

## PERSONAL DATA

Birthplace: Anhui, China

## EDUCATION

2016-2020 PhD Department of Neuroscience and Regenerative Medicine,  
Medical College of Georgia, Augusta University, USA

2003-2007 BS Department of Physics, Huainan Normal University, China

## HONORS

2019 Darrell W. Brann Scholarship in Neuroscience

2019 Virendra B. Mahesh Award in recognition of research excellence in Endocrinology

2018 Virendra B. Mahesh Award in recognition of research excellence in Endocrinology

## SOCIETIES

2015 – Present Society for Neuroscience

## PUBLICATIONS

**Yujiao Lu**, Quanguang Zhang, Jing Wang, Darrell Brann. Senolytic Treatment Attenuates Brain Senescence and Cognitive Deficits after Traumatic Brain Injury. (*In Preparation*)

Jing Wang, Gangadhara R. Sareddy, **Yujiao Lu**, Uday P. Pratap, Fulei Tang, Ratna K. Vadlamudi and Darrell Brann. Astrocyte-derived Estrogen Enhances Astrocyte Activation and is Neuroprotective after Global Cerebral Ischemia. (*In Preparation*)

**Yujiao Lu**, Gangadhara R. Sareddy, Jing Wang, Quanguang Zhang, Fu-Lei Tang, Uday Pratap, Rajeshwar R. Tekmal, Ratna K. Vadlamudi, and Darrell W. Brann. Neuron-Derived Estrogen is Critical for Astrocyte Activation and Neuroprotection of the Ischemic Brain. *J Neurosci.* (*Under Revision*)

**Lu Y**, Sareddy GR, Wang J, Wang R, Li Y, Dong Y, Zhang Q, Liu J, OConnor J, Xu J, Vadlamudi RK, Brann D. Neuron-Derived Estrogen Regulates Synaptic Plasticity and Memory. *J Neurosci.* 2019 Apr 10; 39(15):2792-2809. doi: 10.1523.

Tucker LD<sup>#</sup>, **Lu Y<sup>#</sup>**, Dong Y, Yang L, Li Y, Zhao N, Zhang Q. Photobiomodulation Therapy Attenuates Hypoxic-Ischemic Injury in a Neonatal Rat Model. *J Mol Neurosci.* 2018 Aug;65(4):514-526. doi: 10.1007/s12031-018-1121-3. (*Co-first author*)

**Yujiao Lu**, Yan Dong, Donovan Tucker, Darrell Brann\*, Quanguang Zhang\*. Treadmill Exercise Exerts Neuroprotection and Regulates Microglial Polarization and Oxidative Stress in a Streptozotocin-Induced Rat Model of Sporadic Alzheimer's Disease. *Journal of Alzheimer's disease.* 2017; 56(4):1469-1484. doi: 10.3233/JAD-160869.

## ABSTRACTS

**Yujiao Lu**, Gangadhara R. Sareddy, Jing Wang, Quanguang Zhang, Fu-Lei Tang, Uday Pratap, Rajeshwar R. Tekmal, Ratna K. Vadlamudi, and Darrell W. Brann. Neuron-Derived Estrogen is Critical for Neuroprotective Astrocyte Activation After Ischemic Injury to the Brain. Annual Meeting of the Society for Neuroscience, Chicago, Oct, 2019.

**Yujiao Lu**, Jing Wang, Gangadhara R. Sareddy, Quanguang Zhang, Ratna K. Vadlamudi, and Darrell W. Brann. Neuron-Derived Estrogen is Critical for Endogenous "A2" Astrocyte Activation and Neuroprotection after Ischemic Injury to the Brain. Graduate Research Day, Augusta University, April, 2019.

**Yujiao Lu**, Gangadhara Sareddy, Ruimin Wang, Jing Wang, Yong Li, Yan Dong, Jianhua Xu, Jinyou Liu, Jason OConnor, Quanguang Zhang, Ratna K. Vadlamudi, and Darrell W. Brann. Neuron-Derived Estrogen Regulates Synaptic Plasticity and Memory. Annual Meeting of the Society for Neuroscience, San Diego, Nov, 2018.

