The Faculty of Medicine of Harvard University

Curriculum Vitae

Date Prepared: **November 28th, 2024**

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Education:

02/2011	BSc with honors	Biological Sciences (Prof. Elisabetta Affabris)	University "Roma Tre", Rome, Italy
02/2013	MSc with honors	Biology (Prof. Sandra Incerpi and Prof. Flavio Keller)	University "Roma Tre", Rome, Italy / Campus Bio-medico University of Rome, Rome, Italy
03/2016	PhD with honors (Magna cum Laude)	Molecular Neurophysiology (Prof. Olga A. Sergeeva)	Heinrich-Heine-University, Duesseldorf, Germany

Postdoctoral Training:

04/2016 - 02/2021	PhD	Neurology/ Sleep medicine (Prof. Elda Arrigoni, PhD)	Beth Israel Deaconess Medical Center/ Harvard Medical School

Faculty Academic Appointments:

02/2021 - Present	Instructor in Neurology	Neurology/ Division of Sleep medicine	Harvard Medical School
09/2023 - Present	Adjunct Faculty (Instructor)	College of Natural, Behavioral, and Health Sciences	Simmons College University

Appointments at Hospitals/Affiliated Institutions:

02/2021 - Present	Staff Scientist I	Neurology/ Division of Sleep medicine	Beth Israel Deaconess Medical Center, Boston, USA

Faculty Membership in Harvard Initiatives, Programs, Centers, and Institutes:

03/2023 - Present	Faculty Affiliation to the Division of Sleep Medicine (Member)	Harvard Medical School/ Division of Sleep medicine	Beth Israel Deaconess Medical Center, Boston, USA

Professional Societies:

2013 - Present	Society for Neuroscience (SFN)	Member
2016 - Present	Sleep Research Society (SRS)	Member
2019 - Present	European Histamine Research Society (EHRS)	Member
2023 - Present	Full Member of Sigma Xi – The Scientific Research Honor Society	Member

Editorial Activities (most relevant):

- **Ad hoc Reviewer**

2019 - Present: *Frontiers in Endocrinology* **ISSN:** 1664-2392 (Electronic)
2021 - Guest/invited Reviewer for: Anti-obesity Drug Discovery and Development (*Bentham Science*) (Book chapter: MicroRNAs as Targets for the Management of Obesity) **ISSN:** 2210-2698 (Electronic)
2022 - Present: *Open Journal of Thyroid Research* **ISSN:** 2640-7981 (Electronic)
2022 - Present: *Journal of Biology and Medicine* **ISSN:** 2688-8408 (Electronic)
2022 - Present: *Cancers* **ISSN:** 2072-6694 (Electronic)
2022 - Present: *Scientific Reports* **ISSN:** 2045-2322 (Electronic)
2023 - Present: *International Journal of Peptide Research and Therapeutics* **ISSN:** 1573-3904 (Electronic)
2023 - Present: *Cells* **ISSN:** 2073-4409 (Electronic)
2023 - Present: *Sleep Advances* **ISSN:** 2632-5012 (Electronic)
2023 - Present: *Frontiers in Behavioral Neuroscience* **ISSN:** 1662-5153 (Electronic)
2023 - Present: *Frontiers in Neuroscience* **ISSN:** 1662-453X (Electronic)
2023 - Present: *Frontiers in Pharmacology - Neuropharmacology* **ISSN:** 1663-9812 (Electronic)
2024 - Present: *Nutrients* **ISSN:** 2072-6643 (Electronic)
2024 - Present: *British Journal of Anesthesia* **ISSN:** 1471-6771 (Electronic)
2024 - Present: *Communications Biology* **ISSN:** 2399-3642 (Electronic)
2024 - *Early Career Reviewer (ERC)* as *NIH Grant Reviewer ZRG1 AN - W (55) PAR Panel: Metabolic, Cerebrovascular, Environmental, and Sleep Factors in Alzheimer's Disease and Related Dementias (ADRD) 11/18/24 - 11/19/24*

- **Other Editorial Roles:**

2021 - 2023	Guest Editor	*Frontiers in Neuroscience - Sleep and Circadian Rhythms* **ISSN:** 1662-4548

2023 - Present	Editor (Member of the Editorial Board)	*Annals of Human Biology - Human Neuroscience* **ISSN:** 0301-4460
2023 - Present	Editor (Member of the Editorial Board)	*Scientific Reports* **ISSN:** 2045-2322
2024	Guest Editor (Invited)	*Biomedicines* **ISSN:** 2227-9059
		Frontiers in Neurology **ISSN:** 1664-2295
2024	Guest Editor (Invited): *Optogenetics*	*Scientific Reports* **ISSN:** 2045-2322
2024	Guest Editor (Invited): *The Role of Ventrolateral Preoptic Nucleus (VLPO) in REM Sleep Regulation*	*Brain Sciences* **ISSN:** 2076-3425
2024	Guest Editor (Invited): *Novel insights to sleep disorders*	*Applied Science* **ISSN:** 2076-3417

Honors and Prizes (most relevant):

2014	MSc degree Award	BCC "Giuseppe Toniolo", Italy	MSc degree graduation
2015	"Piero Redaelli" Award	University of Milan, Italy	MSc degree graduation
2016	Travel Grant	VCU, Richmond, Virginia, USA	10th International Meeting on Rapid Responses to Steroid Hormones (RRSH)
2019	Trainee Merit Based Award	Sleep Research Society (SRS)	Trainee Merit Based Award at Sleep Meeting 2019 San Antonio, Texas, USA
2019	Special Commendation Award	European Histamine Research Society (EHRS)	Special Commendation Award in the Young Investigator Awards at 48th EHRS meeting
2023 - 2025	NIH R03 Grant	National Institute of Health (NIH)	
2023	Full Member of Sigma Xi	The Scientific Research Honor Society	
2024	Registration waiver award at Workshop on "Spatial Omics and complexities of human diseases: Resolve and Solve", Rome, Italy	European Molecular Biology Organization (EMBO)	

Report of Funded and Unfunded Projects

Projects Submitted for Funding:

2023-2025

Funded.

