

UConn

Department of Physiology
and Neurobiology

PNB Newsletter

Summer 2021

Department News

Accreditation of IONM (Intraoperative Neuromonitoring) Master's program

We are pleased to announce the accreditation of the Master of Science in Surgical Neurophysiology program from the Commission on Accreditation of Allied Health Education Programs (CAAHEP). This makes it the first graduate Intraoperative Neuromonitoring degree program in the nation to receive such an accomplishment. This great achievement allows IONM graduates to take part in the CNIM exam after 100 cases (instead of 150) and be eligible under Pathway I by ABRET (the organization in charge of certification in the field of IONM).

This success would not have been possible without the incredible dedication of Payam Andalib, the Clinical Director of the program and Radmila Filipovic, the Academic Director and the great support of Amber LaFontaine, the IONM Program's Administrative Assistant, and Joe LoTurco, PNB's previous Department Head. They have all worked incredibly hard to make the program successful.



Move to Gant new teaching laboratory space completed in June

Human Physiology and Anatomy student labs have successfully moved to the newly renovated space in the southwest corner of the first floor of the Gant Science Complex. The new space includes five active learning laboratory classrooms that are designed to foster interactive, flexible, student-centered learning experiences. For example, each classroom has 4 round tables to facilitate discussions, group work, and peer teaching. This interaction zone is surrounded by 7 – 8 computer stations that allow data collection and other lab exercises (see photo). Digital devices, including lab computers, Digital Cadaver table, and other devices, can be readily projected to three big screens/projects, which further facilitate interactions and student presentations. For a practical guide to making the most out of an active learning classroom please see Baepler, P. M., Walker, J. D., Brooks, D. C., Saichaie, K., & Petersen, C. (2016). A guide to teaching in active learning classrooms: History, research, and practice. Stylus Publishing.



The new space also includes offices for the A&P staff Penny Dobbins, Ann Hamlin, and Sonda Parker. Across the hallway is Ed Lechowicz's shop and office. This wing of Gant also houses introductory laboratory classrooms for other biology disciplines.

Congratulations to Penny and her staff, and Ed for your efforts in planning and executing the move!

Faculty and graduate students participate in Healthcare Career Opportunity Program

Associate Professor Alex Jackson and PhD student Kristen Springer have been coordinating with the [Healthcare Career Opportunity Program at UCHC](#). They had their first outreach activity in May, which involved a presentation and panel discussion for 11th and 12th graders in the Hartford area over WebEx. Alex started with an overview of UConn, PNB and what we study in the lab. Graduate students Kristen, Brenda Milla, and Will Armstrong each introduced themselves and what they work on in the lab. Alex then touched on a number of relevant topics including training pathways in neuroscience research and career opportunities following graduate work in neuroscience (and STEM fields in general). This was followed by a Q&A about seeking research opportunities while in high school and in college as well as topics of interest to the students. Some ideas for follow up activities are being discussed, which include organizing a “UConn Brain Day” to offer lab tours and/or presentations for HCOP students.

New light sheet microscope in the Advanced Light Microscopy Facility

A new [Zeiss Lightsheet 7 microscope](#) was purchased using the award from CLAS equipment competition (proposal written by Jianjun Sun in PNB and Spencer Nyholm in MCB with significant contribution from Facility Director Chris O’Connell) and matching funds from all biology departments.

It is now installed in the facility and ready to be used.

New student awards

Graduate students

Excellence in Research Fellowships

Alisa White (Kanadia lab)
Nissi Varghese (Tzingounis lab)
Pratyajit Mohapatra (Menuz lab)

James Romanow Award

Janeth Perez Garza (Ostroff lab)

Undergraduate students

Beckman Scholarship Awards

Katarina Yacuk (Sun lab)

MARC Scholarship Awards

Victoria Cuevas (LoTurco lab)
Teresa Tamborra-Walton (Lynes lab – MCB)
Sara Bernardo (Jackson lab)

Research

Notable papers

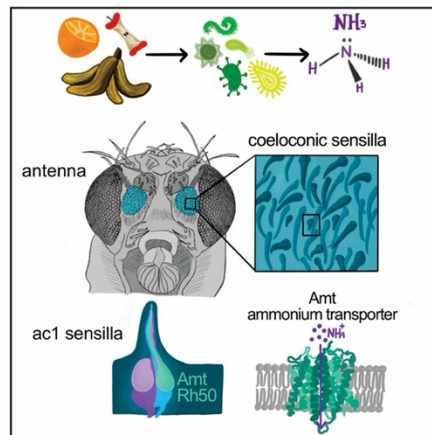
Ali Vulpe et al., Curr Biol 2021 (Menuz lab and collaborators)

