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: Luo, Jian

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

POSITION TITLE: Life Science Research Scientist

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
Hunan Medical University, Hunan, China	B.M.	07/1990	Medicine
Hunan Medical University, Hunan, China	M.S.	07/1993	Medicine
Purdue University, West Lafayette, IN, USA	Ph.D.	12/2003	Neuroscience
Stanford University, Stanford, CA, USA	Postdoctoral	08/2010	Neurology and Neurological Sciences

A. Personal Statement

The overall objective of my research is to understand neuro-immune response and neuroinflammation in brain injury and neurodegeneration. Currently my research focuses on the role of transforming growth factor β (TGF-β), a major injury response factor in the brain, in mild traumatic brain injury and neurodegenerative diseases.

My current research interests have evolved from my PhD dissertation work on traumatic spinal cord injury and postdoctoral training on neurodegenerative diseases. As an instructor after my postdoctoral training, I have successfully established my own research directions in traumatic brain injury and Parkinson's disease, and completed a research project from The Michael J. Fox Foundation (MJFF) for Parkinson's Research as principal investigator. As a principal investigator at the Palo Alto Veterans Institute for Research (PAVIR), I completed a large grant from MJFF (Therapeutic Pipeline Program) and recently was awarded an NIH R01 on traumatic brain injury. I have extensive experience in analyzing animal models of chronic neurodegenerative disease, aging, and brain injury. I have developed multiple unique tools to study (brain) TGF-β signaling and brain injury. I have established several productive collaborations with other researchers, within my institution and from outside. I am a co-inventor of two patents for several neuroprotective agents - one of which is a novel small molecule activator of TGF-β signaling.

B. Positions and Honors

Positions and Employment

1993-1999 Resident Physician, Xiangya Hospital of Hunan Medical University, Hunan, China.
2010-2013 Instructor, Stanford University, Stanford, CA, USA.
2013-2018 Life Science Research Scientist/Principal Investigator, Palo Alto Veterans Institute for Research, Inc. (PAVIR), VA Palo Alto Health Care System, Palo Alto, CA, USA
2018- Life Science Senior Research Scientist/Principal Investigator, Palo Alto Veterans Institute for Research, Inc. (PAVIR), VA Palo Alto Health Care System, Palo Alto, CA, USA

Other Experience and Professional Memberships

1996-1999 Member, Chinese National Medical Association
2000-present Member, The Society for Neuroscience
2007-present The Society for Molecular Imaging

2009 Program Committee Member, The 2nd International Congress on Image and Signal Processing (CISP'09) and the 2nd International Conference on BioMedical Engineering and Informatics (BMEI'09), October 2009, Tianjin, China.
2009-present Member, Institutional Animal Care and Use Committee (IACUC), VA Palo Alto Heath Care System, Palo Alto, CA, USA.
2013-present Manuscript reviewer for: Nat Neurosci, Neuron, Acta Neuropathologica, Exp Brain Res, Molecules, Mol Ther, J Exp Med, Molecular Neurodegeneration, Oncotarget, J Neuroinflammation.
2014-present Editorial Board, Review Editor, Frontiers in Aging Neuroscience (Switzerland).
2015 Research grant reviewer, Dr Hadwen Trust (DHT, now Animal Free Research UK), UK.
2016 Research grant reviewer, Medical Research Council, UK.
2017 Research grant reviewer, NIH/NCATS, USA
2018 Research grant reviewer, Motor Neuron Disease Association, UK.

Honors

1990 Graduation with Distinction, Hunan Medical University, Hunan, China
2004 Purdue University Pfizer Graduate Student Research Award, IN, USA
2007 Stanford Immunology Postdoc Travel Fellowship
2007 Academy of Molecular Imaging Travel Award
2009 Alzheimer's Association Young Scientist Award

C. Contributions to Science

1. TGF-β signaling in neurodegenerative diseases. My postdoctoral research and the expansion afterwards focused on TGF-β signaling in brain injury and neurodegenerative diseases. I generated transgenic luciferase reporter mice, which allow us to monitor TGF-β signaling in live animals. I also employed genetic approaches to abrogate or enhance TGF-β signaling in a cell type-specific manner. The results from these studies revealed several important aspects of TGF-β signaling in response to injury and encouraged us to explore this pathway as a potential therapeutic target: 1) Different organs initiate strikingly different injury responses. 2) Bioluminescence signal of TGF-β signaling can be used as a surrogate marker for neurodegeneration and for therapeutic screening. 3) Activation of TGF-β signaling in the CNS is important for the initiation of neuroinflammation, suggesting a disease-promoting role of TGF-β signaling in autoimmune diseases. 4) Brain TGF-β signaling is impaired during aging and neurodegeneration. 5) Reducing TGF-β signaling in neurons leads to motor deficits and dopaminergic dysfunction in mice, and activating TGF-β signaling in the substantia nigra through adeno-associated virus (*AAV)* blocked 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced motor deficits, neurodegeneration and neuroinflammation in mice. 6) Through collaborations with SRI International and Stanford University, we developed a novel small molecule compound that activates TGF-β signaling and possesses potent neuroprotective effects in vivo.