"The role of neurotensin-expressing neurons of the extended ventrolateral preoptic nucleus in REM sleep regulation"
1 R03 NS128993-01A1
NIH R03 (PA-20-200), BNRS, NS128993-01; Grant #: 13677855
PI, total direct costs requested: $100,000 ($100,000).

Collectively our results from transcriptomic analysis, *in vitro* circuit mapping and whole-animal chemogenetics strongly indicate that eVLPO neurotensin neurons could be the REM sleep-active population in VLPO and that they promote REM sleep by disinhibiting REM-generating neurons in the pontine reticular formation via inhibition of GABA neurons of the vlPAG and monoaminergic neurons of the LC. The proposed studies employ a combination of *in vitro* and *in vivo* electrophysiological methods in *Nts-Cre* mice to identify the cellular and synaptic circuit base by which the eVLPO can promote REM sleep.
Specific Aim 1: Neurotensin neurons in the extended VLPO project to, and inhibit, GABA neurons in the vlPAG and the LC to produce REM sleep. We have found using conditional anterograde labelling that the $eVLPO^{Nts}$ neurons innervate the vlPAG and the LC and that photostimulation of $eVLPO^{Nts}$ axons and terminals in these two regions, in brain slices, produces short-latency, opto-evoked and $GABA_A$-mediated synaptic responses. We will extend these initial studies to identify the postsynaptic targeted neurons in these two regions.
Specific Aim 2: Identify the eVLPO efferent inputs that drive REM sleep. Chemogenetic inhibition of the $eVLPO^{Nts}$ neurons significantly reduces the amount of time that animals spend in REM sleep and our in vitro CRACM work has shown that inputs from the $eVLPO^{Nts}$ inhibit neurons in the vlPAG and the LC. We will use *in vivo* optogenetics to determine which of these efferent inputs are responsible for driving REM sleep.

2024

Submitted

(Resubmission)

"Characterization of Intrinsically Warm Sensitive Neurons of the Hypothalamic Preoptic Area"
1 R21 NS140803-01A1
NIH R21 (PA-21-219), BNRS, NS140803-01; Grant #: 14300511
PI, total direct costs requested: $275,000 ($275,000).

While in vitro Patch clamp recordings in brain slices are limited to one neuron at a time, in vitro single-cell calcium imaging is capable of recording the activity of hundreds of neurons simultaneously. This approach opens the opportunity for sampling the thermosensitivity of a large population of neurons, in an unbiased manner, when brain slices are warmed. Furthermore, the combination of in vitro single-cell calcium imaging and single-cell RNA sequencing to profile recorded neurons after cytoplasmic aspiration (Patch-seq) produces a powerful systematic methodology. This approach bypasses the limits of the past, enabling the identification of the POA's temperature-sensitive neurons with a sufficient sample size. Our laboratory possesses extensive expertise in recording and molecularly profiling neurons from brain slices, establishing a robust foundation for the proposed study. Therefore, we propose to undertake an extensive characterization of iWSNs within the hypothalamic POA. This will be achieved through the pursuit of the Specific Aims outlined as follows:

Specific Aim 1: Anatomical and functional mapping of iWSNs within the hypothalamic POA. We will systematically examine the POA in in vitro brain slices using our newly developed combination of methods for examining fluorescent calcium signaling across large numbers of neurons, in order to identify neurons that are iWSNs and map their locations and response patterns.
Specific Aim 2: Perform Patch-seq on iWSNs to determine their genetic profile. We will characterize 400-450 iWSNs in different regions of the POA and examine their individual RNA transcriptomes using the Patch-seq method. Genetic markers will be identified for potential iWSNs subgroups showing different response characteristics. These findings will give us genetic access to specifically investigate the physiology and connections of these subgroups. In addition, comprehensive knowledge of the receptors and signaling molecules they express may identify druggable targets that can have potential therapeutic implications.

2024
Submitted
(Resubmission)

"Circuitry mediating increased ventilation with EEG arousal"
1 P01 HL149630-01A1
NIH P01 (PA-24-065), NHLBI, HL149630;
Project Director: Clifford B. Saper MD, PhD
ESI PI, Project 3: Roberto De Luca
Total direct costs requested: $1,250,000 ($1,250,000).

Obstructive Sleep Apnea (OSA) is characterized by recurrent upper airway collapse, leading to episodes of apnea, hypercapnia/hypoxia and ensuing brief arousals that restore the airway. While these arousals are crucial for preventing prolonged apneas, they fragment sleep, resulting in excessive daytime sleepiness, neurocognitive impairments, hypertension and increased risk of cardiovascular events. To better manage OSA, it's crucial to define the brain circuits governing breathing and cortical arousals. Recent research suggests that the FoxP2-expressing neurons of Kolliker-Fuse and parabrachial nucleus (PB-KF^{FoxP2}) increase respiration, while CGRP-expressing neurons of the external lateral PB (PB^{CGRP}) regulate hypercapnia-induced cortical arousals. Both of these neuronal populations may contribute to opioid-induced respiratory depression (OIRD), as opioids directly inhibit these neurons to decrease breathing and cause sedation. However, we lack knowledge about the forebrain (FB) inputs targeting the PB-KF^{FoxP2} neurons, that may be crucial for maintaining augmented ventilation without affecting arousal. Therefore, we hypothesize that manipulation of specific FB inputs to the PB-KF^{FoxP2} neurons will enhance ventilatory responses to hypercapnia/hypoxia without triggering cortical arousals. To test this, we propose the following:
Specific Aim 1: Characterize the forebrain inputs to PB-KF^{FoxP2} neurons. Our results from conditional rabies virus retrograde tracing in *FoxP2-Cre* mice indicated strong inputs from the lateral hypothalamus (LH), paraventricular hypothalamus (PVH), central nucleus of the amygdala (CeA) and oval part of the bed nucleus of stria terminalis (ov-BNST) to the PB-KFFoxP2 neurons. To characterize the FB neurons that contact PB-KF neurons we will employ single-nucleus RNA-sequencing (snRNA-seq). Briefly, we will inject a rAAV2-TdTomato-KASH into the PB-KF to selectively label and molecularly profile fluorescent nuclei originating from FB sites that were previously identified as contributors to inputs received by the PB-KF^{FoxP2} neurons with retrograde rabies-tracing. We will also analyze changes in gene expression in these FB neurons that

