BIOGRAPHICAL SKETCH

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NAME: Veronica Galvan, Ph.D.

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

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Center for Advanced Studies in Exact Sciences University, Buenos Aires, Argentina	MS	09/1994	Molecular Biology
University of Chicago	PhD	12/1999	Virology
Buck Institute for Research on Aging	Postdoctoral	12/2005	Neurobiology

A. Personal Statement

The focus of my research is on the molecular processes associated with aging 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, and I pioneered the study of mechanisms that link brain aging to the pathogenesis of AD and other dementias, providing the first evidence for a role of a molecular mediator of aging, the mammalian/ mechanistic target of rapamycin (mTOR), in the etiology of dementia. These studies have led to the first geroscience-based clinical trial in AD, currently ongoing, where I am a co-Investigator. My laboratory also recently provided the first description of pathogenic forms of tau in brain microvasculature of AD and other tauopathies, and singled out the induction of cellular senescence, a 'pillar' of aging, as a major mechanism of tau-induced vascular dysfunction in AD. The goal of our work is to close gaps in our understanding of AD and other tauopathies, determine how key mediators of aging (mTOR and cellular senescence) can be targeted for therapeutic purposes, and fundamentally advance the geroscience, neuroscience, and neurodegeneration fields.

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

5I01BX002211-10 Galvan (PI) 01/01/24 -12/31/28
VA Research and Development Merit Award
Pathogenic Tau Promotes Brain Vascular Dysfunction in Alzheimer's Disease
Role: PI

1RF1 AG068283-01 Galvan, Van Remmen (PI/MPI) 09/15/20 – 09/14/25
NIH/NIA
Tau-induced astrocyte senescence in Alzheimer's disease
Role: Lead PI/MPI

P30AG050911-08 Galvan, Van Remmen (PI/MPI) 06/01/20 - 05/31/25
NIH/NIA
Oklahoma Nathan Shock Center of Excellence in the Basic Biology of Aging
Role: Lead PI/MPI

1 IK6 BX006026-01 Galvan (PI) 04/01/22 – 03/31/27
VA Research Career Scientist Award
Role: PI

1RF1AG065301-01A1 Pickering (PI) 09/30/20 – 08/31/24
NIH/NIA
Proteasome dysfunction as a driver of age-associated risk for Alzheimer's disease onset and progression
Role: Co-Investigator

Alzheimer's Drug Discovery Foundation (ADDF) Grant Lechleiter (PI) 09/01/23 – 08/31/25
Astrocyte Pharmaceuticals
Efficacy of AST-004, an astrocyte-targeted compound, in mouse models of Alzheimer's disease.
Role: Co-Investigator

Recent publications that I would like to highlight include:

1. Hussong SA, Banh AQ, Van Skike CE, Dorigatti AO, Hernandez SF, Hart MJ, Ferran B, Makhlouf H, Gaczynska M, Osmulski PA, McAllen SA, Dineley KT, Ungvari Z, Perez VI, Kayed R, **Galvan V** (2023). Soluble pathogenic tau enters brain vascular endothelial cells, driving cellular senescence and brain microvascular dysfunction in tauopathy. *Nature Comm.* 14:2367. PMID:37185259.
2. Van Skike CE, Hussong SA, Hernandez SF, Banh AQ, DeRosa N and **Galvan V** (2021) mTOR attenuation with rapamycin reverses neurovascular uncoupling and memory deficits in mice modeling Alzheimer's disease. *J Neurosci* 41:4305-4320. *J Neuroscience Featured Research*
3. Van Skike CE, Lin AL, Roberts Burbank R, Halloran JJ, Hernandez SF, Cuvillier J, 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* 19:e13057. PMC6974719.
4. 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. PMC2848616 ***1107 citations*** *F1000 recommended*

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022 - present	NIA P30 Oklahoma Nathan Shock Center of Excellence in the Basic Biology of Aging	Director
2022 - present	US Department of Veterans Affairs	Research Career Scientist
2022 – present	NIA P20 Geroscience Center for Biomedical Research Excellence (CoBRE)	Co-Director
2021 - present	Center for Geroscience and Healthy Brain Aging, University of Oklahoma Health Sciences Center	Co-Director
2021 - present	Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center	Professor
2015 – 2021	Department of Cellular and Integrative Physiology and The Barshop Institute, University of Texas Health San Antonio	Associate Professor
2015 - 2021	US Department of Veterans Affairs	Research Health Scientist
2009 – 2015	Department of Physiology and The Barshop Institute, University of Texas Health Science Center at San Antonio	Assistant Professor
2005 - 2008	Buck Institute for Age Research (*Mentor: Dale Bredesen*)	Staff Scientist
1999 - 2005	Buck Institute for Age Research (*Mentor: Dale Bredesen*)	Postdoctoral Fellow
1994 - 1999	University of Chicago, Department of Molecular Genetics and Cell Biology, Committee on Virology (*Mentor: Bernard Roizman*)	Graduate Student