Recent work from PNB graduate student Ali Vulpe in the Menuz lab identified a surprising type of olfactory receptor for ammonia (Vulpe et al., Current Biology). Research Assistant Sydney Ballou and undergraduate Tiffany Liang (PNB) contributed to this work, as well as collaborators at UC San Diego, Yale, and the Max Planck Institute for Chemical Ecology (Jena, Germany). Although unpleasant to humans, ammonia is an attractive odor for a wide variety of insects, including insect vectors of disease. This discovery was precipitated by their discovery of two previously uncharacterized populations of ammonia-sensing olfactory neurons that both express the ammonium transporters Amt and Rh50. Further investigations revealed that these neurons are selectively tuned to ammonia, mediate ammonia-induced neural spiking activity, and contribute to ammonia-seeking behavior. They next addressed the question of which olfactory receptor mediates ammonia responses in these neurons. There are two olfactory receptor gene families in insects, but the ammonia responses were independent of co-receptors required for the function of each of the known receptor families. Using genetic mutants and ectopic expression experiments, they went on to demonstrate that the ammonium transporter Amt is the olfactory receptor for ammonia in these neurons. This is the first example of a transporter functioning as a receptor in an olfactory system. Additional experiments using an *Anopheles* mosquito ortholog AgAmt together with reports by other labs that AgAmt is expressed by mosquito olfactory neurons suggest that this highly conserved ammonium transporter serves as an olfactory receptor across insect species.

Current Biology

Vulpe A, Kim HS, Ballou S, Wu S-T, Grabe V, Gonzales CN, Liang T, Sachse S, Jeanne JM, Su C-Y, Menuz K.

An ammonium transporter is a non-canonical olfactory receptor for ammonia



Kewa Jiang, Yuping Huang, et al. PNAS 2021 (Sun lab and collaborators)

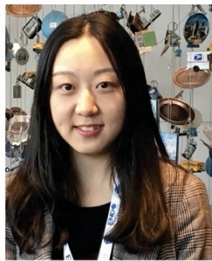
Recent work from PNB Postdoc Yuping Huang and former Research Assistant Kewa Jiang in the Sun lab established a novel platform for nonhormonal contraceptive screening utilizing a fruit fly model (Kewa et al., PNAS). The graduate student Jiyang Zhang (Northwestern University) and Yingzheng Wang (Rutgers University) contributed to this work, as well as other collaborators at UConn Pharmaceutical Sciences, Northwestern University, University of Rutgers, and Michigan State University. Few contraceptive drugs have been developed since the approval of contraceptive pills by the Food and Drug Administration sixty years ago. Although effective, hormonal-based contraceptive pills often lead to undesirable side effects and other risk factors. Development of nonhormonal based contraceptives for women is also completely stalled due to the lack of effective screening platforms. With the recent discovery that the fruit fly utilizes conserved cellular and molecular mechanisms for ovulation as mammals, Sun lab is hoping to utilize fruit fly ovulation as a simple and efficient model to screen compounds that can inhibit ovulation in mammals. Such compounds have great potential to inhibit human ovulation and for nonhormonal contraceptive development. To prove this concept, they screened 1172 FDA-approved drugs using their novel ex vivo follicle rupture assay and identified six compounds that can effectively inhibit fruit fly ovulation. Intriguingly, three out of four candidate drugs showed inhibition of mouse ovulation in an in vitro culture system. Moreover, they demonstrated that chlorpromazine, a psychiatric drug for treating schizophrenia, could inhibit hCG-induced superovulation in mice when injected at 5mg/kg intraperitoneally. Current results suggest that fruit fly ovulation can be a valuable screening platform for the identification of nonhormonal contraceptive compounds. Now, Sun lab is optimizing their screening platform to increase the throughput so that it will provide a faster way to dig more interesting and potent compounds for nonhormonal birth control development.



Jiang K, Zhang J, Huang Y, Wang Y, Xiao S, Hadden KM, Woodruff TK, Sun J. **A platform utilizing *Drosophila* ovulation for nonhormonal contraceptive screening**



Kewa Jiang



Jiyang Zhang



Yuping Huang

Anouk Olthof (Kanadia lab and collaborators)

The central goal of the Kanadia Lab is to understand the role of minor spliceosome in development and disease. The minor spliceosome, which consists of U11, U12, U4atac, U5 and U6atac snRNAs, is responsible for splicing <0.5% of the introns that are found in <2% of the human gene that mostly consist of major introns. In these minor intron-containing genes (MIGs), minor introns are often flanked by major introns. Therefore, the proper splicing of these MIG-transcripts requires coordinated action of both the major and the minor spliceosome. The importance of proper splicing of these introns is underscored by the developmental disorders linked to mutation in the minor spliceosome components. For example, microcephalic osteodysplastic primordial dwarfism type 1, Roifman syndrome, Lowry-Wood syndrome are linked to mutation in U4atac snRNA, while early onset cerebellar ataxia and congenital disorder characterized by Craniosynostosis are linked to mutations in U12 snRNA. U11 snRNA is linked to predisposition to cancer.