project to PB-KF after exposure to hypercarbia and hypoxia. We anticipate that the results obtained (in terms of key marker genes expressed by FB neurons) will be useful in accessing and investigating, using ad hoc recombinase-driver mice, the role of the FB neuronal populations responsible of driving respiratory responses by enhancing PB-KF^{FoxP2} neuron activity. Also they will provide valuable insights into the FB subpopulations, sensitive to hypoxia and hypercarbia, that innervate the PB-KF and may play a crucial role in the respiratory drive triggered by hypercapnia and hypoxia.

Specific Aim 2: Which FB inputs to the PB-KF are activated in advance of the PB-KFFoxP2 neurons during EEG arousal caused by hypercapnia/hypoxia? The GCaMP activity of PB-KF^{FoxP2} neurons increase gradually during hypercarbia, but then sharply increases further with EEG arousal. To investigate which FB inputs are likely to drive this activation of the PB-KF^{FoxP2} neurons, we will simultaneously record the calcium activity from the FB sites and PB-KF^{FoxP2} neurons using dual-fiber photometry during hypoxia and hypercarbia and use cross-correlation analysis to determine whether the activation of specific FB inputs precedes the activation of PB-KF^{FoxP2} neurons.

Specific Aim 3: What role do these FB inputs to the PB-KF^{FoxP2} neurons play in increasing ventilatory responses? To test this, we will first express Channelrhodopsin-2 (ChR2) in FB neurons that are either excitatory or inhibitory and project to the PB-KF. Then we will photo-activate their axons/terminals in PB-KF under normocapnia and after morphine administration. We predict that activation of key inputs to the PB-KF^{FoxP2} neurons will increase respiration and will reverse OIRD. To determine the necessity of the FB inputs for increasing respiration during cortical arousals caused by hypoxia or hypercarbia, we will inhibit these inputs by expressing the inhibitory pump Archaerhodopsin T (ArchT) selectively in the FB sites and photo-inhibiting their terminals in the PB-KF.

Specific Aim 4: Test the synaptic connectivity of FB inputs to PB-KF^{FoxP2} and Tac1-Pet1 medullary raphe neurons and local PB circuitry with ChR2-assisted circuit mapping (CRACM): We will use ChR2 to activate terminals from the FB inputs while performing patch-clamp recordings from the PB-KF^{FoxP2} neurons and Tac1- Pet1 serotonergic medullary respiratory neurons in mouse brain slices. We will also examine possible local inputs from PB^{FoxP2} neurons (in particular those that also express Gpr101; PBGpr101neurons) to the CGRP neurons (PBCalca/CGRP), that drive EEG arousal. We will test with TTX whether inputs are monosynaptic and with pharmacological controls for the receptors used.

Report of Local Teaching and Training

Research Supervisory and Training Responsibilities:

Heinrich-Heine-University, Duesseldorf, Germany

2014 - 2016 **William Baumgaertel**, Medical Student, Heinrich-Heine-University, Duesseldorf, Germany
Supervision: 5 hours per week

Other Mentored Trainees and Faculty:

Beth Israel Deaconess Medical Center/Harvard Medical School

2017-2019 **Somdeb Banerjee**
Research Assistant (Arrigoni Lab)

Supervision: 5 hours per week
Subsequent Role (2019): Medical Student, Tulane School of Medicine, New Orleans, LA

2018-2019 **Bianca Viberti**
Graduate Student (Neurosciences, University of Trieste, Italy) (Arrigoni Lab)
Supervision: 5 hours per week
Subsequent Role (2019): PhD. Program in Neuroscience; Bern University; Switzerland

2018-2019 **Michela Cristofolini**
Graduate Student (Neurosciences, University of Pavia, Italy) (Arrigoni Lab)
Supervision: 5 hours per week
Subsequent Role (2019): PhD. Program in Neuroscience; Trento University; Italy
Current Role: Operation Manager by Pariter Partners, Milan, Italy

2020-2024 **Francesca Raffin**
PhD Student (Neurosciences, University of Pavia, Italy) (Arrigoni Lab)
Supervision: 8 hours per week
Subsequent Role (2024): Post Doc in Neurosciences, University of Pavia, Italy

2021-2022 **Oleksandra (Sasha) Fanari**
Graduate Student (MSc) (Bioengineering, University of Pavia, Italy) (Arrigoni Lab)
Supervision: 2 hours per week
Subsequent Role (2022): PhD. Bioengineering, Northeastern University, Boston, MA, USA

2022-2023 **Andrea Pigozzi**
Graduate Student (MSc) (Bioengineering, University of Pavia, Italy) (Arrigoni Lab)
Supervision: 5 hours per week

2022-2023 **Mustafa Korkutata**
Post Doc (Department of Neurology, Scammell Lab)
Supervision: 1 hour per week

2023-Present **Jinhwan Choi**
Post Doc (Department of Neurology, Scammell Lab)
Supervision: 2 hours per week

2023-2024 **Bridget Fitzgerald**
Research Assistant (Department of Neurology, Scammell Lab)
Supervision: 2 hours per week
Subsequent Role: Medical Student, Renaissance School of Medicine, Stony Brook University Stony Brook, NY.