Memberships, Service and Other Professional Activity

2023	Ad-Hoc Reviewer, NIA Board of Scientific Counselors
2023 – present	External Advisory Board, U Washington Nathan Shock Center
2023 – present	External Advisory Board, U Washington T32 Biological Mechanisms of Healthy Aging Training Program
2023 – present	Vice-Chair, Oklahoma City Veterans Affairs Health Care System IACUC
2021 – 2022	President, American Aging Association
2021 – present	Member, National Scientific Advisory Council, American Federation for Aging Research
2021 – 2023	Member, Oklahoma City Veterans Affairs Health Care System R&D Committee
2010 – 2021	Leader, Nervous System Function Assessment Lab (2010-2015); Co-leader, Healthspan and

Functional Assessment Core (2015-2019); Co-leader, Integrative Physiology of Aging Core (IPAC) (2019-2021); NIA P30 San Antonio Nathan Shock Center of Excellence in the Basic Biology of Aging, University of Texas Health San Antonio

2019 – 2021 Associate Director, T32 Training Program on the Biology of Aging, UT Health San Antonio

2018- present Member, Executive Committee, American Aging Association

2018- present Member, Board of Directors, American Aging Association

2017-2018 Member, Program Committee, 48th Annual Meeting of the American Aging Association

2017 Co-Organizer, 2017 Barshop Symposium on Aging '*Sex Differences in Aging, Age-related Diseases and Interventions*'

2016 Member, Committee to implement Chancellor-initiated University of Texas System Moonshot initiative to tackle Parkinson's disease

2015 Organizer and Chair, 2016 International Conference on Aging and Disease Session III, "*Aging, metabolism and disease*"

2015-2016 Member, Scientific Program Committee, BRAIN & BRAINPET 2017 ISCBFM International Symposium

2015-2016 Member, Young Investigator Committee, BRAIN & BRAINPET 2017 ISCBFM International Symposium

2015–2016 Member, Scientific Program Committee, 2016 International Conference on Aging and Disease, Stanford University

2014–2017 Co-convener, Brain Interest Group (BIG), Gerontological Society of America

2014–2016 Member, Scientific Advisory Board, Rapa Holdings Inc. (currently Emtora Biosciences)

2013–2016 Research Chair, Board of Directors, Alzheimer's Association South Texas Chapter

2011-2019 Member, National Scientific Advisory Council, American Federation for Aging Research

2010–2021 Member, Internal Selection and Steering Committee, NIH T32 Training Program in the Biology of Aging, Barshop Institute, University of Texas Health San Antonio

2003 .. 2010-present Member, Society for Neuroscience; International Behavioral Neuroscience Society; American Aging Association; ISTAART

Honors

2020 Fellow, American Aging Association

2010 Ellison Medical Foundation New Scholar Award in Aging

2006 S.D. Bechtel Jr. Foundation Alzheimer's Award

2003 John D. French Alzheimer's Foundation Fellow

2003 Scholar, National Institute on Aging Summer Institute on Aging Research (currently Butler-Williams Scholar Program)

2002 Eppley Foundation Award

1994 Lucille P. Markey Scholarship in Biomedical Sciences

1994 Baxter Young Investigator Award

Editorial Duties

2021 – present Editor-in-Chief, *Geroscience* (Journal of the American Aging Association)

2022 – present Editorial Board, *Aging Biology*

2019 – 2022 Associate Editor, *Aging Cell*

2020 – 2022 Member, Editorial Board, *Aging Cell*

2019 – 2021 Deputy Editor, *Geroscience* (Journal of the American Aging Association)

2019 – 2020 Associate Editor, eLife Special Issue "Aging, Geroscience and Longevity: A Special Issue"

2018 – 2022 Associate Editor, *Journal of Gerontology: Biological Sciences*

2016 – 2019 Associate Editor, *Geroscience*, Official Journal of the American Aging Association

2014 – 2021 Review Editor, *Frontiers in Molecular Biosciences, Protein Folding and Degradation*