In Olthof et al., *Nucleic Acids Research* Volume 49, Issue 6, 6 April 2021, Pages 3524–3545, (<https://doi.org/10.1093/nar/gkab118>) we leveraged our U11 conditional knockout mouse to study the consequences of aberrant minor spliceosome activity in the developing cortex. We discovered that besides failure to successfully splice minor introns, the inhibition of the minor spliceosome resulted in alternative splicing across minor introns executed by the major spliceosome. We showed that alternative splicing by the major spliceosome is induced when we inhibit the minor spliceosome through morpholinos against U4atac, U12 and U6atac morpholinos or through siRNAs against minor spliceosome proteins such as PDCD7 or RNPC3. We show that aberrantly spliced MIG-transcripts are exported to the cytoplasm. Although these transcripts were bioinformatically predicted to be downregulated through non-sense mediated decay (NMD), they appear to escape NMD and are instead bound to the polysomes. This finding opens the possibility that disease pathogenesis might also occur through aberrant protein products. We go on to show that similar aberrant alternative splicing events are also present in the peripheral blood mononuclear cells from individuals with Lowry-Wood syndrome, Roifman syndrome and early onset cerebellar ataxia. Finally, through immunoprecipitation and Mass Spectrometry, we show that PDCD7, a protein component of the minor spliceosome, directly interacts with the U2AF proteins of the major spliceosome to enable proper splicing of the upstream major introns. This finding provides a mechanism by which the exon-definition model proposed for major intron splicing can be extended to the proper splicing of MIG-transcripts. In all, the findings here shed light onto the mechanism of normal splicing of major introns flanking minor introns and the alternative splicing regulation by the major spliceosome when the minor spliceosome is inactivated. Based on these findings, we are currently exploring how the major spliceosome regulates the recruitment of the minor spliceosome.

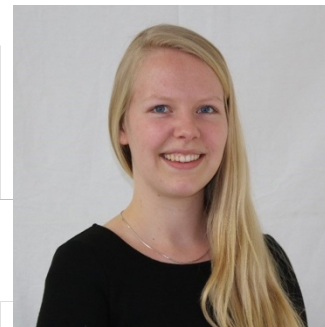
Nucleic Acids Research

Disruption of exon-bridging interactions between the minor and major spliceosomes results in alternative splicing around minor introns

Anouk M Olthof, Alisa K White, Stephen Mieruszynski, Karen Doggett, Madisen F Lee, Almahdi Chakroun, Alice K Abdel Aleem, Justine Rousseau, Cinzia Magnani, Chaim M Roifman, Philippe M Campeau, Joan K Heath, Rahul N Kanadia 

Nucleic Acids Research, Volume 49, Issue 6, 6 April 2021, Pages 3524–3545,
<https://doi.org/10.1093/nar/gkab118>

Published: 28 February 2021 [Article history](#) ▼



Amin Sherafat et al., Nat Commun 2021 (Nishiyama lab)

Recent work from PNB graduate student Amin Sherafat in the Nishiyama lab in collaboration with visiting assistant professor and Marie Skłodowska-Curie fellow Friederike Pfeiffer demonstrated a critical region-specific role for microglia in promoting oligodendrocyte precursor cell (OPC) proliferation during development and the repair of acutely demyelinated lesions. OPCs are resident glial cells in the central nervous system that generate myelinating oligodendrocytes and thus are essential for the fast saltatory conduction of action potentials. The lab had previously shown that OPCs in white matter containing axon tracts but not those in the gray matter containing neuronal cell bodies respond to the mitogenic effects of platelet-derived growth factor (PDGF) AA, despite the presence of the receptor PDGFR α on OPCs in both locations. This has been a topic of interest since the pathology and the efficiency of repair in demyelinated diseases such as multiple sclerosis differ significantly between lesions in the gray and white matter. A bioinformatic search for a potential regulator/coreceptor for PDGFR α that could differentially mediate the effects of PDGF AA led to the identification of an integral membrane protein neuropilin-1 (Nrp1) as a candidate, which had previously been shown to modulate vascular endothelial growth factor signaling in non-neural cells. Surprisingly Nrp1 is not expressed by OPCs but it is present on a subset of activated microglia that appear only in white matter. Deletion of Nrp1 from microglia reduced OPC proliferation in white matter and compromised the repair of demyelinated lesions. Studies using slice and dissociated culture revealed that Nrp1 augments OPC proliferation most prominently in the presence of limiting amounts of PDGF AA, and Nrp1 phosphorylates PDGFR α on OPCs. The study proposes the following novel concepts: 1) The regional differences in the dynamics of oligodendrocytes are mediated by regional differences in the function of microglia and 2) an integral protein on microglia can trans-activate a growth factor receptor on adjacent OPCs. The study has opened a new project in our lab to understand the role of microglia as sensors of changes in myelin and the mechanisms by which they communicate with myelinating cells to restore myelin homeostasis.

