BIOGRAPHICAL SKETCH

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NAME: Bunner, Wyatt Paul

eRA COMMONS USER NAME (credential, e.g., agency login): N/A

POSITION TITLE: PhD Candidate

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
East Carolina University, Greenville, NC	B.S.	05/2017	Exercise Physiology
East Carolina University, Greenville, NC	M.S.	05/2019	Kinesiology
East Carolina University, Greenville, NC	Ph.D.	07/2023	Rehabilitation Sciences

A. Personal Statement

The goal of my doctoral studies is to explore the role of the small GTPase, Rab10 in the cellular and molecular mechanisms of brain resilience against neurodegeneration. To achieve this, I will utilize imaging, transcriptomics, cell biology, biochemistry, and behavioral studies on mice that have reduced Rab10 level ($Rab10^{+/-}$, developed in the lab of Dr. Ryohei Yasuda at Max Planck Institute for Neuroscience).

My interest in neurodegeneration research started during my masters' studies, when I was involved in studies on the role of the hypothalamus in development of Alzheimer's disease-like phenotypes, using the triple transgenic mouse model of the disease (Do, K. et al., 2018, PMID: 30334389). We reported that metabolically significant changes in the hypothalamus precede the build-up of amyloid plaques and neurodegeneration, suggesting that AD may also be a metabolic disorder.

My master thesis titled AgRP neurons are required for exercise induced food intake investigated the change in neuron activity in the homeostatic neurons located in the arcuate nucleus of the hypothalamus responsible for food seeking behavior. I found that food intake increased in mice that weren't accustomed to an exercise regimen that underwent an acute bout of medium intensity exercise. Using coronal staining and patch-clamp electrophysiology I found that the orexigenic arcuate AgRP neurons were much more active in mice immediately after a bout of acute exercise compared to their sedentary counterparts. Finally, I chemogenetically deactivated this AgRP neuron population which abolished this acute exercise induced increase in feeding behavior. This led to my first publication where I was the primary author (Bunner W. et al., 2020, PMID: 32435204) .

Shortly after enrolling in PhD studies, our lab started a collaboration with Dr. Robert Hughes laboratory (ECU Department of Chemistry), to test if a novel optogenetic bio-sensor deemed the "CofActor System" is suitable to report cytoskeletal dysregulations in neurons, an early cellular phenotype of neurodegeneration. This collaboration resulted in two recent publications in prominent journals (Salem and Bunner et al., 2020, PMID: 32424038; Bunner et al., 2021, PMID: 34124292) and set the foundation of my current research on the contribution of Rab10 signaling to actin-cofilin rod formation in neurons under cellular stress responsible for neurodegeneration.

To support this proposed training, I have completed a broad range of courses since becoming a graduate student. These include Methods and Techniques in Chemistry, Neuroscience, Bioenergetics, Physiology of Exercise, Cardiopulmonary Physiology, Advanced Exercise Prescription, Theory and Techniques in Bioenergetics, Cardiopulmonary Rehabilitation Diagnostic Procedures, and Motor Control and Movement

Disorders. Also, I am currently enrolled to take coursed in Molecular Cell Biology, my final of 5 statistics courses to complete my "Graduate Certificate in Quantitative Methods for the Social and Behavioral Sciences", and an apprenticeship course to learn eye blink conditioning surgeries and assessment in mice.

In summary, my record of sustained productivity, combined with my expanding expertise and research at the intersection of Cellular Neuroscience and Metabolism, have prepared me to successfully complete the research outlined in this proposal.

Career Goals

Once I acquire a Ph.D., I anticipate having broadened my technical research capabilities and having gained a greater understanding for unanswered questions that are at the center of Rehabilitation Science. Once equipped with this knowledge, I plan to continue doing research to help resolve some of these questions. The field of Rehabilitation Science, due to its multidisciplinary nature, will continually provide new questions and challenges. I would like to continue to tackle these questions and challenges, with a focus on studying neurodegenerative disorders as a postdoctoral researcher after completing my doctoral studies.

