NAME:	Laura E. Villasana, Ph.D.

Date: October 27, 2020

Present Position and Address

 Title:
 Assistant Scientist

 Department/Division:
 Dow Laboratories of Neuroscience, Legacy Research Institute

 Professional Address:
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 Ivillasana@downeurobiology.org

EDUCATION:

2001, B.S. University of Houston, Houston, TX 2011, Ph.D. Oregon Health & Science University, Portland, OR

Professional Experiences:

- 2020 Assistant Scientist, Dow Laboratories of Neuroscience, Legacy Research Institute, Portland, OR
- 2020 Adjunct Assistant Professor, Anesthesiology & Perioperative Medicine, OHSU, Portland, OR
- 2015 2020 Assistant Professor, Anesthesiology & Perioperative Medicine, OHSU, Portland, OR
- 2015 2020 Director of APOM Behavioral Core, Anesthesiology & Perioperative Medicine, OHSU, Portland, OR
- 2011-2015 Postdoctoral Fellow, Anesthesiology & Perioperative Medicine, OHSU, Portland, OR
- 2005-2011 Graduate Student, Dept. of Behavioral Neuroscience, OHSU, Portland OR
- 2001-2005 Lab manager, Dept. of Molecular Physiology & Biophysics, Baylor College of Medicine, Houston, TX

RESEARCH INTERESTS:

The generation of adult-born neurons, neurogenesis, persists throughout aging and is important for learning and memory and possibly mood regulation. Following different types of brain injury, neurogenesis is increased within the hippocampus, a brain region critical for memory. In contrast to adult-born neurons generated in an uninjured brain, we previously found that neurons generated after traumatic brain injury (TBI) have abnormal developments in their dendritic arborization and migration within the hippocampus. Yet despite their abnormal development, these neurons functionally integrate within their network. The main focus of my current research is to understand how these new neurons integrate themselves within an already established network and determine whether they improve or possibly worsen cognitive recovery after brain injury. To address these questions, my lab utilizes molecular, cellular and behavioral approaches in mouse models of TBI to study acute and long-term changes in the hippocampal cells involved in neurogenesis and in neurogenesis-dependent cognitive function. I am also interested in determining how exposure to clinically relevant sedatives after brain injury influences post-traumatic neurogenesis; the long-term effects of TBI on the integrity of neural stem cells; and the role that sex may play on TBI outcomes.

ACADEMIC HONORS AND AWARDS:

2006Society for Neuroscience Oregon Chapter Travel Award2006OHSU Student Research Forum Poster Presentation Award2006NIA Training Grant

- 2007 Tartar Scholarship
- 2007 Ginger Ashworth Scholarship
- 2008 OHSU Student Research Forum Oral Presentation Award
- 2008 NIA Training Grant
- 2008 NIMH R01 Supplement
- 2010 Society for Neuroscience Oregon Chapter Best Poster Presentation Award
- 2010 American Aging Society Oral Presentation Award
- 2010 PARC/MARC Travel Award
- 2010 American Psychological Association Dissertation Research Award
- 2011 Organization for the Study of Sex Differences New Investigator Travel Award
- 2011 Society for Neuroscience Oregon Chapter Best Oral Presentation Award
- 2013 Ruth L. Kirschstein National Research Service Award (NRSA)
- 2014 Society for Neuroscience Travel Award
- 2015 Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Award
- 2015 American Physiological Society Minority Travel Award
- 2016 Collins Medical Trust
- 2020 Legacy Health Start up Foundation
- 2020 Oregon Tax Checkoff for Alzheimer's Research Fund

PROFESSIONAL MEMBERSHIPS:

- 2002- Society for Neuroscience
- 2010-12 American Aging Society
- 2010-13 American Psychological Association
- 2011-12 Organization for the Study of Sex Differences
- 2008-10 Society for the Advancement of Chicanos and Native Americans in Science

Current Grants:

Legacy Health Start up FoundationVillasana (PI)4/01/20 – 4/01/21Neuronal repair and regeneration following brain injury. The research goal of this proposal is
understand how neurodegenerative processes that occur in response to brain injuries such as
traumatic brain injury and stroke facilitate cognitive recovery.Role: PI

<u>Oregon Tax Checkoff for Alzheimer's Research</u> Villasana (PI) 09/01/20- 09/01/21 *Amyloid beta abnormal neurogenesis after traumatic brain injury and hippocampal dysfunction.* The goals of this research are to determine whether preventing increases in amyloid beta post injury prevents the aberrant development of adult-born neurons and improves learning and memory. Role: PI

