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LASHAE NICHOLSON

PROFILE

I am a Kavli Postdoctoral Research Fellow at Yale University, where I am studying the molecular mechanisms linking neuronal and vascular dysfunction in neurological disorders. Using genetic sequencing approaches, my research investigates complex cellular interactions contributing to disruptive changes in neuronal morphology and function associated with these disorders.

RESEARCH METRICS

H-Index: 8

Total Citations: 320

Publications

Published: 13Under review: 1In preparation: 2

OMICS & DATA SCIENCE SKILLS & EXPERIENCES

- MIT IDSS Course: Data Science and Machine Learning
- snRNA sequencing
 - Sample preparation
 - Seurat, Scanpy, scVI

RESEARCH AREAS

- Alzheimer's Disease, neurodegeneration
- Spinal cord injury, neuro-regeneration
- Neurovascular signaling
- Axonal regeneration
- Gene therapy & gene editing
- Cell & biomaterial implantation
- Translational clinical research

RESEARCH EXPERIENCE

Postdoctoral Training

Yale University, Department of Neuroscience | New Haven, CT Supervisor: Prof. Dr. Stephen Strittmatter, MD, PhD 2019-Present

Graduate Studies

Wolfgang Goethe University | Frankfurt, Germany BLMS & MPI for Brain Research Institutes Supervisor: Prof. Dr. Amparo Acker-Palmer, PhD 2013-2019

EXPERIMENTAL TECHNIQUES

- Animal Models: Rodent husbandry, post-operative care, drug delivery, cell & tissue preparations (Mice & Rats); viral gene therapy (Human & Monkey, SCI project)
- Cell & Tissue Culture: DRGs, CGNs, CHO, PC12, NPCs, iPSCs, SKPCs, astrocytes, fibroblasts, BMSCs, HCNs, OTCs, splenocytes, primary lung endothelial, neuronal cell cultures.
- Assay Systems: DNA / receptor binding, siRNA, gene regulation (Tet, CreERT, temperature inducible systems)
- Biochemistry: WB, ISH / FISH, IP, ICC, IHC, protein modifications, protein purification.
- Microscopy: Laser micro-dissection, Confocal LSM/SD, live cell imaging, FLIP/FRAP.
- Gene and Molecular Biology: Construct libraries, recombinant cloning (gateway, shuttle vector systems), sitedirected mutagenesis, siRNA constructs, viral vector design & production (Tet-On/Off, CreERT tamoxifen-inducible systems).
- Virus Production: AAV (including for human delivery), lentivirus, retrovirus, and bacterial phages.

LaShae K. Nicholson

Curriculum Vitae, January 2024

Present Position

Kavli Postdoctoral Research Fellow

Stephen Strittmatter Lab
Department of Neuroscience
Program in Cellular Neuroscience,
Neurodegeneration and Repair
Yale University
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New Haven, CT, 06510

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Yale Profile; Strittmatter Lab Website

Education & Training

2019 Doctoral Thesis, Dr. ret. nat. Biology

Wolfgang Goethe University, Frankfurt, Germany

"The functional role of cell-type specific VEGF secretion during neuronal development" Buchmann Institute for Molecular Life Sciences, Frankfurt, Germany Supervisor: Prof. Dr. Amparo Acker-Palmer

2013 Master's Degree, Biomedical Sciences & Technology

University of Applied Sciences, Mannheim, Germany

"Whole-cell dynamics of protein exchange in developing neurons"

Max Planck Institute for Brain Research, Department of Synaptic Plasticity, Frankfurt, Germany Supervisors: Prof. Dr. Erin Schuman, Dr. Cyril Hanus

Research Fellowships & Awards

2021- Present Kavli Postdoctoral Research Fellowship
 2013-2014 Max Planck Graduate Student Fellowship

Research Experience

Wolfgang Goethe University, Buchmann Institute for Molecular Life Sciences | 2013 - 2019

Supervisor: Prof. Dr. Amparo Acker-Palmer, Frankfurt, Germany

Investigated the role of the vascular guidance molecule, VEGF, and its receptor VEGFR2, during neuronal development and physiological function.

Wolfgang Goethe University, Neuroscience Center | Nov 2013 - Mar 2014

Supervisor: Prof. Dr. Thomas Deller and Dr. Andreas Vlachos, Frankfurt, Germany

Trained in culturing organotypic hippocampal slice cultures, performing entorhinal cortex lesions, and whole-cell patch clamping. Cloned a cell-type specific AAV library for targeting various neuronal cell sub-populations.