2023-Present **Yaniv Sela**
Post Doc (Department of Neurology, Saper Lab)
Supervision: 3 hours per week

2023-Present **Ida Luisa Boccalaro**
Post Doc (Department of Neurology, Arrigoni Lab)
Supervision: 6 hours per week

2023-Present **Enrico Rillosi**
Research Assistant (Department of Neurology, Arrigoni Lab)

Supervision: 25 hours per week

2024-Present **Caroline Vella**
Graduate Student (BSc) (Department of Neurology, Arrigoni Lab)
Supervision: 15 hours per week

2024-Present **Hannah Pridgeon**
Undergraduate Student (Simmons College University and Department of Neurology, Arrigoni Lab). Supervision: 3 hours per week

Local Invited Presentations:

☐ *No presentations below were sponsored by 3rd parties/outside entities*

☒ *Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.*

2022 GenomeWeb webinar (GenomeWebinars: Recent | Genomeweb), June 2022. Invited speaker for virtual oral presentation: "Investigating Cellular Targets in Narcolepsy and Other Arousal Based Disorders", sponsored by VIZGEN. (*See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings*).

2024 Internal Educational Seminar Series (Medical Affairs Expert Series), January 2024. Invited speaker for virtual oral presentation: "Pitolisant inhibits sleep-active neurons in the ventrolateral preoptic area", sponsored by Harmony Biosciences. (*See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings*).

Report of Regional, National and International Invited Teaching and Presentations

☒ *No presentations below were sponsored by 3rd parties/outside entities*

☐ *Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.*

Regional

2019 Neurophysiology lecture for the LCIS 201 course: "Learning Community Integrated Seminar Bio / Chem" / Guest Lecturer, Simmons College University, Boston, MA.

2022-present Summer Lecture Series (Neuroscience) – Neurology Dept. BIDMC, Boston, MA.

2023-present Simmons Adjunct Faculty (Instructor), Biol 113-02 General Biology and Lab courses, Simmons College University, Boston, MA.

2024 2nd Edition of Neurology World Conference (NWC 2024) 2024, San Francisco Airport, CA, USA. September 4th-6th. Invited Speaker for virtual oral presentation: "Effect of Noradrenaline in the Ventrolateral Preoptic Area". (*See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings*).

2025 GenEd 1038 'Sleep' serving as teaching fellow (TF) - Harvard Medical School

International

2013-2016	"Sleep and Anaesthesia: Cellular and molecular mechanisms" Lecturer, Assistant Supervisor, Heinrich-Heine-University, Duesseldorf, Germany.
2016	Neurophysiology course (Sleep lecture) and Doctoral Seminars / Invited Lecturer University "Roma Tre", Rome, Italy.
2022	Associated Professional Sleep Societies (APSS) meeting 2022, Charlotte, USA, June 4-8th Invited speaker: "The Preoptic Area in Sleep and Arousal" - "Orexin promotes arousal by inhibiting the sleep-promoting neurons of the ventrolateral preoptic nucleus". (*See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings*).
2022	GenomeWeb webinar (GenomeWebinars: Recent | Genomeweb), event that was sponsored by VIZGEN in June 2022 (*See also Local invited presentations*).
2023	Society for Neuroscience (SFN) meeting 2023, Washington DC, USA, November 11-15th. Nanosymposium presenting author (speaker): "Effect of noradrenaline in the ventrolateral preoptic area". (*See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings*).
2024	Global summit on Neurology and Neurological Disorders (Neuro2024) 2024, Kuala Lumpur, Malaysia, August 22nd-24th. Keynote Invited Speaker for virtual oral presentation: "Effect of Noradrenaline in the Ventrolateral Preoptic Area". (*See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings*).
2024	European Molecular Biology Organization (EMBO) Workshop on "Spatial Omics and complexities of human diseases: Resolve and Solve" 2024, Rome, Italy. October 23rd-25th. Invited Speaker for oral presentation: "The Role of Noradrenaline and Adrenergic Receptors Mapped by Spatial Transcriptomics in the Ventrolateral Preoptic Area in Arousal and Narcolepsy". *(See Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings).*

Report of Scholarship

* denotes equal authorship contribution
** denotes mentored trainee.

Peer-Reviewed Scholarship in print or other media (most relevant):

Research Investigations

1. Biamonte F, Latini L, Giorgi FS, Zingariello M, Marino R, **De Luca R**, D'Ilio S, Majorani C, Petrucci F, Violante N, Senofonte O, Molinari M, Keller F. Associations among exposure to methylmercury, reduced Reelin expression, and gender in the cerebellum of developing mice. *Neurotoxicology*. 2014 Dec; 45:67-80. PMID: 25305366.
2. **De Luca R**, Suvorava T, Yang D, Baumgärtel W**, Kojda G, Haas HL, Sergeeva OA. Identification of histaminergic neurons through histamine 3 receptor-mediated autoinhibition. *Neuropharmacology*. 2016 July; 106:102-15. PMID: 26297536. (** Mentored trainee).

3. Sergeeva OA, **De Luca R**, Mazur K, Chepkova AN, Haas HL, Bauer A. N-oleoyldopamine modulates activity of midbrain dopaminergic neurons through multiple mechanisms. *Neuropharmacology*. 2017 June; 119:111-122. PMID: 28400256.

4. Anaclet C, **De Luca R**, Venner A, Malyshevskaya O, Lazarus M, Arrigoni E, Fuller PM. Genetic Activation, Inactivation, and Deletion Reveal a Limited And Nuanced Role for Somatostatin-Containing Basal Forebrain Neurons in Behavioral State Control. *J Neurosci*. 2018 May 30; 38(22):5168-5181. PMID: 29735555.

5. **De Luca R**, Mazur K, Kernder A, Suvorava T, Kojda G, Haas HL, Sergeeva OA. Mechanisms of N-oleoyldopamine activation of central histaminergic neurons. *Neuropharmacology*. 2018 Dec; 143:327-338. PMID: 30219501.