B. Positions and Honors

Positions and Scientific Appointments

07/2017 –05/ 2019 Master Student, Kinesiology Graduate Program; East Carolina Diabetes and Obesity Institute, East Carolina University, Greenville, NC

07/2019 – Present PhD Student, Rehabilitation Sciences Graduate Program; College of Allied Health Sciences, East Carolina University, Greenville, NC

Professional Memberships

2016 American Physiological Society
2017 American College of Sports Medicine
2020 Society for Neuroscience
2021 American Heart Association

Honors

2017 Poster Award (1st place), Undergraduate Research Opportunity Symposium, East Carolina University

2018 Poster Award (1st place, Graduate Students), East Carolina University Annual Neuroscience Symposium

C. Contributions to Science

1. Identifying the mechanisms of neuroprotection by moderate long-term voluntary exercise

During my undergraduate and master studies, I researched the peripheral and central effects of long-term and acute exercise, focusing on AgRP/NPY and POMC neurons in the arcuate nucleus of the hypothalamus. These are orexigenic and anorexigenic neuron populations respectively and are major contributors to food seeking behavior. We reported that long-term voluntary exercise is sufficient to attenuate the loss of Arcuate AgRP/NPY and POMC neurons in AD model mice compared to AD mice that didn't undergo a voluntary exercise regimen. In my first-author publication, we showed that acute exercise in mice who weren't accustomed to an exercise routine, caused food seeking behavior. This behavior can be abolished by turning off Arcuate AgRP neurons, indicating that this population is required for food seeking behavior.

a. Rao, Z., Wang, S., **Bunner, W.P.**, Chang, Y. and Shi, R., 2016. Exercise induced right ventricular fibrosis is associated with myocardial damage and inflammation. Korean Circ J. 2018 Nov;48(11):1014-1024. doi: 10.4070/kcj.2018.0084. PubMed PMID: 30334389.
b. Do, K., Laing, B.T., Landry, T., **Bunner, W**., Mersaud, N., Matsubara, T., Li, P., Yuan, Y., Lu, Q. and Huang, H., 2018. The effects of exercise on hypothalamic neurodegeneration of Alzheimer's disease

mouse model. PLoS One. 2018;13(1):e0190205. doi: 10.1371/journal.pone.0190205. eCollection 2018. PubMed PMID: 29293568 .

c. **Bunner, W.**, Landry, T., Laing, B.T., Li, P., Rao, Z., Yuan, Y. and Huang, H., 2020. ARC AgRP/NPY Neuron Activity Is Required for Acute Exercise-Induced Food Intake in Un-Trained Mice. Front Physiol. 2020;11:411. doi: 10.3389/fphys.2020.00411. eCollection 2020. PubMed PMID: 32435204.

2. Identifying neuronal targets of the anti-aging factor, α-klotho

As a master studies I also collaborated on projects that evaluated the metabolic properties of the protein α-klotho, a circulating factor with anti-aging properties. We found that central administration of α-klotho reduces the activity of orexigenic neurons, which in turn decreases blood glucose in mice fed a high fat diet. We also found a negative correlation between central levels of α-klotho and BMI in humans.

a. Rao Z, Landry T, P Li, **Bunner W**, Laing BT, Yuan Y, Huang H. 2019. Administration of alpha klotho reduces liver and adipose accumulation in obese mice. Heliyon. 2019 Apr;5(4):e01494. doi: 10.1016/j.heliyon.2019.e01494. eCollection 2019 Apr. PubMed PMID: 31049427

b. Landry, T., Laing, B.T., Li, P., **Bunner, W.**, Rao, Z., Prete, A., Sylvestri, J. and Huang, H., 2020. Central α-Klotho Suppresses NPY/AgRP Neuron Activity and Regulates Metabolism in Mice. Diabetes. 2020 Jul;69(7):1368-1381. doi: 10.2337/db19-0941. Epub 2020 Apr 24. PubMed PMID: 32332158

c. Landry T, Li P, Shookster D, Jiang Z, Li H, Laing BT, **Bunner W**, Langton T, Tong Q, Huang H. Centrally circulating α-klotho inversely correlates with human obesity and modulates arcuate cell populations in mice. Mol Metab. 2021 Feb;44:101136. doi: 10.1016/j.molmet.2020.101136. Epub 2020 Dec 7. PubMed PMID: 33301986