a. Lin AH, Luo J, Mondshein LH, ten Dijke P, Vivien D, Contag CH, Wyss-Coray T (2005). Global analysis of Smad2/3-dependent TGF-β signaling in living mice reveals prominent tissue-specific responses to injury. *J Immunol* 175:547-54. PMID:15972691
b. Luo J, Lin AH, Masliah E, Wyss-Coray T (2006). Bioluminescence imaging of Smad signaling in living mice shows correlation with excitotoxic neurodegeneration. *Proc Natl Acad Sci USA* 103:18326-31. PMID:11710447.
c. Luo J, Ho PP, Buckwalter MS, Hus T, Lee LY, Zhang H, Kim D, Kim S, Gambhir SS, Steinman L, Wyss-Coray T (2007). Glia-dependent TGF-β signaling, acting independent of the TH17 pathway, is critical for initiation of autoimmune encephalomyelitis. *J Clin Invest* 117: 3306-3315. PMID:17965773.
d. Tesseur I, Nguyen A, Chang B, Li L, Woodling NS, Wyss-Coray T*, Luo J* (2017). Deficiency in Neuronal TGF-beta Signaling Leads to Nigrostriatal Degeneration and Activation of TGF-beta Signaling Protects against MPTP Neurotoxicity in Mice. *J Neurosci* 37:4584-92. PMID: 28363982. (*, corresponding authors)

2. Neuro-immune interactions in brain function and cognition. I discovered that modulating macrophage colony-stimulating factor 1 (CSF-1)-mediated neuron-microglia interactions may provide therapeutic benefits, since activating CSF-1 signaling promotes neuronal survival and reduces neuroinflammation. During my senior postdoc years and as an instructor, I supervised two Stanford graduate students (SA Villeda and ZQ Ding, under Dr. Tony Wyss-Coray's guidance) to study neuro-immune interactions. I refined the parabiosis model (where two mice are joined together and share blood) and improved the survival rate of the surgery. This model is now widely used in the lab to study how immune components in the systemic milieu affects brain function and

cognition in mice. I have trained a dozen scientists from the US, Canada, China and Japan to use this model in their research.

a. Luo J, Elwood F, Britschgi M, Villeda S, Zhang H, Ding Z, Zhu L, Alabsi H, Getachew R, Narasimhan R, Wabl R, Fainberg N, James ML, Wong G, Relton J, Gambhir SS, Pollard JW, Wyss-Coray T (2013). Colony-stimulating factor 1 receptor (CSF1R) signaling in injured neurons facilitates protection and survival. *J Exp Med* 210:157-72. PMID:23296467.
b. Ding ZQ, Mathur V, Ho PP, James ML, Lucin KM, Hoehne A, Alabsi HS, Gambihr SS, Steinman L, Luo J*, and Wyss-Coray T* (2014). Antiviral drug Ganciclovir is a potent inhibitor of microglial proliferation and neuroinflammation. *J Exp Med* 211:189-98. PMID:24493798. (*, corresponding authors).
c. Villeda SA, Luo J, Mosher KI, Zou B, Britschgi M, Bieri G, Stan TM, Fainberg N, Ding Z, Eggel A, Lucin KM, Czirr E, Couillard-Després S, Aigner L, Li G, Peskind ER, Kaye JA, Quinn JF, Galasko DR, Xie X, Rando TA, Wyss-Coray T (2011). The aging systemic milieu negatively regulates neurogenesis and cognitive function. *Nature* 477(7362):90-4. PMID:21886162.
d. Castellano JM, Palner M, Li SB, Freeman GM Jr, Nguyen A, Shen B, Stan T, Mosher KI, Chin FT, de Lecea L, Luo J*, Wyss-Coray T* (2016). In vivo assessment of behavioral recovery and circulatory exchange in the peritoneal parabiosis model. *Sci Rep* 6:29015. PMID: 27364522 (*, corresponding authors).