6. Venner A, Mochizuki T, **De Luca R**, Anaclet C, Scammell TE, Saper CB, Arrigoni E, Fuller PM. Reassessing the Role of Histaminergic Tuberomammillary Neurons in Arousal Control. *J Neurosci*. 2019 Nov 6; 39(45):8929-8939. PMID: 31548232.

7. Venner A*, **De Luca R***, Sohn LT, Bandaru SS, Verstegen AMJ, Arrigoni E, Fuller PM. An Inhibitory Lateral Hypothalamic-Preoptic Circuit Mediates Rapid Arousals from Sleep. *Curr Biol*. 2019 Dec 16; 29(24):4155-4168.e5. PMID: 31761703. * Equally contributing authors.

8. Segal M, Biscans A, Gilles ME, Anastasiadou E, **De Luca R**, Lim J, Khvorova A, Slack FJ. Hydrophobically Modified let-7b miRNA Enhances Biodistribution to NSCLC and Downregulates HMGA2 In Vivo. *Mol Ther Nucleic Acids*. 2020 Mar 6; 19:267-277. PMID: 31855835.

9. Kaur S, **De Luca R**, Khanday MA, Bandaru SS, Thomas RC, Broadhurst RY, Venner A, Todd WD, Fuller PM, Arrigoni E, Saper CB. Role of serotonergic dorsal raphe neurons in hypercapnia-induced arousals. *Nat Commun*. 2020 June2; 11(1):2769. PMID: 32488015.

10. Todd WD, Venner A, Anaclet C, Broadhurst RY, **De Luca R**, Bandaru SS, Issokson L, Hablitz LM, Cravetchi O, Arrigoni E, Campbell JN, Allen CN, Olson DP, Fuller PM. Suprachiasmatic VIP neurons are required for normal circadian rhythmicity and comprised of molecularly distinct subpopulations. *Nat Commun*. 2020 Sept2; 11(1):4410. PMID: 32879310.

11. Candelotti E, **De Luca R**, Megna R, Maiolo M, De Vito P, Gionfra F, Percario ZA, Borgatti M, Gambari R, Davis PJ, Lin HY, Polticelli F, Persichini T, Colasanti M, Affabris E, Pedersen JZ, Incerpi S. Inhibition by thyroid hormones of cell migration activated by IGF-1 and MCP-1 in THP-1 monocytes: focus on signal transduction events proximal to integrin avß3. *Front Cell Dev Biol*. 2021 Apr 8; 8;9: 651492. PMID: 33898447.

12. Chung CC, Huang TY, Chu HR, **De Luca R**, Candelotti E, Huang CH, Yang YSH, Incerpi S, Pedersen JZ, Lin CY, Huang HM, Lee SY, Li ZL, ChangOu CA, Li WS, Davis PJ, Lin HY, Whang-Peng J, Wang K. Heteronemin and tetrac derivatives suppress non-small cell lung cancer growth via ERK1/2 inhibition. *Food Chem Toxicol*. 2022 Feb 10; 112850. PMID: 35151786.

13. Sergeeva OA, Mazur K, Kernder A, Haas HL, **De Luca R**. Tachykinins amplify the action of capsaicin on central histaminergic neurons. *Peptides*. 2022 Apr; 170729. PMID: 34958850.

14. **De Luca R**, Nardone S, Grace KP, Venner A, Cristofolini M**, Bandaru SS, Sohn LT, Kong D, Mochizuki T, Viberti B**, Zhu L, Zito A, Scammell TE, Saper CB, Lowell BB, Fuller PM Arrigoni E. Orexin neurons inhibit sleep to promote arousal. *Nat Commun.* 2022 Jul 18;13(1):4163. PMID: 35851580. (** Mentored trainee).

15. Kroeger D, Thundercliffe J, Phung A, **De Luca R**, Geraci C, Bragg S, McCafferty KJ, Bandaru SS, Arrigoni E, Scammell TE. Glutamatergic PPT neurons control wakefulness and locomotion via distinct axonal projections. *Sleep.* 2022 Dec 12; 45(12): zsac242. PMID: 36170177.
16. Nardone S, **De Luca R**, Zito A, Klymko N, Nicoloutsopoulos D, Amsalem O, Brannigan C, Resch JM, Jacobs CL, Pant D, Veregge M, Srinivasan H, Grippo RM, Yang Z, Zeidel ML, Andermann ML, Harris KD, Tsai LT, Arrigoni E, Verstegen AMJ, Saper CB, Lowell BB. A spatially-resolved transcriptional atlas of the murine dorsal pons at single-cell resolution. bioRxiv [Preprint]. 2023 Nov 17:2023.09.18.558047. doi: 10.1101/2023.09.18.558047. PMID: 38014113; PMCID: PMC10680649.
17. Nardone S, **De Luca R**[#], Zito A[#], Klymko N[#], Nicoloutsopoulos D, Amsalem O, Brannigan C, Resch JM, Jacobs CL, Pant D, Veregge M, Srinivasan H, Grippo RM, Yang Z, Zeidel ML, Andermann ML, Harris KD, Tsai LT, Arrigoni E, Verstegen AMJ, Saper CB, Lowell BB. A spatially-resolved transcriptional atlas of the murine dorsal pons at single-cell resolution. *Nat Commun*. 2024, Mar 4;15(1):1966. PMID: 38438345; PMCID: PMC10912765. [#,] equally contributing authors.
18. Korkutata M**, **De Luca R**, Fitzgerald B**, Arrigoni E, Scammell TE. Afferent projections to the *Calca* /CGRP-expressing parabrachial neurons in mice. bioRxiv [Preprint]. 2024 May 8:2024.05.07.593004. doi: 10.1101/2024.05.07.593004. PMID: 38766214; PMCID: PMC11100666. (** Mentored trainee).
19. Ramirez-Plascencia OD[#], **De Luca R**[#], Machado NLS, Eghlidi D, Khanday MA, Bandaru SS, Raffin F, Vujovic N, Arrigoni E, Saper CB. A hypothalamic circuit for circadian regulation of corticosterone secretion. *Res Sq [Preprint]*. 2024 Jul 12:rs.3.rs-4718850. PMID: 39041039; PMCID: PMC11261983. (*Nature.* In revision, 2024). [#,] equally contributing authors.

