BIOGRAPHICAL SKETCH

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NAME: Stacy A. Hussong

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POSITION TITLE: Assistant Professor of Research, Research Health Scientist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of South Dakota, Vermillion, SD	B.S.	08/2005	Biology
University of South Dakota, Vermillion, SD	B.S.	08/2005	Chemistry
University of Minnesota, Minneapolis, MN	Ph.D.	10/2010	Biochemistry (major) Gerontology (minor)
University of Texas Health Science Center at San Antonio, San Antonio, TX	Postdoctoral	2010-2017	Physiology

A. Personal Statement

The broad goal of my research is to determine the role of the mechanistic target of rapamycin complex 1 (mTORC1) in the aging brain as well as in the pathogenesis of Alzheimer's disease (AD). Specifically, my goal is to determine the contribution of mTORC1 signaling from neurons in the brain and to the pathogenesis of Alzheimer's-like disease in a mouse model. I received extensive training in chemistry and biochemistry during my undergraduate and graduate studies. My training in neurobiology began during my graduate studies with a project that focused on role of the immunoproteasome, a subtype of proteasome that is thought to function primarily in the immune system, in age-associated retinal dysfunction. As a postdoctoral fellow in the laboratory of Veronica Galvan at the Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center at San Antonio, I continued my training in neuroscience, focused on the molecular mechanisms that link the regulation of brain aging to those driving the pathogenesis of Alzheimer's disease (AD).

mTOR is a major regulator of mammalian aging. A major focus of my lab is to identify the mechanisms that link the regulation of aging to the pathogenesis of Alzheimer's disease, and thus explain the increased vulnerability of aged brain to AD. As a postdoctoral fellow I made critical contributions to studies that demonstrated that a major target of mTOR-dependent aging processes in brain maps to brain vascular endothelium, specifically as the inhibition of nitric oxide-dependent mechanisms of vascular reactivity, critical for neurovascular coupling, a central homeostatic mechanism adjusting cerebral blood flow (CBF) to the increased metabolic needs of activated neuronal tissue. Neuronal networks and brain vasculature form an indivisible functional unit in the brain. While we know that critical mTOR-dependent mechanisms of AD operate in endothelium, whether mTOR signaling in neurons contributes to AD-like pathogenesis in mouse models is still unknown. I am currently studying this question by genetically reducing mTORC1 specifically in neurons to define the contribution of neuronal mTORC1 to AD-like cognitive, synaptic, and brain vascular deficits in AD model mice. This research has broad implications for our understanding of the mechanisms of AD pathogenesis, and will define neuron-specific mTOR-dependent pathways of AD. Ongoing experiments will utilize my expertise and strengths but will also provide me with critical training that will expand competencies critical for the development of my own research program and for my continuing development as an independent investigator.

I have received numerous awards and honors that recognized academic and professional career accomplishments during my graduate and postgraduate training, as well as a faculty member at UT Health San Antonio and a Research Health Scientist at the South Texas Veterans Health Care System. I recently moved to the University of Oklahoma Health Sciences Center and the Oklahoma City Veterans Health Care System. I am currently funded by a Career Development Award (CDA-2) through the Department of Veterans Affairs and on the path to becoming and independent investigator.

B. Positions and Honors

Positions and Employment

2005-2010	Graduate Research Assistant, Department of Biochemistry, Molecular Biology, & Biophysics, University of Minnesota (Mentor, Deborah Ferrington, Ph.D.)
2010-2017	Postdoctoral Fellow, Department of Cellular and Integrative Physiology and Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center at San Antonio (Mentor, Veronica Galvan, Ph.D.)
2017-2021	Instructor/Research, Department of Cellular and Integrative Physiology and the Barshop Institute for Longevity and Aging Studies, University of Texas Health at San Antonio
2018-2021	Research Health Scientist, South Texas Veterans Health Care System, Department of Veterans Affairs
2021-present	Assistant Professor of Research, Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center
2021-present	Research Health Scientist, Oklahoma City Veterans Health Care System, Department of Veterans Affairs