nature communications

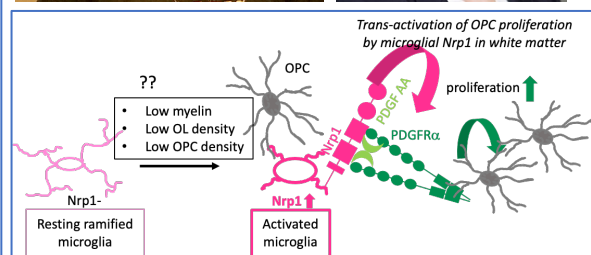
nature > nature communications > articles > article

Article | [Open Access](#) | Published: 15 April 2021

Microglial neuropilin-1 promotes oligodendrocyte expansion during development and remyelination by trans-activating platelet-derived growth factor receptor

Amin Sherafat, Friederike Pfeiffer, Alexander M. Reiss, William M. Wood & Akiko Nishiyama [✉](#)

Nature Communications **12**, Article number: 2265 (2021) | [Cite this article](#)



New Grants

The following new grants were awarded during the past year:

PI	Sponsor	Title	Award Period	Total Award
Tasso Tzingounis (Professor)	NIH/R21	Identification and validation of the epilepsy associated KCNQ2 complexes in the brain	7/1/20-6/30/22	\$ 442,750
Linnaea Ostroff (Assistant Professor)	NIH/R21	Quantum dot probes for electron microscopy	7/1/20-6/30/22	\$ 442,750
Linnaea Ostroff (Assistant Professor)	NSF	*NeuroNex: Enabling Identification and Impact of Synaptic Weight in Functional Networks	8/15/20-7/31/25	\$ 901,894
Xinnian Chen (Professor-in-Residence)	NSF	Collaborative Research: Defining and Measuring Student Trust of Instructor in College STEM Courses	10/1/20-9/30/23	\$ 115,229
Linnaea Ostroff (Assistant Professor)	NSF (conference)	Third Annual NeuroNex Investigator Meeting	11/1/20-10/31/21	\$ 33,617
Dan Mulkey (Professor)	NIH/R01	Glial chemosensitivity and control of breathing in Rett syndrome	1/1/21-12/31/24	\$ 2,109,559
Joanne Conover (Professor)	NIH/R21	Control of Forebrain Neuroblast Migration in Mouse and Human	9/1/20-8/31/21	\$ 442,750
Natale Sciolino (Assistant Professor)	NIH/R00	Defining locus coeruleus-norepinephrine (LC-NE) circuits in feeding	1/31/21-1/31/24	\$ 729,913
Gulcan Akgul (Assistant Research Professor)	Brain and Behavior Research Foundation	The Effects of Schizophrenia Associated Somatic Mutations on Connectivity and Function in Prefrontal Neocortical Circuits	1/15/21-1/14/22	\$ 35,000
Xinnian Chen (Professor-in-Residence)	HHMI	Broadening Participation to Advance Inclusive Teaching	7/1/21-12/31/23	\$ 313,633
Brenda Milla (PhD student)	NIH/F31	Roles of glycinergic neurons in Dravet Syndrome-associated disordered breathing and mortality	1/1/21-12/31/24	\$ 168,643
Jaseph Soto (PhD student)	NIH/F31	Proposed roles of KCNQ2 channels in Respiratory Homeostasis	12/1/20-11/30/24	\$ 165,788

The following grants have been transferred to UConn

PI	Sponsor	Title	Award Period	Total Award
Jianzong Yi (Assistant Professor)	NSF	Molecular Regulation of Insulin Signaling in Nutrient Stress Response in Drososphila	8/23/20-6/30-23	\$ 673,366
Jianzong Yi (Assistant Professor)	NIH/R01	Upstream Regulations of the Hippo Signaling Pathway	1/31/21-1/31/24	\$ 1,620,598

[NeuroNex](#) (Next Generation Network for Neuroscience Program) consists of 21 multidisciplinary teams across the US and are developing tools and resources to advance neural and cognitive research.

Alex Jackson (Associate Professor) received a large supplement (total \$420,634) to his NIH/R01 grant Hypothalamic spatial transcriptomics and connectomics in a mouse model of Alzheimers disease (7/21/21-3/31/22).

Other research news

Alex Jackson's application for a new Gordon Research Conference focused on the hypothalamus, which he and three other investigators proposed, was approved last fall. Alex is co-Vice Chair of the inaugural [Hypothalamus Gordon Research Conference](#) in July 2022 and co-Chair in 2024. Congratulations Alex!

Teaching and Mentoring

University and CLAS awards

Jeff Devino

2021 CLAS Strategic Goal Award for Teaching, Learning, and Student Success

Rahul Kanadia

2021 CETL University Teaching Innovation Award - This is awarded to individuals who show a demonstrated commitment to continuously improving teaching through innovation and reflective practice. They are dedicated to teaching effectiveness and support enhanced levels of student engagement and learning.