Max Planck Institute for Brain Research, Dept. of Synaptic Plasticity | Mar - Sept 2013 Supervisor: Prof. Dr. Erin Schuman and Dr. Cyril Hanus, Frankfurt, Germany

Developed a computational model to quantify and correlate protein mobility with respect to neuronal cell morphology in post-microscopy time-lapse images.

Ruprecht-Karls-Universitäts Heidelberg, BioQuant | Aug - Oct. 2011

Supervisor: Prof. Dr. Dirk Grimm, Heidelberg, Germany

Trained in AAV virus production and purification. Optimized tissue laser dissection protocol for AAV shuttle vector collaboration project.

Heidelberg Universitätsklinikum, Klinik für Paraplegiologie | 2010 - 2013

Supervisor: Dr. Armin Blesch, Heidelberg, Germany

Worked in an interdisciplinary environment to develop translational combinatorial approaches (gene therapy, biomaterials, physiotherapy) for treating spinal cord-injured clinical patients.

UC San Diego, School of Medicine, Dept. of Neurosciences | 2006—2010

Supervisors: Dr. Mark Tuszynski and Dr. Armin Blesch, San Diego, California, USA

Developed viral vector systems to regulate gene expression *in vivo* to study neuronal degeneration and promote axonal regeneration in a spinal cord injury model.

Societies & Organizations

German Neuroscience Society | Hertie Foundation Alumni Association | FENS | Minerva FemmNet | Max Planck Society | SciMento | Young Entrepreneurs in Science (Falling Walls Organization) | Science Innovation Union | Deutsche Neurowissenschaften Olympiade e.V.

Leadership Positions

Diversity, Equity, and Inclusion Committee Co-Chair | 2020-2021

Department of Neurology, Yale University

International Brain Bee (IBB) Organization, World Neuroscience Championship | June 2018

11th FENS Forum of Neuroscience, Berlin, Germany

Invited committee chair on behalf of the IBB Organization and its board members: SfN, APA, FENS, Dana Alliance, iBro.

Position: Committee Chair, Host Country

IMPRS for Neural Circuits, Science Retreat | April 2018

Bordeaux NeuroCampus, Université de Bordeaux, Bordeaux, France

Position: Scientific coordinator co-chair

IMPRS for Neural Circuits, Science Retreat | April 2016 Champalimaud Center for the Unknown, Lisbon, Portugal

Position: Scientific coordinator

Teaching, Training & Mentorships

Graduate & Post-bachelor Student Research Projects

- Zheyun X (Graduate Student Rotation, 2024, Yale University):
 Comparative transcriptomic profiling of cortical gene expression changes in APOE2 and APOE4 mice post spinal cord injury.
- Christine W (Graduate Student Rotation, 2023, Yale University)

 Characterization of the spatial localization of mGluR5 and PrP proteins in iPSC, primary neuron cultures, and mouse brain tissues using expansion microscopy.
- Tejaswini K (Postbach trainee, 2021-2023, Yale University):
 The impact of Type 2 Diabetes on the pathological development of Alzheimer's Disease.

Master's Students

 Madhuri M. (Master's Thesis, 2016, Wolfgang Goethe University): Characterization of VEGF / VEGFR2 expression in cultured astrocytes under normal and KCl stimulation conditions

- Adesanoye B. (Rotation Project, 2015, Wolfgang Goethe University): Characterization of VEGF-induced VEGFR2 activation and downstream signaling in cultured neurons.
- Benjamin M. (Rotation Project 2014, Wolfgang Goethe University):
 Characterization of VEGF / VEGFR2 expression in the adult mouse hippocampus.

Bachelor Student Research Projects

- Jacqueline W. (Bachelor's Thesis, 2023-2024, Yale University: Characterization of vascular network changes during the pathological development of Alzheimer's Disease.
- Sapphire M.(Yale Summer Research Fellow, 2021, Yale University):
 Comparative analysis of the brain vasculature in two different Alzheimer's Disease mouse models.
- Christina O. (Bachelor's Thesis, 2020-2021, Yale University):
 Characterization of ROCK1 expression within the neurovascular unit in the Alzheimer's Disease mouse brain.

High School Student Research Project

• Jimin K. (IMPRS Scholar's program, 2018-2019, MPI for Brain Research): Cloning of endothelial cell-targeted AAV GCaMP6 vectors for functional vascular Imaging.