Other Experience and Professional Memberships

2006-2010	Member, Association of Research in Vision and Ophthalmology
2011-present	Member, American Aging Association
2011-present	Ad hoc reviewer, *Journal of Alzheimer's Disease*
2012-present	Ad hoc reviewer, *Journal of Gerontology*
2016-present	Ad hoc reviewer, GeroScience-*Journal of the American Aging Association*
2018-present	Ad hoc reviewer, *Journal of Integrative Neuroscience*
2018-present	Ad hoc reviewer, *Scientific Reports*
2019-present	Ad hoc reviewer, *Journal of Nutrition and Healthy Aging*
2020-present	Editorial board member, *Frontiers in Aging: Interventions in Aging*

Academic and Professional Honors

1999	Alpha Lambda Delta Honor Society
2002	Dr. Joseph R. Spies Chemistry Scholarship, University of South Dakota
2002	Dean Joseph H. Cash Award for Excellence in Writing, University of South Dakota
2002	Golden Key International Honor Society
2003-2004	Senior Merit Award in Chemistry, University of South Dakota
2005	Phi Beta Kappa Society
2005	Magna Cum Laude, University of South Dakota
2007	Best Poster Award, Biochemistry, Molecular Biology, & Biophysics Departmental Retreat, University of Minnesota
2007, 2008	Travel Fellowship Award, Department of Biochemistry, Molecular Biology, & Biophysics, University of Minnesota
2007	Invited Speaker, San Antonio Nathan Shock Aging Center Conference on Aging
2008-2010	National Research Service Award (NRSA) Institutional Training Grant, University of Minnesota, Functional Proteomics in Aging
2009	Graduate and Professional Student Assembly Scholarly Travel Award, University of Minnesota
2009	Invited Speaker, Scientists in Aging Research Fall Symposium, University of Minnesota
2009	Best Poster Award, Gordon Research Conference, Biology of Aging
2010	Outstanding Poster Presentation, Midwest Eye Research Symposium
2010-2013	NRSA Institutional Training Grant, UTHSCSA, Biology of Aging
2012	Third Place Best Poster Award, Center for Biomedical Neuroscience, 10th Annual Retreat, University of Texas Health Science Center at San Antonio
2013	Research Poster Award – 3rd Place, 1st Annual Postdoctoral Research Forum and Distinguished Lecture
2014	San Antonio Life Sciences Institute Best Poster Presentation, 2nd Annual Postdoctoral Research Forum and Distinguished Lecture

2015	Joe and Bettie Ward Award for Excellence in the Study of the Biology of Aging
2016	Superior Postdoctoral Poster Award, 45th Annual Meeting of the American Aging Association
2018-2023	Career Development Award (CDA-2), Department of Veterans Affairs
2018	Outstanding Junior Faculty Poster Presentation, Center for Biomedical Neuroscience 16th Annual Retreat, UT Health San Antonio
2018	Poster Presentation Award – Junior Faculty, 21st Annual Department of Medicine Research Day, UT Health San Antonio
2018	Junior Faculty Travel Award, American Aging Association 47th Annual Meeting
2019	Poster Presentation Award – VA Non-Clinical Research – Faculty, 22nd Annual Department of Medicine Research Day, UT Health San Antonio
2019	Junior Faculty Travel Award, American Aging Association 47th Annual Meeting

