BIOGRAPHICAL SKETCH

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NAME: Taylor, Anne Marion

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

POSITION TITLE: Chief Scientific Officer

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
Washington University, St. Louis, MO	BS	05/1995	Civil Engineering
Washington University, St. Louis, MO	BS	05/1995	Engineering & Public Policy
University of California, Irvine, CA *Mentor: Noo Li Jeon*	MS/PhD	03/2006	Biomedical Engineering
Institute for Brain Aging & Dementia, Irvine, CA *Mentor: Carl W. Cotman*	Postdoctoral	08/2006	Neurobiology
California Institute of Technology, Pasadena, CA *Mentor: Erin M. Schuman*	Postdoctoral	08/2010	Neurobiology
Cold Spring Harbor Laboratory, NY		06/2007	Biology of Memory summer course

A. Personal Statement

My graduate training in biomedical engineering focused on developing methods to spatially and temporally manipulate neurons for multiple applications in experimental neurobiology. While a graduate student I invented a microfluidic device for compartmentalizing neurons that is now extensively used in neurobiology. Our Nature Methods paper described this device along with several experimental paradigms for its use, including examining axonal outgrowth, regeneration, transport, local protein synthesis, and co-culture interactions (Taylor et al., ***Nat Meth***, 2005). This technology was patented by UC Irvine and exclusively licensed to Xona Microfluidics, LLC (now Xona Microfluidics, Inc.). I continued to use novel micro-scale approaches to study neurons during my postdoctoral training in neurobiology under Dr. Carl Cotman at UC Irvine where I examined the axonal transcriptome in mature axons and how its composition changes in regenerating axons following axotomy. As a postdoc in Dr. Erin Schuman at Caltech (now a Director of the Max Planck for Brain Research in Frankfurt, Germany) I developed a novel approach to pharmacologically manipulate synapses for studies of synaptic plasticity (Taylor et al., ***Neuron***, 2010).

As an independent investigator at both UNC-Chapel Hill and now Xona Microfluidics, Inc., I have continued to use novel approaches to investigate synapse development and plasticity (Nagendran et al., ***Nat Commun***, 2017; Nagendran & Taylor, ***Front Cell Neurosci***, 2019). Microfluidic devices provide unprecedented access to somatic and axonal compartments for experimental manipulations needed to study axon-to-soma signaling. One of our interests at Xona Microfluidics is the study of how cellular mechanisms of axon damage, an early event in acute neural injuries and neurodegenerative disease, cause synaptic remodeling (Nagendran et al., ***Nat Commun***, 2017).

Importantly, I have a demonstrated record of success managing projects. I was the PI for an R41/R42 project funded through the NIMH and am currently PI of an R21 project awarded to Xona Microfluidics. I was one of a select few to receive the Alfred P. Sloan Foundation Research Fellowship to continue the pursuit of innovative research in the field of neuroscience. I have served as PI on multiple other grants, including from private foundations.

1. **Taylor, A.M.**, Blurton-Jones, M., Rhee, S.W., Cribbs, D.H., Cotman, C.W. & Jeon, N.L.* *A microfluidic culture platform for CNS axonal injury, regeneration and transport.* Nature Methods, 2005. 2(8):599-605, PMID: 16094385
2. **Taylor, A.M.**, Dieterich, D.C., Ito, H. T., Kim, S.A. & Schuman, E.M.* *Microfluidic local perfusion chambers for the visualization and manipulation of synapses.* Neuron, 2010. 66, 57-68, PMID: 20399729
3. Nagendran, T. Larsen, R.S., Bigler, R.L., Frost, S.B., Philpot, B.D., Nudo, R.J. & **Taylor, A.M.*** *Distal axotomy enhances retrograde presynaptic excitability onto injured pyramidal neurons via trans-synaptic signaling.* Nature Communications**,** 2017. 8(1):625, PMID: 28931811
4. Nagendran, T., **Taylor, A.M.*** Unique Axon-to-Soma Signaling Pathways Mediate Dendritic Spine Loss and Hyper-Excitability Post-axotomy. Frontiers in Cellular Neuroscience, 2019. 13, PMID: 31607869