New proposal funded

UConn FIRST in Biology: Fostering Ideal Regional Student Transitions in Biology

PIs:

- Michael Finiguerra (Associate Professor-in-Residence, EEB)
- John Redden (Associate Professor-in-Residence, PNB)

Co-PIs:

- Jeff Divino (Assistant Professor-in-Residence, PNB)
- Dylan Audette (Assistant Professor-in-Residence, MCB, Hartford)
- John Cooley (Assistant Professor-in-Residence, EEB, Hartford)
- Susan Herrick (Associate Professor-in-Residence, EEB)
- Elizabeth Kline (Assistant Professor-in-Residence, MCB)
- Claudia Kraemer (Associate Professor-in-Residence, EEB, Stamford)
- Luciana Santoferrara (Assistant Professor-in-Residence, EEB, Stamford)
- Colleen Spurling (Assistant Professor-in-Residence, MCB)
- Stephen Trumbo (Professor, EEB, Waterbury)

The goal of the project is to identify barriers to successful campus change in biology and test an intervention strategy to create academic support and equity for campus change students in biology, build community, and strengthen faculty and peer relationships.

NEXT-STEP Seminar Series successfully launched

Alex Jackson organized the NEXT-STEP Virtual Seminar Series in the fall 2020 and spring 2021 semesters to give PNB trainees perspective on different career paths. Five speakers in a variety of professions in science, technology, and engineering gave a presentation followed by a Q&A session with the trainees. This will be continued in the next academic year.

Syllabus Design Tips

The syllabus is the first impression students receive about the instructor and course so it is important to be mindful of the message and tone we want to communicate. In addition to the usual details (assignments, grading policies, etc.) a well-constructed syllabus can define class expectations, provide a roadmap to successfully meeting course objectives, and set the tone for the type of learning environment you plan to foster. Below are some tips for making an inclusive syllabus.

Sources include <https://www.csus.edu/college/natural-sciences-mathematics/center-science-math-success/center-communications.html>.

Use inviting language. Warm language will give the impression you are approachable and interested in helping students learn. The opposite is also true. This is particularly important for large enrollment courses. [Find more details on warm vs. cold language.](#)

Diversity Statement. The point of a diversity statement is to communicate your belief that you respect and value the opinions of all students in your class. Explicitly stating this will help create a welcoming environment for your students regardless of cultural, racial or gender background. Also, consider making clear how you will make sure everyone's voice will be heard. This statement can also help establish classroom etiquette and standards of behavior. [Find design tips and examples.](#)

Promote growth mindset. The growth mindset is the idea that the ability to learn can develop with effort. Conversely, the fixed mindset is the idea that intellectual capacity is set at birth, therefore people with a more fixed mindset are often discouraged by challenges and give up easily. Cultivating a growth mindset among all students, especially underrepresented minority students, is of particular importance. As students encounter inevitable challenges and setbacks, a growth mindset can help battle stereotype threats, embrace challenges, persist, respond well to feedback, and find inspiration in the success of others.

Tips to cultivate a growth mindset:

- Provide encouragement throughout the learning process
- set realistic goals
- promote effort and learn from mistakes.
- cultivate a positive/supportive classroom environment.

Be encouraging. Let students know that you want them to succeed. Use explicit language that defines expectations and provide guidance for achieving success.

Use accessible language. Avoid using slang, jargon or acronyms and use gender neutral language. [Find tips on how to create a culturally responsive classroom.](#)

Share personal details. Providing the students with a few details about yourself will make you seem more approachable to students. A description of your professional training will bolster your credibility and help the students understand what motivated you to teach this class.

Other helpful resources:

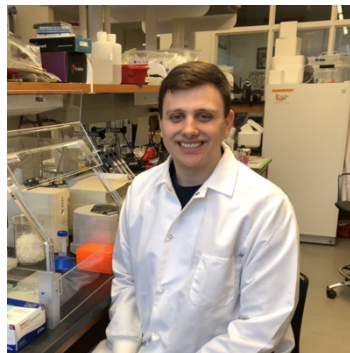
- [A Learner-Centered Syllabus Helps Set the Tone for Learning](#)
- [Inclusion By Design - Survey Your Syllabus and Course Design](#)

New PhDs

Recent Graduates, Summer 2020 – Spring 2021

Colin M. Cleary, Ph.D. (2017-2021) (Major Advisor Dan Mulkey)

Colin is originally from Woodbury, CT. He completed his undergraduate studies here at UConn and graduated cum laude in 2017. Colin joined our graduate program that summer and by August had successfully submitted a predoctoral fellowship to the NIH that supported his research for the duration of his thesis. Colin's research focused broadly on understanding how the brain controls breathing in response to changes in tissue CO₂/H⁺. In particular, he discovered that regulation of blood flow in a brainstem respiratory center is opposite to most parts of the body and is specialized to support the CO₂/H⁺ dependent drive to breathe. He went on to identify the cellular and molecular basis of this mechanism involves activation of P2Y₂ receptors on vascular smooth muscle cells. In separate work, Colin led efforts to understand the basis of disordered breathing in neurological disorders including Dravet syndrome and Pitt Hopkins syndrome. As part of this work, Colin identified two previously unrecognized populations of brainstem inhibitory neurons with functionally discrete roles in controlling breathing or arousal/sleep. He also provided the most convincing evidence to date for the existence of a specific group of neurons dedicated to regulating expiratory activity. These discoveries will fuel research in the Mulkey lab for many years to come.