C. Contribution to Science

1. The research from graduate career focused on describing novel roles of the immunoproteasome in the retina. The immunoproteasome was previously thought to primarily function in the immune system. The data from my research has shown that the immunoproteasome plays an important role in the retinal stress response as well as retinal function. Immunoproteasome is upregulated with many types of stress including retinal injury, oxidative stress, age, and light damage. Mice lacking immunoproteasome respond differently to stress and are more resistant to retinal injury. However, immunoproteasome is required for normal retinal function and immunoproteasome deficient mice have impaired retinal function as measured by electroretinogram. Overall, my research findings have shown that the immunoproteasome is important in the retinal stress response and also retinal function.
   a. Ethen, C.M., **Hussong, S.A.**, Reilly, C., Feng, X., Olsen, T.W. and Ferrington, D.A. (2007) Transformation of the proteasome with age-related macular degeneration. *FEBS Letters* 581: 885-890. PMCID: PMC1850528
   b. Ferrington, D.A., **Hussong, S.A.**, Roehrich, H., Kapphahn, R.J., Kavanaugh, S., Heuss, N. and Gregerson, D.S. (2008) Immunoproteasome responds to injury in the retina and brain. *J. Neurochem.* 106: 158-169. PMCID: PMC4401486
   c. **Hussong, S.A.**, Kapphahn, R.J., Phillips, S.L., Maldonado, M. and Ferrington, D.A. (2010) Immunoproteasome deficiency alters retinal proteasome's response to stress. *J. Neurochem.* 113: 1481-1490. PMCID: PMC2909641
   d. **Hussong, S.A.**, Roehrich, H., Kapphahn, R.J., Maldonado, M., Pardue, M.T. and Ferrington, D.A. (2011) A novel role for immunoproteasome in retinal function. *IOVS* 52: 714-723. PMCID: PMC3053103
   e. Schuld, N.J.*, **Hussong, S.A.* (*authors contributed equally)**, Kapphahn, R.J., Lehmann, U., Roehrich, H., Rageh, A., Heuss, N., Gregerson, D.S., Ferrington, D.A. (2015) Immunoproteasome deficiency protects the retina after optic nerve crush. *PlosOne*. 10(5): e0126768. PMCID: PMC4433222
   f. Heuss, N.D., Pierson, M.J., Montaniel, K.R., McPherson, S.W., Lehmann, U., **Hussong, S.A.**, Ferrington, D.A., Low, W.C., Gregerson, D.S. (2014) Retinal dendritic cell recruitment, but not function, was inhibited in MyD88 and TRIF deficient mice. *J. Neuroinflammation*. 11:143. PMCID: PMC4149240

2. Aging is the major risk factor for Alzheimer's disease. A major focus of my current research is on the investigation of pathways that mechanistically link the mTORC1 regulation of the rate of brain aging and the pathogenesis of Alzheimer's disease. We have identified mTOR-dependent inhibition of autophagy in neurons and the inhibition of endothelial nitric oxide (NO)-dependent release of NO in brain vasculature as two critical mechanisms that render aged brains vulnerable to AD-like pathogenesis in mice. Our work demonstrated that systemic attenuation of mTOR activity with rapamycin, an intervention that extends lifespan by delaying aging can prevent and also *treat* established Alzheimer's-like deficits in mice modeling the disease and that this hinges on two critical mechanisms: The relief of mTOR-dependent inhibition of (a) autophagy, decreasing levels of production of Aβ in brain parenchyma, and (b) restoration of vascular integrity, enabling sustained Aβ clearance from brain in a manner dependent on eNOS-mediated NO release and vasodilation mediated by vascular endothelial cells. Because mTOR inhibitors such as rapamycin are FDA-approved, our studies have significant immediate translational implications for the treatment of Alzheimer's, and potentially other neurological diseases of aging beyond Alzheimer's alone.

a. Halloran, J.*, **Hussong, S.A.* (*authors contributed equally)**, Burbank, R.R., Podlutskaya, N., Fischer, K., Sloane, L., Austad, S., Strong, J.R., Richardson, A., Hart, M. and Galvan, V. (2012) Chronic inhibition of mammalian target of rapamycin by rapamycin modulates cognitive and non-cognitive components of behavior throughout lifespan in mice. *Neuroscience.* 223C:102-113. PMCID: PMC3454865. *This article was recommended by Faculty of 1000*

b. Pierce, A., Podlutskaya, N., **Hussong, S.A.**, Halloran, J.J., Burbank, R.R., Strong, J.R., Richardson, A., Hart M.J. and Galvan, V. (2013) Upregulation of heat shock proteins by chronic rapamycin treatment lowers Aβ and prevents cognitive impairment in mice modeling Alzheimer's disease. *J. Neurochem.* 124: 880-893.