R01AG064016-A1Walker (PI)04/01/20 – 03/31/25Large artery stiffness and cerebrovascular dysfunction: Implications for cognitive impairment and
neuropathologyneuropathologyRole: ConsultantNeuropathologyNeuropathology

GRANTS HELD:

Collins Medical TrustVillasana (PI)10/01/17 - 10/01/18The role of neurogenesis on cognitive recovery after brain injury. The research goals of this project
were to confirm whether labeled TBI-induced adult-born neurons integrate into the hippocampal
circuitry in a functional manner using behavioral approaches and to determine whether inhibition of
post-traumatic neurogenesis with sedatives improves or worsens performance on hippocampal-
dependent behavioral tests.
Role: PI

K-12 BIRCWH	Guise/Dorsa (PI)	10/01/15 - 09/30/17
The role of sex on long-term changes in hippoc	ampal neurogenesis after	traumatic brain injury. The
research goals of this project were to gain a be	ter understanding of the m	echanisms underlying long-
term deficits in neurogenesis after TBI and to estimate	stablish whether these defi	cits are influenced by sex.
Role: BIRCWH trainee		
F32-NINDS, NRSA	<u>Villasana (PI)</u>	09/20/13 - 04/30/15
Synaptic integration of newborn neurons after t	raumatic brain injury.	
The major goal of this project was to determine	whether hippocampal new	/born neurons induced by a
controlled cortical impact injury integrate into th	e hippocampal circuitry and	d to determine the functional
significance of post-traumatic neurogenesis.		
Role: Post-doctoral trainee.		
T32-NIH Training Grant	Kirch (PI)	12/15/11-06/15/13
Integrated and Translational Training in Anasth	esiology Research	12/13/11-00/13/13
The major goal of this project was to determine	whether closed head injur	v induced hippocampal
neurogenesis and to determine whether clinical	ly relevant sedative influen	induced inproceampair
integration of neurons born after injury		lee the generation and
Role: Post-doctoral trainee.		
NIMH (RO1 Supplement)	Raber (PI)	04/01/08 - 06/31/11
Role of mGluR8 in anxiety.		
The major goal of this project was to determine	the role of the mGluR8 rec	ceptor in anxiety and to test
the hypothesis that effects of mGluR8 signaling	on the neuropeptides CRF	F and AVP contribute to the
increased anxiety of mGluR8 deficient mice.		
Role: Graduate Student		
NIA, Training Grant	Janowsky (PI)	07/19/06 - 7/19/08
The major goals of this project were to determine	ne the role of neurogenesis	on apoE-isoform dependent
effects of ⁵⁶ Fe and 137Cs irradiation on cognitiv	e function and to determin	e whether these effects were
sex- and age-dependent.		
Role: Graduate Student		
NIAAA, Training Grant	Neve (PI)	07/19/05 - 7/19/06
The major goal of this project was to determine	the role of Edinger-Westpl	hal (EW) on anxiety-like
behaviors.		
Role: Graduate Student		

PEER REVIEWED PUBLICATIONS:

- Denfeld, Q., Erickson, E., Valent, A., Villasana, L. Zhang, Z., Myatt, L., and Guise, J. (2020) COVID-19: Challenges and lessons learned from early career investigators. J. Womens Health. 29(6):752-754. PMID 32469620
- Villasana, L.E., Peters, A., McCallum, R., Liu, C., and Schnell, E. (2019) Diazepam inhibits posttraumatic neurogenesis and blocks aberrant dendritic development. J. Neurotraum. 36(16): 2454-2467. PMID 30794026
- Peters, A., Villasana, L.E, and Schnell, E. (2018) Ketamine alters hippocampal cell proliferation and improves learning in mice after traumatic brain injury. Anesthesiology 129(2): 278-295. PMID 29734230
- 4. **Villasana, L.E.**, Akinyeke, T., Weber, S., and Raber, J. (2017) Paradoxical effects of 137Cs irradiation on pharmacological stimulation of reactive oxygen species in hippocampal slices from apoE2 and apoE4 mice. Oncotarget. 1;8(44): 76587-76605. PMID 29100334
- 5. Villasana, L.E., Weber, S., Akinyeke, T., and Raber, J. (2016) Genotype differences in anxiety and fear learning and memory of WT and ApoE4 mice associated with enhanced generation of hippocampal reactive oxygen species. J. Neurochem. 138(6): 896-908. PMID 27412623