B. Positions and Honors

Positions and Employment

2019-	Chief Scientific Officer, Xona Microfluidics, Inc.
2010-2019	Assistant Professor, UNC/NC State Joint Department of Biomedical Engineering
2010-	Member, UNC-Chapel Hill Neuroscience Center

Other Experience and Professional Memberships

1999-2011	Professional Engineer, California, License #59568
2004-	Member, Society for Neuroscience
2008-	Co-founder and member, Xona Microfluidics, LLC (now Xona Microfluidics, Inc.), Research Triangle Park, NC
2015-2019	Editorial Board Member, Scientific Reports (Nature)

Honors and Awards

2004-2006	NRSA Predoctoral Fellowship, NINDS
2007-2008	Postdoctoral Fellowship, Johnson & Johnson
2010	Max Planck Institute for Brain Research scholarship for foreign scientists
2010	Keystone Symposia scholarship (Synapses: Formation, Function, and Misfunction)
2013-2014	K12 Engineering Career Development Scholar in Movement & Rehabilitation Sciences
2013-2015	Sloan Research Fellowship (1 of 16 selected in Neuroscience throughout the US and Canada)
2017	Symposium organizer for Pittcon 2017, session entitled *Scalable Neuron-Based Cell Culture Assays for Drug Discovery and Toxicity Testing*
2017	NIH Reviewer for NIBIB Trailblazer Award for New and Early Stage Investigators (R21) ZRG1 BST-H(50)
2017	Keynote speaker, μTAS 2017, Savannah, Georgia
2017	Keynote speaker, Neurofluidics 2017, Grenoble, France
2019-2020	NIH Reviewer, IMST (15) Small Business: Cell and Molecular Biology
2020	INSERM grant reviewer: ITMO Cancer of the French National Alliance for Life and Health Sciences (AVIESAN) jointly with the French National Cancer Institute (INCa).
2020-2021	NIH Reviewer, Commercialization Readiness (CRP) Study Section

C. Contributions to Science

1. Microfluidic tools for studying neurons

Neurons are highly specialized, polarized cells with a cell body, an axon that transmits signals, and dendrites that receive signals. Traditional neuron-cell culture approaches result in random outgrowth of processes, which prevent the study of neurons in their unique polarized morphology. Neurons extend processes over long distances and can experience multiple local environments; thus, their study demands an approach able to examine soma, axon and dendrite domains separately. One of my major contributions to science has been the invention of the first microfluidic device to compartmentalize neurons, which has opened the door for multiple novel investigations that were not previously possible. The resulting paper in Nature Methods has been cited close to 1,000 times. While in Erin Schuman's lab, I developed another novel microfluidic device to visualize and manipulate synapses (Taylor et al., ***Neuron***, 2010). In my own laboratory, I developed a microfluidic device to expose axons to extremely stable soluble gradients for axon guidance studies (Taylor et al., ***Lab***

Chip, 2015). This latter device uses only passive forces (no pumps), making it easily accessible to biologists. Our collaborator at UNC (Stephanie Gupton) adopted this method for her axon guidance studies.