2013 – present Member, Editorial Board, *Archives of Physiology*

2010 – present Member, Editorial Board, *Aging and Disease*

Review Panel Participation (federal only)

2021 Member, P01 Special Emphasis Panel, NIA Special Emphasis Committee

2020 – 2026 Standing (permanent) Member, NIH/CSR Cellular Mechanisms in Aging and Development (CMAD)

2020 Member, P01 Special Emphasis Panel, NIA Special Emphasis Committee

2020 - 2021	Member, NIH/CSR NIA-B Scientific Review Group
2020	Member, NIH RFA-NS-20-004 Neuroscience Special Emphasis Panel
2019	Member, NIH/CSR Chronic Dysfunction and Integrative Neurodegeneration (CDIN)
2018	Member, NIH Special Emphasis Panel ZAG1 ZIJ-P A1
2018	Member, VA Neurobiology C (NURC) Study Section, Veterans Administration
2016 - 2018	Member, NIH/CSR Cellular Mechanisms in Aging and Development (CMAD)
2016	Member, NIH/CSR Study Section ZRG1 MDCN-T
2015 – 2018	Member, VA Neurobiology D Study Section (NURD), Department of Veterans Affairs

C. Contributions to Science (selected from 94 total publications)

h-index=53 i10 index=79
Total citations: 9,468 (4,413 citations since 2019)

1. Molecular mechanisms of Alzheimer's disease (AD). A major focus of my research is on the molecular processes associated with aging that lead to dementia, with an emphasis on those that link brain aging to the pathogenesis of AD. mTOR is a central driver of aging. We have identified mTOR-dependent deactivation of endothelial and neuronal nitric oxide (NO) synthases as critical mTOR-dependent molecular abnormalities that initiate AD-like disease in mouse models. Our work also demonstrated that systemic attenuation of mTOR with rapamycin prevents and treats established AD-like disease in model mice 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). The first Phase 2 clinical trial of rapamycin in MCI and early AD is currently ongoing at our institution.

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 ***1148 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 ***223 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. PMC3764385 ***222 citations***

d. Van Skike CE, Hussong SA, Hernandez SF, Banh AQ, DeRosa N and **Galvan V** (2021) mTOR attenuation with rapamycin reverses neurovascular uncoupling and memory deficits in mice modeling Alzheimer's disease. *J Neurosci* 41:4305-4320. PMC8143195. *J Neuroscience Featured Research*

2. Vascular tau pathology and the induction of cellular senescence in Alzheimer's disease and other tauopathies. We recently provided 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 cells, potently inducing endothelial cell senescence. Our ongoing studies seek to define (a) the impact of soluble tau aggregate propagation on the induction of senescence in brain endothelial cells and in astrocytes; (b) the molecular abnormalities triggered by transmission of soluble tau aggregates to brain vascular endothelium; and (c) the potential for removal of pathogenic tau via immunotherapy to block the induction of tau-induced braom vascular senescence in AD.

a. Hussong SA, Banh AQ, Van Skike CE, Dorigatti AO, Hernandez SF, Hart MJ, Ferran B, Makhlouf H, Gaczynska M, Osmulski PA, McAllen SA, Dineley KT, Ungvari Z, Perez VI, Kayed R, **Galvan V** (2023). Soluble pathogenic tau enters brain vascular endothelial cells, driving cellular senescence and brain microvascular dysfunction in tauopathy. *Nature Comm.* 14:2367. PMID:37185259. ***23 citations since 2023***

b. 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. ***105 citations***

3. Role of APP C-terminal proteolytic processing in Alzheimer's disease. 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 proteolytic products, providing novel insights into mechanisms of AD neurodegeneration. New knowledge that was generated resulted in 2 patents and led to a clinical trial.

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
298 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) ***124 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-terminal cleavage of APP. *J Neurosc*. 26:13428. PMCID: PMC6674728 ***154 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
130 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 programmed cell death at the earliest steps in infection and has evolved functions to block all programmed death pathways triggered in infected cells. These studies opened up a new area of research in HSV-1-host cell interactions, providing seminal insights into the initial steps of productive and latent infection by HSV-1 and prompting similar or divergent discoveries in other members of the Herpesvirus family. Data reported in Galvan and Roizman (1998) provided a foundation for 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. *PNAS. USA* 95:3931-36. PMCID:PMC19940 ***295 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.
118 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 ***205 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.
74 citations

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1jkK1ehNbwzQp/bibliography/public/