- 6. Villasana, L.E., Kim, K.N., Westbrook, G.L. and Schnell, E. (2015) Functional integration of adultborn neurons after traumatic brain injury. eNeuro. 2(5): 1-17. PMID 26478908
- Villasana, L.E., Westbrook, G. and Schnell, E. (2014) Neurologic impairment following experimental closed head injury predicts post-traumatic neurogenesis. Exp Neurol. 261:156-62. PMID 2486142
- Villasana, L.E., Dayger, C. and Raber, J. (2013) Dose- and apoE isoform-dependent cognitive injury following cranial ⁵⁶Fe irradiation in female mice. Radiat Res. 179 (4): 493-500. PMID 23496055
- Villasana, L.E., Rosenthal, R.A., Doctrow, S.R., Pfankuch, T., Zuloaga, D.G., Garfinkel, A.M., and Raber, J. (2013) Effects of alpha-lipoic acid on associative and spatial memory of sham-irradiated and ⁵⁶Fe-irradiated C57BI/6J male mice. Pharmacol Biochem Behav. 103(3):487-93. PMID 23051895
- Yeiser L.A., Villasana, L.E., and Raber, J. (2013) ApoE isoform modulates effects of cranial ⁵⁶Fe irradiation on spatial learning and memory in the water maze. Behav Brain Res. 15;207-14. PMID 23018124
- Haley, G.E., Villasana, L.E., Dayger, C., Davis, M.J., and Raber, J. (2012) Apolipoprotein E genotype-dependent paradoxical short-term effects of (56) Fe irradiation on the brain. Int J Radiat Oncol Biol Phys. 84(3): 793-9. PMID 22401921 PMCID: PMC3742074
- Raber, J. Rossi, S., Chakraborti, A., Fishman, K., Dayger, C., Davis, M.J., Villasana, L.E., and Fike, J.R. (2011) Effects of (56)-particle cranial radiation on hippocampus-dependent cognition depend on salience of the environmental stimuli. Radiat Res. 176(4):521-6. PMID 21823976
- Dayger C., Villasana, L., Pfankuch, T., Davis, M., and Raber, J. (2011) Effects of the SARM ACP-105 on rotorod performance and cued fear conditioning in sham-irradiated and irradiated female mice. Brain Res. 1381:134-40. PMID 21219889 PMCID: PMC3048897
- Duvoisin, R.M., Villasana, L., Davis, M., Winder, D.G., and Raber, J. (2011) Opposing roles of mGluR8 in measures of anxiety involving non-social and social challenges. Behav Brain Res. 221(1):50-4. PMID 21382421 PMCID: PMC3079808
- Villasana, L.E. Benice, T.S., and Raber J. (2011) Long-term effects of ⁵⁶Fe irradiation on spatial memory of mice: Role of sex and apoE-isoform. Int J Radiat Oncol Biol Phys. 80(2): 567-73. PMID 21549250
- Raber, J., Villasana, L., Rosenberg, J, Zou, Y., Huang, T., and Fike, J. (2011) Irradiation enhances hippocampus-dependent cognition in extracellular superoxide dismutase deficient mice. *Hippocampus* 21(1):72-80. PubMed PMID: 20020436; PubMed Central PMCID: PMC2891276.
- Villasana, L., Pfankuch, T., and Raber, J. (2010) Isoform-dependent effects of apoE on doublecortin-positive cells and microtubule-associated protein 2 immunoreactivity following (137) Cs irradiation. *Radiat Environ Biophys.* 49(3): 421-6. PMID 20458592
- Duvoisin, R.M., Villasana, L., Pfankuch, R., and Raber, J. (2010) Sex-dependent cognitive phenotype of mice lacking mGluR8. *Behav Brain Res.* 209(1): 21-6. PMID 20080129 PMCID: PMC2832071
- 19. Villasana, L., Rosenberg, J., and Raber, J. (2010) Sex-dependent effect of ⁵⁶Fe irradiation on contextual fear condition. *Hippocampus* 20(1):19-23. PMID 19489001 PMCID: PMC2850563
- 20. Hu, L., Sun, Y., Villasana, L., Paylor, R., Klann, E., and Pautler, R. (2009) Early changes in the apparent diffusion coefficient (ADC) in a mouse model for Sandhoff's disease occur prior to disease symptoms and behavioral deficits. *Magn Reson Med.* 62(5):1175-84. PMID 1978015 PMCID: PMC 3238566
- 21. Villasana L., Poage, C., van Meer, P., and Raber, J. (2008) Passive avoidance learning and memory of 56Fe sham-irradiated and irradiated human apoE transgenic mice. *Radiats Biol Radioecol*, 48(2):167-70. PMID 18666648
- 22. Villasana L, Acevedo S, Poage C, Raber J. (2006) Sex- and APOE isoform-dependent effects of radiation on cognitive function. *Radiat Res*, 166(6):883-91 PMID 17149978
- 23. Tejada-Simon, M.V., Villasana, L.E., Serrano, F., and Klann, E. (2006) NMDA receptor activation induces translocation and activation of Rac in mouse hippocampal area CA1. *Biochem Biophys Res Commun*, 343(2): 504-512. PMID 16546126 PMCID: PMC 2013301