A. **Taylor, A.M.**, Dieterich, D.C., Ito, H. T., Kim, S.A. & Schuman, E.M.* *Microfluidic local perfusion chambers for the visualization and manipulation of synapses.* Neuron, 2010. 66, 57-68, PMID: 20399729
B. **Taylor, A.M.***, Menon, S., & Gupton, S.L.* *Passive microfluidic chamber for long-term imaging of axon guidance in response to soluble gradients.* Lab Chip, 2015. 15: 2781 - 2789, PMID: 26000554
C. Menon, S., Boyer, N., Winkle, C., McClain, L.M., Hanlin, C., Rueckel, J., Rothenfußer, S., **Taylor, A.M.**, & Gupton, S.L.* *The E3 ubiquitin ligase TRIM9 is a filopodia off switch required for netrin dependent axon guidance.* Developmental Cell, 2015. 35(6): 698-712, PMID: 26702829
D. Nagendran, T., Poole, V., Harris, J., **Taylor, A.M.*** *Use of Pre-Assembled Plastic Microfluidic Chips for Compartmentalizing Primary Murine Neurons* J Vis Exp, 2018. Nov 2;(141), PMID: 30451222

2. Cellular determinants of synaptic remodeling after axotomy in pyramidal neurons

Brain injury and stroke induce significant synaptic reorganization, even in remote uninjured cortical regions. This enhanced plasticity makes the brain particularly receptive to therapeutic interventions following injury. While this plasticity is a guiding principle in clinical rehabilitation, very little is known about its cellular basis. Long projection pyramidal neurons extend axons into numerous distant areas of the CNS, including the spinal cord and apposing cortical hemisphere. Following distal axon injury, enhanced excitability occurs in cortical layers containing pyramidal somatodendritic regions due to loss of local GABAergic inhibition and unmasking of preexisting excitatory connections. While enhanced excitability contributes to neural plasticity, there are also negative aspects of hyper-excitability such as excitotoxicity and increase risk of seizures. Because of the importance of pyramidal neurons in injury and disease, we set out to determine the progression of events that occur intrinsically within pyramidal neurons following distal axonal injury to affect retrograde synaptic remodeling and alter excitability. We used a novel microfluidic approach to specifically identify long projecting pyramidal neurons using retrograde labeling and subject them to axonal injury at an unprecedented distance away from their somatodendritic compartments. This allowed us, for the first time, to examine how synapses onto these directly injured neurons are altered over time and to examine the trans-synaptic changes that influence excitability of their uninjured synaptic inputs (Nagendran et al., ***Nat Commun***, 2017). Our data suggests that retrograde signaling from the postsynaptic compartment of injured neurons may be responsible for the enhancements in presynaptic excitability. To examine this further, we used an unbiased approach to identify differentially expressed genes 24h following injury, but before trans-synaptic excitability changes occurred. Our results showed that several transcripts show altered levels following injury, including netrin-1, a secreted cue that is critically involved in synaptogenesis and brain development. Our microarray results showed that netrin-1 was significantly down-regulated post-injury. Very encouragingly, we found that exogenous netrin-1 application normalized the injury-induced hyper-excitability effects at 40h post-axotomy. Thus, our data suggest that netrin-1 and other differentially expressed genes may provide therapeutically-relevant targets within a tractable time-window for modulating hyper-excitability following brain injury and stroke. Future studies will focus on (1) determining the signaling cascade triggering synaptic remodeling and (2) evaluating the therapeutic potential of netrin-1 *in vivo* in collaboration with Prof. Randolph Nudo at the University of Kansas Medical Center.

A. **Taylor, A.M.**, Berchtold, N.C., Perreau, V.M., Tu, C.H., Jeon, N.L. & Cotman, C.W.* *Axonal mRNA in uninjured and regenerating cortical mammalian axons.* J Neurosci, 2009. 29: p. 4697-4707. PMID: 19369540 (highlighted in “This Week in the Journal”)
B. Nagendran, T. Larsen, R.S., Bigler, R.L., Frost, S.B., Philpot, B.D., Nudo, R.J. & **Taylor, A.M.*** *Distal axotomy enhances retrograde presynaptic excitability onto injured pyramidal neurons via trans-synaptic signaling.* Nat Commun 2017. 8(1):625, PMID: 28931811
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3. Axonal mRNA translation during synaptogenesis and synaptic plasticity

During development pyramidal neurons extend long axons to form appropriate connections in remote regions of the CNS. These distal axons have considerable autonomy to form and modify functional synapses in response to local cues from target cells. During synapse maturation changes occur locally at presynaptic

terminals, including an enlargement of the synaptic vesicle pool and a reduced rate of synaptic vesicle release. The mechanism by which synaptic vesicles accumulate and release rate is modified at distal presynaptic terminals with autonomy from the rest of the neuron is of fundamental importance to brain development, learning and memory.