Seminars

Modern topics in neuroscience: Gene & Molecular Networks
 Max Planck Institute for Brain Research, IMPRS for Neural Circuits, Doctoral Students

Teaching Lab & Practical Courses

- Introduction to basic methods in neuroscience: Histology preparations and microscopy
 Wolfgang Goethe University, Dept. of Molecular and Cellular Neurobiology, Master's Course
- Methods in neuroscience: Cloning, PCR, and genotyping techniques
 Max Planck Institute for Brain Research, Teaching Lab, High School Students

Talks & Presentations

Why vessels matter in neuronal brain diseases (Talk) | 2021 Neuroscience Seminar Series, Yale University, New Haven, CT

Growing dendritic trees with vascular endothelial growth factor (Talk) | March 2019 Neuroscience Seminar Series, MPI for Brain Research, Frankfurt, Germany

Driving connectivity in neuroscience research (Talk) | April 2019 Neuroscience Seminar Series, Donders Center for Cognition, Nijmegen, Netherlands

Vessels and astrocytes coordinate hippocampal development and circuit integration (Poster) | March 2018 Dutch-German Vascular Biology Meeting, Amsterdam, Netherlands

VEGFR2-ephrinB2 cooperative signaling controls dendritic arborization and synapse formation (Poster) | March 2017 German Neuroscience Society Conference, Göttingen, Germany

Extracurricular Activities

Business Start-Ups

NeuroXP | STEM program development consulting for academic, industry, and organizations. Position: Founder

Deutsche Neurowissenschaften Olympiade e.V. (DNO e.V.) | Non-profit neuroscience outreach and educational platform for high school students.

Position: Brand & partnerships manager, Co-founding Member

Program Management (self-initiated)

GRADE Brain: University-wide career development training program for early career scientists. **Postdoc teaching training program:** A teaching training program for Postdocs working at non-university neuroscience research institutions.

Neuroscience Education Initiative Working with several stakeholders to establish a neuroscience training program for high school teachers. The overall goal is to establish a high school-level neuroscience curriculum.

Publications (*First Author)

H-index: 8 Total Citations: 320

In preparation for submission

*Nicholson L, Karra T, Tang J, Strittmatter SM. Hyperglycemia alters the disease state functionality of activated microglia, causing accelerated synapse loss in a double knock-in mouse model of Alzheimer's Disease. (*In preparation for submission, target date March 2024*)

Under review:

Zhang L, He CH, Coffey S, Yin D, Hsu IU, Su C, Ye Y, Zhang C, Spurrier J, **Nicholson L**, Rothlin CV, Ghosh S, Gopal PP, Hafler DA, Zhao H, Strittmatter SM. *Single-cell transcriptomic atlas of Alzheimer's disease middle temporal gyrus reveals region, cell type, and sex specificity of gene expression with novel genetic risk for MERTK in females.* medRxiv [Preprint]. 2023 Feb 23:2023.02.18.23286037. PMID: 36865305, PMCID: PMC9980267, DOI: 10.1101/2023.02.18.23286037