- Villasana, L.E., Tejada-Simon, M.V., Kanterwicz, B., Klann, E. (2006) Rapid isolation of synaptoneurosomes and postsynaptic densities from adult mouse hippocampus. *J Neuroscience Methods*, 158(1), 30-6. PMID 16797717 PMCID: PMC 2014514
- Tejada-Simon, M.V., Serrano, F., Villasana L.E., Klann, E., Kanterwicz, B., Quinn, M.T. and Wu G.Y. (2005) Synaptic localization of a functional NADPH-oxidase in the mouse hippocampus. *Mol Cell Neurosci*, 29: 97-106. PMID 15866050 PMCID: PMC 2013304

ABSTRACTS AND PRESENTATIONS:

<u>National</u>

- 1. **Villasana, L.E.** (2017) The influence of sex and diazepam on hippocampal neurogenesis following traumatic brain injury. Building Interdisciplinary Research Careers in Women's Health Conference, Bethesda, MD
- 2. Villasana, L.E., Peters, A., McCallum, R., Westbrook, G., and Schnell, E. (2016) Diazepam inhibits post-traumatic neurogenesis and blocks aberrant neuronal maturation. Society for Neuroscience, San Diego, CA. Poster
- 3. Schnell, E., Villasana, L.E., Kim, K.N., and Westbrook, G.L. (2015) Granule cells born during posttraumatic neurogenesis functionally integrate into the hippocampus. Society for Neuroscience, Chicago IL. Poster
- 4. Villasana, L.E., Kim, K.N., McCallum, R., Westbrook, G.L., and Schnell, E. (2014) Developmental changes in adult-born neurons following controlled cortical impact injury. Society for Neuroscience, Washington D.C. Poster
- 5. Villasana, L.E., Kim, K.N., Westbrook, G.L., and Schnell, E. (2013) Post-traumatic hippocampal neurogenesis in POMC-EGFP mice following a controlled cortical impact injury. Society for Neuroscience, San Diego, CA Poster.
- Villasana, L.E., Kim, K.N., Westbrook, G.L., and Schnell, E. (2013) Morphologic changes in adultborn hippocampal granule cells following controlled cortical impact injury in POMC-EGF mice. Society for Neuroscience in Anesthesiology and Critical Care Conference, San Francisco, CA. Poster.
- 7. Villasana, L.E., Pandit, N., Westbrook, G.L., and Schnell, E. (2012) Mouse closed head injury increases the production and dispersion of adult-born hippocampal granule cells. Society for Neuroscience Conference, New Orleans, LA. Poster
- 8. Villasana, L.E., and Raber, J. (2011) Ameliorative effect of alpha lipoic acid on radiation-induced deficits in water maze reversal learning is sex-dependent. Organization for the Study of Sex Differences, Oklahoma City, OK. Poster presentation
- 9. Duvoisin, R., **Villasana, L.E.,** Davis, M. Gosnell, H., Winder, D., and Raber, J. (2010) Opposing roles of mGluR8 in measures of anxiety and social interaction. Society for Neuroscience Conference, San Diego, CA.
- 10. Villasana, L.E. and Raber, J. (2010) Effects of cranial irradiation and the antioxidant alpha-lipoic acid on hippocampal-dependent learning and memory of mice in the water maze. American Aging Society Conference, Portland, OR.
- 11. Villasana, L., van Meer, P., Pfankuch, T., and Raber, J. (2008) Enhanced Spatial Memory Retention of hApoE4 Female Mice in the Water Maze Following 56Fe Irradiation. Society for Neuroscience, Annual Conference, Washington D.C.
- Villasana, L., Poage, C., Pfankuch, T. and Raber, J. (2006) Effects of Cranial Cesium Irradiation on Neuronal Markers in Human ApoE Transgenic Female Mice. Society for Neuroscience, Annual Meeting, San Diego, CA.
- 13. Villasana, L.E., Acevedo S., Poage, C., and Raber, J. (2006) Sex- and ApoE isoform-dependent effects of radiation on cognitive function. Society for Neuroscience, Annual Conference, Atlanta, Georgia.
- 14. **Villasana, L.E.**, Tejada-Simon, M.V., Serrano, F., and Klann, E. (2004) Phorbol ester-induced activation of NADPH oxidase and production of superoxide in mouse hippocampus. Society for Neuroscience Annual Conference, San Diego, CA.

