailey Alzheimer's Fund Galvan (PI) No expiration
The goal of this project is to determine the mechanisms that link signaling
through the mTOR pathway and the production of nitric oxide in vascular endothelial cells.
Role: PI

Completed (selected from last 3 years)

I01 BX002211-01A2 Galvan (PI) 01/26/15 – 12/31/19
Veterans Administration Research and Development Merit Award
Inhibiting the TOR Pathway to Combat Alzheimer's Disease
Goals of this project are to establish the therapeutic potential for rapamycin or other TOR inhibitors in the treatment of Alzheimer's disease (AD) and to determine rapamycin's mechanisms of action in AD brain.
Role: PI