**Yujiao Lu**, Gangadhara Sareddy, Ruimin Wang, Jing Wang, Yong Li, Yan Dong, Jianhua Xu, Jinyou Liu, Jason OConnor, Quanguang Zhang, Ratna K. Vadlamudi, and Darrell W. Brann. Neuron-Derived Estrogen Regulates Synaptic Plasticity and Memory. Graduate Research Day, Augusta University, March, 2018.

**Yujiao Lu**, Yan Dong, Donovan Tucker, Ruimin Wang, Mohammad Ejaz Ahmed, Darrell Brann\* and Quanguang Zhang\*. Beneficial Effects of Treadmill Exercise in a Rat Model of Sporadic Alzheimer's Disease. Annual Meeting of the Society for Neuroscience, Washington DC, Nov, 2017.

TITLE OF DISSERTATION: NEURON-DERIVED ESTROGEN AND  
NEURAL FUNCTION

ABSTRACT:

17 $\beta$ -estradiol (E2) is produced from androgens via the action of the enzyme aromatase. E2 is known to be made in neurons in the brain, but its precise functions in the brain are unclear. We created a forebrain neuron-specific aromatase knockout (FBN-ARO-KO) mouse model to deplete neuron-derived E2 in the forebrain of mice. Under normal conditions, FBN-ARO-KO mice showed a 70-80% decrease in aromatase and forebrain E2 levels. Male and female FBN-ARO-KO mice exhibited significant deficits in forebrain spine and synaptic density, as well as hippocampal-dependent cognitive functions. Reinstating forebrain E2 levels via exogenous in vivo E2 administration was able to rescue both the molecular and behavioral defects in FBN-ARO-KO mice. Furthermore, electrophysiological study suggested normal long-term potentiation (LTP) induction, but significantly decreased amplitude in FBN-ARO-KO mice which could be fully rescued by acute E2 treatment in vitro. Mechanistic studies revealed that FBN-ARO-KO mice had compromised rapid kinase (AKT, ERK) and CREB-BDNF signaling in the hippocampus and cerebral cortex. After global cerebral ischemia (GCI), ovariectomized female FBN-ARO-KO mice had significantly attenuated aromatase and hippocampal E2 levels. Intriguingly, FBN-ARO-KO mice exhibited a robust reduction in astrocyte activation, as well as exacerbated neuronal damage and worse cognitive dysfunction after GCI. Similar results were observed in intact male mice. RNA-seq analysis revealed alterations in pathways and genes associated with astrocyte activation, neuroinflammation and oxidative stress in FBN-ARO-KO mice. The compromised astrocyte activation in FBN-ARO-KO mice was associated with robust downregulation of the astrocyte-derived neurotrophic factors, BDNF and IGF-1, as well as the astrocytic glutamate transporter, GLT-1. In vivo E2 replacement rescued the compromised reactive astrogliosis and cognitive deficits. Moreover, neuronal FGF2, which acts in a paracrine manner to suppress astrocyte activation, was dramatically increased in FBN-ARO-KO neurons. Interestingly, blocking FGF2 signaling in astrocytes by central injection of an FGFR3 antibody was able to reverse the diminishment in neuroprotective astrocyte reactivity, and attenuate neuronal damage in FBN-ARO-KO mice. Collectively, our data provides novel genetic evidence for the roles of neuron-derived E2 in regulating synaptic plasticity, cognitive function in the non-injured brain, and astrocyte activation and neuroprotection in the injured brain.

The Graduate School- Augusta University

Final Oral Examination

for

YUJIAO LU

For the Degree of

DOCTOR OF PHILOSOPHY

Friday, March 27<sup>th</sup>, 2020  
9:00 A.M.

Department of Neuroscience and Regenerative Medicine

Interdisciplinary Research Center  
Room CA1002

COMMITTEE

Advisor: Darrell Brann Ph.D.

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Anilkumar Pillai, Ph.D.

READER

Sangeetha Sukumari-Ramesh, Ph.D.