The identification of polyribosomes within dendrites has directed attention for local mRNA translation toward the postsynaptic compartment. Little is known about axonal translation in the CNS, mainly because of the difficulty in visualizing and manipulating presynaptic terminals in isolation without the overwhelming signal from the larger-diameter postsynaptic compartment. Using microfluidic tools (Taylor et al., ***Nat Meth***, 2005), I initiated and led a project to characterize the uninjured and regenerating axonal transcriptome of mature cortical neurons while a postdoc in Carl Cotman's lab (Taylor et al., ***J Neurosci***, 2009). I subsequently identified ribosomal RNA and β-catenin mRNA within presynaptic terminals and found that β-catenin mRNA was locally translated within rat hippocampal axons and regulated vesicle release rate (Taylor et al., ***J Neurosci***, 2013). This work has provided some of the first evidence for local mRNA translation in mammalian axons during synaptogenesis. More recently we have investigating the axonal transcriptome of human axons using glutamatergic neurons differentiated from NIH-approved human stem cells and compared these with the axonal transcriptome in rat hippocampal axons (Bigler et al., ***Sci Rep***, 2017).

A. **Taylor, A.M.**, Berchtold, N.C., Perreau, V.M., Tu, C.H., Jeon, N.L. & Cotman, C.W.* *Axonal mRNA in uninjured and regenerating cortical mammalian axons.* J Neurosci, 2009. 29: p. 4697-4707. PMID: 19369540 (highlighted in "This Week in the Journal")
B. **Taylor, A.M.***, Wu, J.R., Tai, H.C. & Schuman, E.M.* *Axonal translation of β-catenin regulates synaptic vesicle dynamics*. J Neurosci, 2013. 33(13): 5584-9. PMID: 23536073 (highlighted in "This Week in the Journal")
C. Bigler, R.L., Kamande, J.W., Dumitru, R., Niedringhaus, M., & **Taylor, A.M.*** *Messenger RNAs localized to distal projections of human stem cell derived neurons.* Scientific Reports**,** 2017. 7(1): 611, PMID: 28377585

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1BaineZg5bmQ9/bibliography/46761835/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1R21NS109750-01A1 (PI: Taylor) 04/2020-03/2022
NIH/NINDS
Title: The Role of ER in Axon-to-Soma Injury Signaling in Pyramidal Cells
The goal of this grant is to investigate calcium-dependent axon-to-soma signaling following axotomy that causes somatic ER stress and synapse loss.

1R41NS108895-01 (PI: Taylor) 09/2018-08/2020 (No cost extension)
NIH/NINDS
Title: A user-friendly microfluidic chip for anti-epileptogenic drug screening
The goal of this grant is to develop a new anti-epileptogenic drug screen using Xona's patented platform technology.

Completed Research Support

1R42MH097377 (PI: Taylor) 05/2013-08/2019
A user-friendly scalable microfluidic platform for enhanced neuron-cell culture
The goal of this Phase II small business technology transfer grant is to develop user-friendly and robust technology for neuron-cell culture including the development of novel technology to examine and manipulate synapses.

17GRNT33700108 (PI: Taylor) 07/2017-06/2019
AHA Grant-in-Aid ***Received impact score of 1.39 (out of 100) and percentile rank of 0.13%***
Title: Molecular mechanisms triggering synaptic remodeling following stroke

The goal of this grant is to identify critical signaling pathways and molecules triggering synaptic remodeling following stroke.