c. Lin, A.-L., Zheng, W., Halloran, J.J., Burbank, R.R., **Hussong, S.A.**, Hart, M.J., Javors, M., Shih, Y.-Y., Muir, E., Solano Fonseca, R., Strong, R., Richardson, A.G., Lechleiter, J.D., Fox, P.T., and Galvan, V. (2013) Chronic rapamycin restores brain vascular integrity and function through NO synthase activation and improves memory in symptomatic mice modeling Alzheimer's disease. *J. Cereb. Blood Flow Metab.* 33: 1412-1421. PMCID: PMC3764385

d. Lin, A.L., Pulliam, D.A., Deepa, S.S., Halloran, J.J., **Hussong, S.A.**, Burbank, R.R., Bresnen, A., Liu, Y., Podlutskaya, N., Soundararajan, A., Muir, E., Duong, T.Q., Bokov, A.F., Viscomi, C., Zeviani, M., Richardson, A.G., Van Remmen, H., Fox, P.T., Galvan, V. (2013) Decreased in vitro mitochondrial function is associated with enhanced brain metabolism, blood flow, and memory in Surf1-deficient mice. *J. Cereb. Blood Flow Metab.* 33: 1605-1611. PMCID: PMC3790931
This article was recommended by Faculty of 1000

e. Jahrling, J.B., Lin, A-L., DeRosa, N., **Hussong, S.A.**, Van Skike, C.E., Girotti, M., Javors, M., Zhao, Q., Maslin, L.A., Asmis, R., Galvan, V. (2018) mTOR Drives Cerebral Blood Flow and Memory Deficits in LDLR-/- Mice Modeling Atherosclerosis and Vascular Cognitive Impairment. *J. Cereb. Blood Flow Metab.* 38(1): 58-74. PMCID: PMC5757441

f. Van Skike, C.E.,Jahrling, J.B., Olson, A.B., Sayre, N.L., **Hussong, S.A.**, Ungvari, Z., Lechleiter, J.D., Galvan, V. (2018) 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(4): 58-74. PMCID: PMC5966773

g. Van Skike, C.E., Lin, A-L., Burbank Roberts, R.R., Halloran, J.J., Hernandez, S.F., Cuvillier, J., Soto, V., **Hussong, S.A.**, Jahrling, J., Javors, M., Hart, M.J., Fischer, K., Austad, S.A., and Galvan, V. 2020. mTOR drives cerebrovascular, synaptic, and cognitive dysfunction in normative aging. *Aging Cell.* **19(1):** e13057. PMCID: PMC6974719.

h. Dorigatti, A.O.*, **Hussong, S.A.* (*authors contributed equally)**, Hernandez, S.F., Sills, A.M., Salmon, A.B., Galvan, V. 2020. Primary neuron and astrocyte cultures from postnatal *Callithrix jacchus*: a non-human primate in vitro model for research in neuroscience, nervous system aging, and neurological diseases of aging. *GeroScience* **43(1)**: 115-124. PMCID: PMC8050148.

i. Van Skike, C.E., **Hussong, S.A.**, Hernandez, S.F., Banh, A.Q., 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(19)**: 4305-4320. PMCID: PMC8143195.

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/pubmed/?term=Hussong+SA%5BAuthor%5D

D. Research Support

Current

1 IK2 BX003798-01A1 (Hussong) 04/01/2018-3/31/2023

Veterans Administration Career Development Award (CDA-2)

The Role of Neuronal mTORC1 in Alzheimer's Disease

The goal of this project is to define the contribution of neuronal-driven mTOR-dependent mechanisms of Alzheimer's disease pathogenesis by measuring cognitive behaviors, synaptic function, and vascular function.

Completed

1 I01 BX002211-01A2 (Galvan) 01/26/15 – 01/25/19

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: Key Personnel

OWENS FUND 2014 (Galvan) 03/01/2014-02/28/15
William & Ella Owens Medical Research Foundation
Rapamycin as a therapy for vascular damage in Alzheimer's disease
The goal of this project is to determine whether rapamycin maintains memory in AD mice by blocking Aβ-induced vessel damage.
Role: Postdoctoral Fellow

AG-NS-0726-10 (Galvan) 08/01/10-07/31/14
Ellison Medical Foundation – New Scholar Award in Aging
Neuronal mTOR in Mammalian Aging
The goal of this project is to determine the role of mTOR signaling from the nervous system in the control of aging in mammals.
Role: Key Personnel

T32 AG021890 (Austad/Strong) 11/01/10-10/31/13
NIH/NIA
Training Grant: Biology of Aging
This grant supports the training of pre-doctoral and postdoctoral fellows in aging research.
Role: Postdoctoral trainee