3. Mild traumatic brain injury (mTBI): model, pathophysiology and therapeutic options. I developed a mouse model of repetitive mild traumatic brain injury with long-term behavioral and pathological sequelae, which resemble those observed in human patients. This model allows us to study the long-term neurological and pathological consequences of mild head injuries, and the molecular mechanisms of repetitive concussive injury to the brain. Through collaborations with Dr. Hongjie Dai at Stanford University, we developed a novel near infrared molecular fluorophore that allowed us to characterize dynamic vascular damages after mTBI through in vivo imaging. This model also allows us to evaluate potential therapeutic interventions (activating TGF-β signaling, NIH R01 NS092868 and modulating CSF-1-mediated neuron-microglia interactions, Department of Veterans Affairs I01 RX001218) for mTBI.

a. Luo J*, Nguyen A, Villeda S, Zhang H, Ding Z, Lindsey D, Bieri G, Castellano JM, Beaupre G and Wyss-Coray T* (2014). Long-term cognitive impairments and pathological alterations in a mouse model of repetitive mild traumatic brain injury. *Front Neurol* 5:12. doi: 10.3389/fneur.2014.00012. PMID:24550885. (*, corresponding authors).
b. Zhang XD, Wang H, Antaris AL, Li L, Diao S, Ma R, Nguyen A, Hong G, Ma Z, Wang J, Zhu S, Castellano JM, Wyss-Coray T, Liang Y*, Luo J*, Dai H* (2016). Traumatic brain injury imaging in the second near-infrared window with a molecular fluorophore. *Adv Mater* 28:6872-9. PMID: 27253071. (*, corresponding authors).

4. Oxidative stress and secondary injury in traumatic spinal cord injury. During my PhD thesis work, my advisor, Dr. Riyi Shi gave me a great deal of flexibility and freedom in the development and progression of my doctoral project, allowing me to work outside of his laboratory's primary focus of studying traumatic spinal cord injury using electrophysiological recording techniques. My research was on the effect of membrane repair on secondary injury mechanisms. I discovered that repairing the membrane with polyethylene glycol (PEG) 2000, reduces oxidative stress and apoptosis, and improves functional recovery after traumatic spinal cord injury. I also found that acrolein, a product from oxidative stress, is increased after traumatic spinal cord injury. Acrolein induces membrane damage, oxidative stress and causes mitochondrial function deficits. My work opened a new research area for the lab and built the foundation for another 20 publications by later lab members and for an NIH R01 grant (Role of acrolein in spinal cord injury, R01NS073636) by Dr. Shi after I graduated.

a. Luo J, Borgens RB and Shi R (2002). Polyethylene glycol immediately repairs neuronal membranes and inhibits free radical production after acute spinal cord injury. *J Neurochem* 83: 471-80. PMID:12423257.
b. Luo J, Borgens RB and Shi R (2004). Polyethylene glycol improves function and reduces oxidative stress in synaptosomal preparations after spinal cord injury. *J Neurotrauma* 21:994-1007. PMID:15318999.
c. Luo J and Shi R (2004). Diffusive oxidative stress after spinal cord injury and its inhibition by polyethylene glycol. *Neurosci Lett* 359:167-70. PMID:15050690.
d. Luo J, Uchida K, Shi R (2005). Accumulation of acrolein-protein adducts after traumatic spinal cord injury. *Neurochem Res* 30:291-5. PMID:16018572.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/sites/myncbi/jian.luo.1/bibliography/48250668/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

NIH R01 NS092868 Luo (PI) 04/01/2016-03/31/2021
TGF-β signaling as a novel therapeutic target for mild traumatic brain injury.
The goal of this R01 is to examine the long-term changes and role of TGF-β signaling in repetitive mild traumatic brain injury and whether increasing TGF-β signaling can reduce long-term cognitive deficits and neuropathology associated with repetitive mTBI.
Role: PI

Department of Veterans Affairs I01 RX001218 Wyss-Coray (PI) 01/01/2014-12/31/2018
Aging and inflammation in mild traumatic brain injury.
The goal of this I01 is to refine our mouse model of repetitive mild traumatic brain injury and assess long-term pathological and cognitive changes in wildtype mice, and to examine the efficacy of colony-stimulating factor 1 and/or IL-34 in reducing pathology and alleviating symptoms in mouse models of mTBI.
Role: Co-Investigator

Completed Research Support

The Michael J. Fox Foundation for Parkinson's Research Luo (PI) 10/01/2013-12/31/2015
Novel Small Molecule TGF-β Agonist for the Treatment of Parkinson's
The goal of this Therapeutic Pipeline Program is to examine the efficacy of a TGF-β agonist in a chronic MPTP model of Parkinson's disease.
Role: PI

The Michael J. Fox Foundation for Parkinson's Research Luo (PI) 12/01/2011-11/30/2012
TGF-β signaling as novel therapeutic treatment for Parkinson's disease
The goal of this Target Validation program is to determine whether activation of the TGF-β signaling pathway in dopaminergic neurons will protect them against the Parkinsonism inducing neurotoxin MPTP.
Role: PI