Peer-Reviewed Scholarship in revision and/or in preparation (most relevant):

1. Mahoney CE, Joyal A, **De Luca R**, Woods C, Zhu W, Coffey A, Zhu L, Kurimoto E, Fenselau H, Grinevich V, Arrigoni E, Lowell BB, Scammell TE. Oxytocin neurons promote socially-triggered cataplexy. (*Nat Neurosci.* In revision, 2023). https://doi.org/10.21203/rs.3.rs-2530781/v1.
2. Gionfra F, D' Ezio Veronica, **De Luca R**, Candelotti E, Leone S, Percario ZA, Persichini T, Colasanti M, Affabris E, Pedersen JZ, Davis PJ, Lin HY, Incerpi S. Modulation of integrin αvβ3 activation and signaling in BV-2 3 microglial cells and THP-1 monocytes by thyroid hormones. (*Front Endocrinol.* In revision, 2023).
3. Wu Y-E, **De Luca R**, Broadhurst RY, Venner A, Sohn LT, Bandaru SS, Schwalbe DC, Campbell J, Arrigoni E, Fuller PM. Suprachiasmatic Neuromedin-S Neurons Regulate Arousal. (*Nature.* In revision, 2024).
4. Lynch N, **De Luca R**, Spinieli RL, Rillosi E**, Thomas RC, Sailesh S, Gangeddula N, Lima JD, Bandaru SS, Arrigoni E, Burstein R, Thankachan S, Kaur S. Unraveling the intricate brain circuits that regulate awakenings to pain stimulus. (*Science Translational Medicine*, in revision, 2024). (** Mentored trainee).
5. Zhao Y, Parmentier R, **De Luca R**, Baumgärtel W**, Xie X, Wu S, Anaclet C, Akaoka H,Gervasoni D, Miao C-Y,Haas HL, Sergeeva OA, Lin J-S.Sexual arousal, role of histamine and orexin/hypocretin neurons. (In submission to *Prog Neurobiol*). (** Mentored trainee).
6. **De Luca R**, Nardone S, Haas HL, Sergeeva OA. Neurokinin 1 receptor signaling in mouse histaminergic neurons. (In preparation).

7. **De Luca R**[#], Choi J[#,**], Nardone S, Raffin F**, Cano CA, Rillosi E**, Fitzgerald B**, Pigozzi A**, Fanari O**, Palmer MR, Zhu L, Burgess CR, Scammell TE, Arrigoni E. The role of noradrenaline in the preoptic area in arousal and narcolepsy (In preparation). [#,] equally contributing authors, (** Mentored trainee).
8. **De Luca R**[#], Arrè V[#], Nardone S, Incerpi S, Trivedi P, Anastasiadou E and Negro R. Navigating the complexity of the microbiota within the gastrointestinal tract: a new perspective. (In preparation) [#,] equally contributing authors.

Other peer-reviewed scholarship

1. Kernder A, **De Luca R**, Yanovsky Y, Haas HL, Sergeeva OA. Acid-sensing hypothalamic neurons controlling arousal. *Cell Mol Neurobiol*. 2014 Aug; 34(6):777-89. PMID: 24798513.

2. **De Luca R**, Davis PJ, Lin HY, Gionfra F, Percario ZA, Affabris E, Pedersen JZ, Marchese C, Trivedi P, Anastasiadou E, Negro R, Incerpi S. Thyroid Hormones Interaction With Immune Response, Inflammation and Non-thyroidal Illness Syndrome. *Front Cell Dev Biol*. 2021 Jan 21; 8:614030. PMID: 33553149.

3. Cheng TM, Chang WJ, Chu HY, **De Luca R**, Pedersen JZ, Incerpi S, Li ZL, Shih YJ, Lin HY, Wang K, Whang-Peng J. Nano-strategies Targeting on Integrin avß3 Network for Cancer Therapy. *Cells.* 2021 Jul 3;10: 1684. PMID: 34359854.

4. Incerpi S, Gionfra F, **De Luca R**, Candelotti E, De Vito P, Percario ZA, Leone S, Gnocchi D, Rossi M, Caruso F, Davis PJ, Lin H-Y, Affabris E and Pedersen JZ. Extranuclear effects of thyroid hormones and analogs during development. An old mechanism with emerging roles. *Front Endocrinol - Cancer Endocrinology.* 2022 Sept 23; PMID: 36213288.

5. **De Luca R**, Todd WD and Burgess CR. Editorial: Novel pharmacological treatments in sleep disorders. *Front Neurosci - Sleep and Circadian Rhythms*. 2022 Dec 1; 16:1086983. PMID: 36532280.

6. Fraigne JJ, Luppi PH, Mahoney CE, **De Luca R**, Shiromani PJ, Weber F, Adamantidis A, Peever J. Dopamine neurons in the ventral tegmental area modulate REM sleep. Chapter: Why do we have REM sleep? (**De Luca R** and Mahoney CE) *Sleep.*2023 Feb 13; zsad024. doi: 10.1093/sleep/zsad024. PMID: 36775897.

Thesis:

2011 **De Luca R**, University "Roma Tre", Rome, Italy. *HIV-1 Nef protein is transmitted by infected macrophages to B cells and influences the humoral response*. BSc Thesis; Curriculum: Microbiology and Immunology.

2013 **De Luca R**, University "Roma Tre" and Campus Bio-medico University of Rome, Rome, Italy. *Interactions between exposure to methylmercury, reduced Reelin expression, and gender in developing mice*. MSc Thesis; Curriculum: Physiology and Neuroscience.