This spring, Colin successfully defended his thesis and this fall will matriculate to UConn Medical School to continue his training as a physician scientist. He also managed to marry his college sweetheart, Jen, and the couple is looking forward to their future adventures together as a family.

Papers

Hawkins VE, Takakura AC, Trinh A, Malheiros-Lima MR, Cleary CM, Wenker IC, Dubreuil T, Rodriguez EM, Nelson MT, Moreira TS*, Mulkey DK*. Purinergic regulation of vascular tone in the retrotrapezoid nucleus is specialized to support the drive to breathe. *elife*. 2017 Apr 7;6. pii: e25232. Rated by F1000Prime as Very Good. Highlighted in [Elife](#). 2017 May 17;6. pii: e27563.

Kuo FS, Cleary CM, LoTurco JJ, Chen X, Mulkey DK. [Disordered breathing in a mouse model of Dravet syndrome](#). *elife*. 2019 Apr 26;8. (PMID: 31025941).

Cleary CM, Moreira TS, Takakura AC, Nelson MT, Longden TA, Mulkey DK. [Vascular control of the CO₂/H⁺-dependent drive to breathe](#). *elife*. 2020 Sep 14;9:e59499. (PMID: 32924935)

Mulkey DK, Olsen ML, Ou M, Cleary CM, Du G. Putative roles of astrocytes in general anesthesia. *Current Neuropharm* 2021 Feb 15. (PMID: 33588730).

Cleary CM, Milla BM, Kuo FS, James S, Flynn WF, Robson P, Mulkey DK. [Somatostatin-expressing parafacial neurons are CO₂/H⁺ sensitive and regulate baseline breathing](#). *eLife*. 2021 May 20;10:e60317. (PMID: 34013884).

Cleary CM, James S, Maher BJ, Mulkey DK. Disordered breathing in Pitt Hopkins syndrome involves disruption of parafacial respiratory neurons and aberrant expression of Nav1.8. In revision.

Funding

Title: Role of P2Y₂ in the Regulation of Vascular Tone and Control of Breathing

Source: NIH/NHLBI (F31 HL142227) (PI: CM Cleary)

Funding period: 5/1/18 to 4/31/21

Akie Fujita (Major Advisor Alex Jackson)

Dr. Akie Fujita successfully defended her PhD thesis in December, 2020. Dr. Fujita pursued a PhD in Biomedical Engineering working with advisor Dr. Alexander Jackson in the Department of Physiology and Neurobiology. Her thesis focused on the anatomical and electrophysiological properties of hypothalamic cells and circuits that control sleep and wakefulness. During her time in graduate school, Dr. Fujita published several papers, was a UConn Neuroscience Fellow and recipient of several awards including the Neuroscience at Storrs Graduate Poster Award (2019), SciComm-petition Poster Award (2019) and the Suzannah Bliss Tieman Outstanding Poster Award at NEURON, 2020. Dr. Fujita is currently a postdoctoral fellow in Dr. Bruce Bean's lab in the Department of Neurobiology at Harvard Medical School.



Papers

Mickelsen LE*, Bolisetty M*, Chimileski BR, Fujita A, Beltrami E, Costanzo J, Naparstek J, Robson P† and Jackson AC†. (2019) Single cell transcriptomic analysis of the lateral hypothalamic area reveals molecularly distinct populations of inhibitory and excitatory neurons. *Nature Neuroscience*. Apr; 22(4): pp. 642-656. *Equal contribution, †co-corresponding.

Fujita A*, Bonnavion P*, Wilson MH, Mickelsen LE, de Lecea, L† and Jackson AC†. (2017) Hypothalamic tuberomammillary nucleus neurons: electrophysiological diversity and essential role in arousal stability. *Journal of Neuroscience*. Sep 27; 37(39): pp. 9574-9592. *Equal contribution, †equal contribution.

Bonnavion P*, Mickelsen L*, Fujita A, de Lecea L and Jackson AC. (2016) Hubs and Spokes of the Lateral Hypothalamus: Cell Types, Circuits and Behavior (Invited Review). *Journal of Physiology*. 594(22): pp. 6443-6462. *Equal contribution.

She's also first author on the following manuscript, which is still under review:

Fujita A, Zhong L, Antony M, Chamiec-Case, E, Mickelsen, LE, Kanoski, SE, Flynn W and Jackson AC. Parallel cell type-specific limbic forebrain pathways mediate tachykininergic/GABAergic modulation of melanin-concentrating hormone neuron subpopulations (under review).

Shanu George (Major Advisor Angel De Blas)

Dr. Shanu George, Ph.D., Physiology and Neurobiology. Shanu is currently a Postdoctoral Fellow in Dr. Linda Van Aelst's laboratory at Cold Spring Harbor Laboratory.