3. Dissecting the signaling pathways involved in abnormal neuronal cytoskeletal dynamics using novel optogenetic tools

In my current research, I study the formation of actin-cofilin rods in neurons exposed to cellular stress using novel molecular optogenetic sensors. These rods or bundles are involved in the early stages of neurodegeneration. Our first sensor, the “CofActor system” allowed me to monitor reversible rod formation in cortical and hippocampal neurons exposed to cellular stress, induced by ROS formation and amyloid oligomers. The next stage of this line of research as outlined in this proposal is to employ the CofActor system for evaluation of rod formation in subcellular compartments of neurons isolated from Rab10$^{+/-}$ transgenic mice.

a. Salem FB*, **Bunner WP*,** Prabhu VV, Kuyateh A-B, O’Bryant CT, Murashov AK, Szatmari EM, Hughes RM (2020) CofActor: A light- and stress-gated optogenetic clustering tool to study disease-associated cytoskeletal dynamics in living cells. J Biol Chem. 2020 Aug 7;295(32):11231-11245. doi: 10.1074/jbc.RA119.012427. Epub 2020 May 18. PubMed PMID: 32424038. (*equal contribution)

b. **Bunner WP**, Dodson R, Hughes RM, Szatmari EM. Transfection and Activation of CofActor, a Light and Stress Gated Optogenetic Tool, in Primary Hippocampal Neuron Cultures. Bio Protoc. 2021 Apr 20;11(8):e3990. doi: 10.21769/BioProtoc.3990. eCollection 2021 Apr 20. PubMed PMID: 34124292

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/wyatt.bunner.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Scholastic Performance

YEAR	COURSE TITLE	GRADE
2013	Abnormal Psychology	B
2013	Comp App in Exercise and Sport Science	A
2014	Physiology of Exercise	A-

YEAR	COURSE TITLE	GRADE
2014	Introduction to Biomechanics	A-
2014	Organic Chemistry	B-
2014	Survey Human Physiology and Anatomy	A
2014	Introduction to Neuroscience	B
2015	Human Physiology and Anatomy I	A-
2015	Exercise Evaluation and Prescription	B-
2015	Exercise Adherence	A
2015	Exercise Prescription for Clinical Populations	A-
2015	Independent Research in Exercise Physiology	A
2015	Medical Terminology for Health Professionals	A
2016	Human Physiology and Anatomy II	B+
2016	Microbiology	A
2016	Professional Ethics	A
2017	Graduate Physiology of Exercise	A
2017	Research Techniques in Kinesiology	A
2017	Research Seminar in Kinesiology	A
2018	Cardiopulmonary Physiology	A
2018	Advance Exercise Prescription	A
2018	Cardiopulmonary Rehabilitation and Diagnostic Procedures	A
2018	Bioenergetics	A
2019	Motor Control and Movement Disorders	B
2019	Ethics & Research: Humanities & Basic Med Sciences	A
2019	Statistics and Research Design	B
2019	Doctorial Colloquium	A
2019	Biostatistics for Health Professionals	B
2020	Advanced Research Design	B
2020	Research Internship	A
2020	Methods and Techniques in Chemistry	A
2020	Neuroscience	B
2020	Techniques in Biomechanical Assessment	A
2021	Structural Equations and Hierarchical Learning Models	B
2021	Research Internship II	A

Current Research Support

N/A

Completed Research Support

N/A