2016 **De Luca R**, Heinrich-Heine-Universität Düsseldorf, Germany. *Interactions of dopaminergic and histaminergic systems in health and disease*. https://d-nb.info/1156007771/34. PhD Thesis; Curriculum: Physiology and Molecular Neuroscience

Abstracts, Poster Presentations, and Exhibits Presented at Professional Meetings (most relevant):

1. Society for Neuroscience (SFN) meeting 2013, San Diego, USA, November 7-13th. Poster presenting author: "TRPV1 expression in central histaminergic neurons of rat and mouse".
2. Society for Neuroscience (SFN) meeting 2014, Washington DC, USA, November 15-19th. Poster presenting author: "Neurokinin 1 and capsaicin receptors in mouse histaminergic neurons".
3. Rapid Responses to Steroid hormones, 10th meeting 2016, Richmond, VA, USA, November 2nd-5th. Talk presenting author: "Thyroxine (T4) and negative effective factor (Nef) crosstalk: a new model for thyroid dysfunctions during human immunodeficiency virus (HIV) infection?"
4. Associated Professional Sleep Societies (APSS) meeting 2017, Boston, USA, June 3rd-7th. Poster presenting author: "Orexin mediates feed-forward inhibition of VLPO sleep-active neurons – A mechanism for controlling arousal".
5. Society for Neuroscience (SFN) meeting 2017, Washington DC, USA, November 11-15th. Poster presenting author: "Orexin mediates feed-forward inhibition of VLPO sleep-active neurons – A mechanism for controlling arousal". Invited Speaker at Neuroscience of Sleep and Circadian Biology Data Blitz, 13th November 2017.
6. 7th International Symposium on Narcolepsy 2018, Beverly, USA, September 9– 13th Poster presenting author: "Effects of orexin on ventrolateral preoptic neurons".
7. Society for Neuroscience (SFN) meeting 2018, San Diego, USA, November 3rd-6th. Poster presenting author: "Ascending projections from parafacial zone to the medial parabrachial neurons".
8. 48th European Histamine Research Society (EHRS) meeting 2019, Krakow, Poland, 15-18th. Talk presenting author in YIA session: "Activation of neurokinin-1 receptor pathway in central histaminergic neurons".
9. Associated Professional Sleep Societies (APSS) meeting 2019, San Antonio, USA, June 8-12th. Poster presenting author: "Ascending projections from parafacial zone to the medial parabrachial neurons".
10. Associated Professional Sleep Societies (APSS) meeting 2021, Virtual, June 10-13th. Poster presenting author: "Noradrenaline and acetylcholine inhibit sleep-promoting neurons of ventrolateral preoptic area through a local GABAergic circuit".
11. GenomeWeb webinar (GenomeWebinars: Recent | Genomeweb) June 2022. Invited Speaker for virtual oral presentation: "Investigating Cellular Targets in Narcolepsy and Other Arousal Based Disorders", sponsored by VIZGEN.
12. Associated Professional Sleep Societies (APSS) meeting 2022, Charlotte, USA, June 4-8th. Invited speaker: "The Preoptic Area in Sleep and Arousal" - "Orexin promotes arousal by inhibiting the sleep-promoting neurons of the ventrolateral preoptic nucleus".
13. Society for Neuroscience (SFN) meeting 2022, San Diego, USA, November 12-16th. Poster presenting author: "Noradrenaline in the ventrolateral preoptic area".
14. NextGen Omics US meeting 2023, Boston, USA, March 30th-31st. Chair: Novel Spatial Analysis Technologies - Morning Session.

15. Society for Neuroscience (SFN) meeting 2023, Washington DC, USA, November 11-15th. Nanosymposium presenting author (speaker): “Effect of noradrenaline in the ventrolateral preoptic area”.
16. Society for Neuroscience (SFN) meeting 2023, Washington DC, USA, November 11-15th. Poster presenting author: “Pitolisant inhibits sleep-active neurons in the ventrolateral preoptic area”.
17. 2nd NIH Annual Investigator Meeting for Interoception Research 2023, Bethesda, MD, USA, November 11th. Selected Poster presenting author: “Effect of noradrenaline in the ventrolateral preoptic area”.
18. Internal Educational Seminar Series (Medical Affairs Expert Series), Harmony Bioscience, Boston, MA, USA, January 29th, 2024. Invited Speaker for virtual oral presentation: “Pitolisant inhibits sleep-active neurons in ventrolateral preoptic area".
19. Global Summit on Neurology and Neurological Disorders (Neuro2024), Kuala Lumpur, Malaysia, August 22-24th, 2024. Keynote Invited Speaker for virtual oral presentation: “Effect of noradrenaline in the ventrolateral preoptic area”.
20. 2nd Edition of Neurology World Conference (NWC 2024) San Francisco Airport, CA, USA. September 4th-6th, 2024. Invited Speaker for virtual oral presentation: “Effect of Noradrenaline in the Ventrolateral Preoptic Area".
21. Society for Neuroscience (SFN) meeting 2024, Chicago IL, USA, October 5-9th. Poster presenting author: “A hypothalamic circuit for circadian regulation of corticosterone secretion”.
22. European Molecular Biology Organization (EMBO) Workshop on “Spatial Omics and complexities of human diseases: Resolve and Solve” 2024, Rome, Italy. October 23rd-25th. Invited Speaker for oral presentation: “The Role of Noradrenaline and Adrenergic Receptors Mapped by Spatial Transcriptomics in the Ventrolateral Preoptic Area in Arousal and Narcolepsy”.
23. European Molecular Biology Organization (EMBO) Workshop on “Spatial Omics and complexities of human diseases: Resolve and Solve” 2024, Rome, Italy. October 23rd-25th. Co-chair of the session: “Transferring emerging paradigms in Spatial Omics to Clinic“ at the conference on 25th October 2024.