Published

- 1. Stoner A, Fu L, *Nicholson L, Zheng C, Toyonaga T, Spurrier J, Laird W, Cai Z, Strittmatter S. Neuronal transcriptome, tau and synapse loss in Alzheimer's knock-in mice require prion protein. Alzheimer's Research & Therapy 2023, 15: 201. PMID: 37968719, PMCID: PMC10647125, DOI: 10.1186/s13195-023-01345-z.
- Zheng C, Toyonaga T, Chen B, Nicholson L, Mennie W, Liu M, Spurrier J, Deluca K, Strittmatter SM, Carson RE, Huang Y, Cai Z. Decreased synaptic vesicle glycoprotein 2A binding in a rodent model of familial Alzheimer's disease detected by [18F]SDM-16. Front Neurol. 2023, 14: 1045644. doi: 10.3389/fneur.2023.1045644. PMID: 36846134, PMCID: PMC9945093, DOI: 10.3389/fneur.2023.1045644
- 3. Zheng C, Mennie W, Gravel P, Balayeva T, Chen B, Holden D, Kapinos M, Felchner Z, **Nicholson L**, Toyonaga T, Zheng M, Fowles K, Ropchan J, Nabulsi N, Strittmatter, SM, Carson R, Huang Y, Cai Z. *Synthesis and preclinical evaluation of 18F-labeled radioligands for imaging rho-associated protein kinase 2 in the brain*. Journal of Nuclear Medicine. 2023;64(supplement 1):P779-P.
- 4. Zheng C, Chen B, Toyonaga T, **Nicholson L**, Holden D, Zhang L, Gao H, Zheng M, Fowles K, Ropchan J, Strittmatter SM, Carson R, Huang Y, Cai Z. *Preclinical evaluation of [11C]ROCK201 for imaging rho-associated protein kinase 2 in brain*. Journal of Nuclear Medicine. 2022;63(supplement 2):2301-2301.
- 5. Zheng C, Chen B, Toyonaga T, Liu M, **Nicholson L**, Deluca K, Strittmatter S, Carson R, Huang Y, Cai Z. *Visualization of synaptic vesicle protein 2A in a rodent model of familial Alzheimer's disease with a metabolically stable PET probe*. Alzheimer's & Dementia 2022, 18 DOI: 10.1002/alz.063890.
- Spurrier J, *Nicholson L, Fang XT, Stoner AJ, Toyonaga T, Holden D, Siegert TR, Laird W, Allnutt MA, Chiasseu M, Brody AH, Takahashi H, Nies SH, Pérez-Cañamás A, Sadasivam P, Lee S, Li S, Zhang L, Huang YH, Carson RE, Cai Z, Strittmatter SM. Reversal of synapse loss in Alzheimer mouse models by targeting mGluR5 to prevent synaptic tagging by C1Q. Science Translational Medicine 2022, 14: eabi8593. PMID: 35648810, PMCID: PMC9554345, DOI: 10.1126/scitranslmed.abi8593.
- *Nicholson L, Gervasi N, Falières T, Leroy A, Miremont D, Zala D, Hanus C. Whole-Cell Photobleaching Reveals Time-Dependent Compartmentalization of Soluble Proteins by the Axon Initial Segment. Frontiers In Cellular Neuroscience 2020, 14: 180. PMID: 32754013, PMCID: PMC7366827, DOI: 10.3389/fncel.2020.00180.

- 8. Harde E, **Nicholson L**, Cuadrado B, Bissen D, Wigge S, Urban S, Segarra M, de Almodóvar C, Acker-Palmer A. *EphrinB2 regulates VEGFR2 during dendritogenesis and hippocampal circuitry development*. ELife 2019, 8: e49819. <u>PMCID: PMC6927743</u>, <u>DOI: 10.7554/elife.49819</u>.
- 9. Luck R, Urban S, Karakatsani A, Harde E, Sambandan S, **Nicholson L**, Haverkamp S, Mann R, Martin-Villalba A, Schuman EM, Acker-Palmer A, de Almodóvar C. *VEGF/VEGFR2 signaling regulates hippocampal axon branching during development*. ELife 2019, 8: e49818. PMID: 31868583, PMCID: PMC6927742, DOI: 10.7554/elife.49818.
- Liu S, Sandner B, Schackel T, Nicholson L, Chtarto A, Tenenbaum L, Puttagunta R, Müller R, Weidner N, Blesch A. Regulated viral BDNF delivery in combination with Schwann cells promotes axonal regeneration through capillary alginate hydrogels after spinal cord injury. Acta Biomaterialia 2017, 60: 167-180. PMID: 28735026, DOI: 10.1016/j.actbio.2017.07.024.
- McCall J, Nicholson L, Weidner N, Blesch A. Optimization of adult sensory neuron electroporation to study mechanisms of neurite growth. Frontiers In Molecular Neuroscience 2012, 5: 11. PMID: 22347167, PMCID: PMC3274834, DOI: 10.3389/fnmol.2012.00011.
- 12. Hou S, **Nicholson L**, van Niekerk E, Motsch M, Blesch A. *Dependence of Regenerated Sensory Axons on Continuous Neurotrophin-3 Delivery*. Journal Of Neuroscience 2012, 32: 13206-13220. PMID: 22993437, PMCID: PMC3513675, DOI: 10.1523/jneurosci.5041-11.2012.
- Kenyon WJ, Nicholson KL, Rezuchova B, Homerova D, Garcia-Del Portillo F, Finlay BB, Pallen MJ, Kormanec J, Spector MP. Sigma(s)-Dependent carbon-starvation induction of pbpG (PBP 7) is required for the starvation-stress response in Salmonella enterica serovar Typhimurium. Microbiology (Reading, England) 2007, 153: 2148-2158. PMID: 17600059, DOI: 10.1099/mic.0.2007/005199-0.

References

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Chair Of Neuroscience

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Professional connection: Current Postdoctoral Supervisor

Prof. Amparo Acker-Palmer, PhD

Head Of Department

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Professional connection: Ph.D. Supervisor

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Professional connection: Former Supervisor