During his graduate studies, Shanu was the recipient of the UCONN Neuroscience Fellowship Award (2016-2018) and PNB Teaching Excellence Award (2017). Shanu's research focused on the role of the rho guanine exchange factor, collybistin, on the clustering of GABA type-A receptors at inhibitory GABAergic synapses in the brain. Shanu has also designed a viral vector to manipulate the expression of collybistin in selective neurons and synapses, enhancing the strength of inhibitory GABAergic neurotransmission in these neurons. Shanu has shown that this viral-mediated targeted delivery of collybistin protects an experimental mouse models from induced seizures.

Publications during PhD

George S, James S, de Blas AL. Selective overexpression of Collybistin in mouse hippocampal pyramidal cells enhances GABAergic neurotransmission and protects against PTZ-induced seizures. *eNeuro*. 2021 Jun 2;ENEURO.0561-20.2021. doi: 10.1523/ENEURO.0561-20.2021. Epub ahead of print. PMID: 34083383.

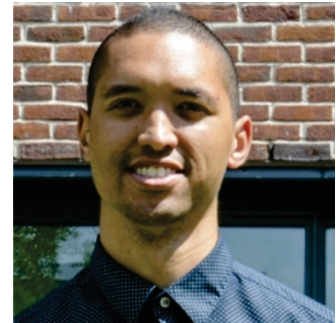
George S, Chiou TT, Kanamalla K, De Blas AL. Recruitment of Plasma Membrane GABA-A Receptors by Submembranous Gephyrin/Collybistin Clusters. *Cell Mol Neurobiol*. 2021 Feb 5. doi: 10.1007/s10571-021-01050-1. Epub ahead of print. PMID: 33547626.

George S, Bear J Jr, Taylor MJ, Kanamalla K, Fekete CD, Chiou TT, Miralles CP, Papadopoulos T, De Blas AL. Collybistin SH3-protein isoforms are expressed in the rat brain promoting gephyrin and GABA-A receptor clustering at GABAergic synapses. *J Neurochem*. 2021 May;157(4):1032-1051. doi: 10.1111/jnc.15270. Epub 2021 Jan 5. PMID: 33316079.

Miralles CP, Taylor MJ, Bear J Jr, Fekete CD, George S, Li Y, Bonhomme B, Chiou TT, De Blas AL. Expression of protocadherin-γC4 protein in the rat brain. *J Comp Neurol*. 2020 Apr 1;528(5):840-864. doi: 10.1002/cne.24783. Epub 2019 Nov 6. PMID: 31609469; PMCID: PMC6987019.

Shaun James, Ph.D. (2016-2021) (Major Advisor Dan Mulkey)

Shaun hails from Lawrence Kansas. He did his undergraduate studies at Drake University and received a MS in Exercise Science and Nutrition from Sacred Heart University in 2016. He joined our graduate program in 2016. His thesis work focused on characterizing adenosine modulation of neurons that regulate breathing in response to changes in tissue CO₂/H⁺. Shaun found that adenosine signaling via A1 receptors inhibited respiratory neurons directly by activation of an inward rectifying potassium conductance, and indirectly suppressing excitatory synaptic activity. This work provided the first characterization of synaptic properties of respiratory neurons in the retrotrapezoid nucleus (RTN). He also showed how cellular and synaptic properties of RTN neurons are disrupted in a disease model of Pitt Hopkins syndrome. Shaun is currently a postdoctoral fellow at the Yale School of Medicine.



Papers

James SD, Hawkins VE, Falquetto B, Ruskin DN, Masino SA, Moreira TS, Olsen ML, Mulkey DK. Adenosine signaling through A1 receptors inhibits chemosensitive neurons in the retrotrapezoid nucleus. *eNeuro* Accepted Nov. 26, 2018 (PMID: 30627640).

Cleary CM, Milla BM, Kuo FS, James S, Flynn WF, Robson P, Mulkey DK. [Somatostatin-expressing parafacial neurons are CO₂/H⁺ sensitive and regulate baseline breathing.](#) *eLife*. 2021 May 20;10:e60317. doi: 10.7554/eLife.60317. (PMID: 34013884)

Cleary CM, James S, Maher BJ, Mulkey DK. Disordered breathing in Pitt Hopkins syndrome involves disruption of parafacial respiratory neurons and aberrant expression of Nav1.8. In revision.

Amin Sherafat (Major Advisor Akiko Nishiyama)

Amin joined our program in 2014. He obtained his MS from Tarbiat Modares University in Tehran and then worked as a research assistant for several years in Dr. Su-Chun Zhang's lab at the Waisman Center of the University of Wisconsin at Madison. His interest in demyelinating diseases led him to seek further training in Akiko Nishiyama's lab at UConn. His thesis work led to the discovery that a subpopulation of microglia in the white matter containing axon tracts differ from those in the gray matter where neuronal cell bodies reside and promote oligodendrocyte precursor proliferation and subsequent oligodendrocyte differentiation and myelination during development and after myelin damage. This is mediated by an integral membrane protein expressed on this subset of microglia activating a growth factor receptor on adjacent oligodendrocyte precursor cells in trans. This was published in *Nature Communications* in April. The findings from this study have led to a more fundamental question of whether and how microglial cells signal to maintain homeostasis of oligodendrocyte lineage cells and myelin. Amin has left for this important and new question for the lab to investigate. His work has led us to become a part of the MBP Hypomyelination Consortium initiated by Dr. Alan Peterson at McGill University.