- 15. Tejada-Simon, M.V., Villasana, L.E., and Klann, E. (2004) Rac translocation and activation is associated with NMDA receptor activation and memory formation in the mouse hippocampus. Society for Neuroscience Annual Conference, San Diego, CA.
- 16. Serrano, F., Tejada-Simon, M.V., **Villasana, L.E.**, Quinn, M.T., Wientjes, F.B., Segal, A.W. and Klann, E. (2002) Characterization of NADPH Oxidase in the mouse hippocampus. Society for Neuroscience Annual Conference, Orlando, FL.

Regional and Local

- 1. Villasana, L.E. (2020) Functional significance of hippocampal neurons generated after traumatic brain injury: good, bad or no role in memory processing? Biology for Neurodegeneration Interest Group (BOND) Meeting, OHSU, Portland, OR. Oral Presentation
- Villasana, L.E. (2019) Paradoxical effects of traumatic brain injury on neurogenesis: Implications for short and long-term cognitive recovery. Legacy Research Institute, Portland, OR. Oral Presentation
- 3. Raphael, S., Bah, T.M., Mader, S., and **Villasana, L.E**. (2019) A history of traumatic brain injury to a neural stem cell. APOM Research Conference, OHSU, Portland, OR.
- 4. **Villasana, L.E.** (2018) Generating new neurons after traumatic brain injury. University of Oregon, Eugene, OR. Oral Presentation.
- 5. **Villasana, L.E.,** Westbrook, G.L., and Schnell, E. (2014) Changes in hippocampal adult-born neurons following controlled cortical impact injury. OHSU Research Forum, Portland, OR. Oral Presentation
- 6. **Villasana, L.E**. and Schnell, E. (2013). Post-traumatic hippocampal neurogenesis in mice. OHSU Stroke Meeting, Stevenson , WA. Oral presentation.
- 7. Villasana, L.E., and Schnell, E. (2013) A concussion story. Vollum Research Seminar Series, Portland OR. Oral presentation.
- 8. **Villasana, L.E.,** and Schnell, E. (2012) Post-traumatic hippocampal neurogenesis in mice. APOM Research Conference, Portland, OR. Oral presentation.
- Villasana, L.E., van Meer, P. and Raber, J. (2010) Effects of ⁵⁶fe irradiation and lipoic acid on spatial memory retention of apoe2 and apoe4 female mice in the water maze. Society for Neuroscience Oregon Local Chapter Meeting, McMinnville, OR.
- Villasana, L.E., Pfankuch, T., and Raber, J. (2008) Enhanced spatial memory of apoE3 and apoE4 female mice following 56Fe irradiation associated with reduced hippocampal MAP-2 levels. OHSU Student Research Forum, Portland, OR
- Villasana L.E., Acevedo S., Poage, C., and Raber, J. Sex- and ApoE isoform-dependent effects of radiation on cognitive function. (2006) Society for Neuroscience Local Chapter, Gleneden Beach, OR

MENTORSHIP

- 2019 Simone Helfrich, Summer Intern, APOM, OHSU Undergraduate, California Polytechnic Institute
- 2019 Sree Neha Yenturu, summer intern, APOM, OHSU High school student, Westview High School
- 2019 Nikhil Samudrala, summer intern, APOM, OHSU High-school student, Lincoln High School
- 2019 Marquitta Smith, (summer project) APOM, OHSU Postdoctoral Fellow, APOM
- 2018 Sam Raphael, summer intern APOM, OHSU Undergraduate, Lewis & Clark
- 2018 Thierno Madjou, (summer project) APOM, OHSU Postdoctoral Fellow, APOM
- 2018 Chang, Liu, summer intern, APOM, OHSU Undergraduate, College of Osteopathic Medicine of the Pacific Northwest
- 2015 Khanh Doan, Lab Volunteer, APOM, OHSU

Undergraduate, Portland State University

- 2014 Raluca McCallum, research internship, Vollum OHSU Medical Student, OHSU
- 2012 Kristine Kim, summer intern, Vollum Institute, OHSU Undergraduate, MIT
- 2012 Peters, Austin, Research internship, Vollum, OHSU Medical Student, OHSU