Amin is currently a postdoctoral scientist at Boehringer Ingelheim Pharmaceuticals in Ridgefield, CT, working on the immunology of respiratory diseases. His passion for science was not deterred by the pandemic, and he continued to engage in heated discussions across the safe distance of 2 meters on a variety of topics with whomever happened to be in the lab within hearing distance, particularly with visiting assistant professor Friederike Pfeiffer from Tübingen. Amin is a recipient of the UConn Neuroscience Fellowship and has contributed to the following papers.

Papers

Zuo H, Wood WM, Sherafat A, Hill RA, Lu QR, Nishiyama A. Age-dependent decline in fate switch from NG2 cells to astrocytes after *Olig2* deletion. *J Neurosci*. 2018 Feb 28;38(9):2359-2371. doi: 10.1523/JNEUROSCI.0712-17.2018. Epub

Sherafat A, Hill RA, Nishiyama A. Organotypic slice cultures to study oligodendrocyte proliferation, fate, and myelination. *Methods Mol Biol*. 2018;1791:145-156. doi: 10.1007/978-1-4939-7862-5_11.

Boshans LL, Sherafat A, Nishiyama A. The effects of developmental and current niches on oligodendrocyte precursor dynamics and fate. *Neurosci Lett*. 2020 Jan 10;715:134593. doi: 10.1016/j.neulet.2019.134593.

Medved J, Wood WM, van Heyst MD, Sherafat A, Song JY, Sakya S, Wright DL, Nishiyama A. Novel guanidine compounds inhibit platelet-derived growth factor receptor alpha transcription and oligodendrocyte precursor cell proliferation. *Glia*. 2021 Mar;69(3):792-811. doi: 10.1002/glia.23930.

Nishiyama A, Shimizu T, Sherafat A, Richardson WD. Life-long oligodendrocyte development and plasticity. *Semin Cell Dev Biol*. 2021 Mar 16, 116:25-37. doi: 10.1016/j.semcdb.2021.02.004.

Sherafat A, Pfeiffer F, Reiss AM, Wood WM, Nishiyama A. Microglial neuropilin-1 promotes oligodendrocyte expansion during development and remyelination by trans-activating platelet-derived growth factor receptor. *Nat Commun*. 2021 Apr 15;12(1):2265. Doi: 10.1038/s41467-021-22532-2.

Pfeiffer F, Sherafat A, Nishiyama A. The impact of fixation on the detection of oligodendrocyte precursor cell morphology and vascular associations. *Cells*. 2021 May 24;10(6):1302. doi: 10.3390/cells10061302.

Sherafat A, Pfeiffer F, Nishiyama A. Shaping of regional differences in oligodendrocyte dynamics by regional heterogeneity of the pericellular microenvironment. *Front Cell Neurosci*. Under revision.

Other Recent Graduates, March 2020 – Summer 2020

Linda Boshans (Major Advisor Akiko Nishiyama)

Wei Shen (Major Advisor Jianjun Sun)

Anouk Olthof (Major Advisor Rahul Kanadia)

Alumni News

Marie Cantino, Associate Professor Emeritus

It's been almost four years since I left UConn employment behind. One reason I retired was to meet the divergent needs of a 96-year-old mother in Pennsylvania and a 32-year-old daughter expecting her first baby in Toronto.



My mother passed away in late 2018, and I am grateful for the time I had to help her navigate her final years. At the other end of the life-event spectrum. Peter and I have been able to get to know our two Canadian grandsons from infancy. Last summer, a planned

two week visit after the birth of our second grandson expanded into eleven weeks of pandemic assistance.

My second retirement goal, after 44 years in windowless electron microscopy labs, was to spend as much time outside as possible. Daily hikes in the area, volunteer work on Joshua's Trust trails, and my expanding garden pull me outside often and reaffirm the wisdom of our decision, 30 years ago, to move to this beautiful part of the country.

Retirement is sweet, but I do miss my friends and colleagues in PNB and hope to visit in the coming year.

A bit of history....

Did you know that our department was established in 1986? It emerged from the Physiology Section of the Department of Biological Sciences under the leadership of Guillermo Pilar as one of the three new departments, along with MCB and EEB. Shortly thereafter, the new PNB department moved from Torrey Life Sciences Building to a newly built facility on Horsebarn Hill Road (see pictures on the right), a mile away from the center of the campus. Undergraduate students had to run across the campus between classes to do research in our labs. We eventually outgrew that facility and returned to the science quad in 2005 into Pharmacy Biology and Torrey Life Sciences Buildings.