List of published abstracts (most relevant):

1. Haas HL, **De Luca R**, Sergeeva OA (2014). Glutamatergic excitation of histaminergic neurons (2014). The European histamine research society 43rd annual meeting, May 7-10/2014, Lyon, France. *Inflammation Research.* 63(1): S32-S32.
2. **De Luca R**, Kernder A, Sergeeva OA (2014). Substance P amplifies capsaicin signalling in mouse histaminergic neurons. The European histamine research society 43rd annual meeting, May 7-10/2014, Lyon, France. *Inflammation Research.* 63(1): S32-S33.
3. **De Luca R**, Sergeeva OA (2016). N-oleoyldopamine (OLDA) modulates activity of central aminergic neurons through multiple and region-specific mechanisms. The 95th annual meeting of the German Physiological Society, March 3-5/2016, Luebeck, Germany. *Acta Physiologica.* 216(707):93.

4. **De Luca R**, Park D, Bandaru S, Arrigoni E (2017). Orexin mediates feed-forward inhibition of VLPO sleep-active neurons - a mechanism for controlling arousal. APSS 2017, June 3-7/2017. *Sleep.* 40 (Suppl 1), S50-S50.
5. Venner A, **De Luca R**, Arrigoni E, Fuller PM (2018). Functional and Anatomical Characterization of Lateral Hypothalamic GABA Arousal Circuitry. APSS 2018, June 2-6/2018.*Sleep.* 41 (Suppl 1) A26-A26.
6. Haas HL, **De Luca R**, Mazur K, Sergeeva OA (2018). Histaminergic and dopaminergic neurons. The European histamine research society 47th annual meeting, May 31-June 2/2018, Dublin, Ireland *Inflammation Research.* 67(1): S11-S11.
7. Zhao Y, **De Luca R**, Baumgaertel W**, Xie X, Haas HL, Lin JS, Sergeeva OA (2018). Activation of histaminergic and orexinergic neurons by testosterone.The European histamine research society 47th annual meeting, May 31-June 2/2018, Dublin, Ireland *Inflammation Research.* 67(1): S35-S35. (** Mentored trainee).
8. **De Luca R**, Xie X, Zhao Y, Haas HL, Sergeeva OA, Lin JS (2018). Activation des neurons histaminergiques et orexinergiques par la testosterone. *Médecine du Sommeil.* 15(1) CO 2-2; 6-7.
9. **De Luca R**, Broadhurst RY, Fuller PM, Arrigoni E (2019). Ascending projections from parafacial zone to the medial parabrachial neurons. APSS 2019, June 8-12/2019. *Sleep.* 42 (Suppl 1), S58-S58.
10. **De Luca R**, Haas HL, Sergeeva OA (2019). Activation of neurokinin-1 receptor pathway in central histaminergic neurons. The European histamine research society 48th annual meeting, May 15-18/2019, Krakow, Poland. *Inflammation Research.* 68(1): S8-S8.
11. Kroeger D, Thundercliffe JA, Phung A, Geraci C, **De Luca R**, Bragg S, Arrigoni E, Scammell TE (2020). Activation of Glutamatergic PPT Neurons and Their Projections Promotes Arousal, and Distinct Wake Behaviors. APSS 2020, August 27-30/2020. *Sleep.* 43 (Suppl 1), A61-A62.
12. **De Luca R**, Nardone S, Zhu L, Arrigoni E (2021). Noradrenaline and acetylcholine inhibit sleep-promoting neurons of ventrolateral preoptic area through a local GABAergic circuit. APSS 2021, June10-13/2021. *Sleep.* 44 (Suppl 2), A27-A28.
13. Cristofolini M**, **De Luca R**, Venner A, Ferrari L, Grace K, Fuller P, Arrigoni E (2021). Basal Forebrain GABAergic Neurons Promote Arousal by Disinhibiting the Orexin Neurons via Local GABAergic Interneurons. APSS 2021, June 10-13/2021. *Sleep.* 44 (Suppl 2), A31. (** Mentored trainee).

Narrative Report

Research

I am a young neuroscientist at Harvard Medical School, working in the Department of Neurology at Beth Israel Deaconess Medical Center. My primary focus is on comprehending the mechanisms and neuronal circuits involved in the brain's control over wake-sleep states and their reciprocal transitions. Through my ongoing experiments, I aim to shed light on the synaptic circuits and neural foundations responsible for regulating arousal and sleep within the brain. My research aims to establish connections between the activity of neurochemically-identified circuits and physiological responses observed in behaving animals. During my postdoc training at Harvard Medical School, I further developed my skills and expertise in electrophysiology by incorporating *in vitro* optogenetics and single-cell molecular biology techniques. Optogenetics is a highly effective method that enables the manipulation of neuronal physiology, both *in vivo* and *in vitro*, by utilizing light-sensitive proteins, such as Channelrhodopsin. By expressing these proteins, we can selectively and temporally control the activity of neurons through light-dependent

activation. One of the key advantages of optogenetics is its ability to induce the release of neurotransmitters from specific neuronal terminals that express Channelrhodopsin. This allows us to study the evoked synaptic responses in downstream neurons that receive inputs exclusively from targeted neuronal populations. This approach provides valuable insights into the functional connectivity and communication between distinct types of neurons. Channelrhodopsin-assisted circuit mapping (CRACM) offers several advantages. Firstly, it allows for the mapping of long-range synaptic inputs from specific neuronal cell types that are localized in well-defined anatomical regions and also it can dissect complex neuronal circuits and gain insights into their functional connectivity. However, it is important to note that CRACM has limitations when it comes to revealing the neurochemical composition of the input-recipient neurons. To address this limitation and uncover the neurochemical identity of the recorded neurons, I established the use of single-cell PCR and single-cell RNA sequencing techniques in the Arrigoni Lab. By employing these powerful tools, I can simultaneously map and characterize the connections from input neurons while obtaining the gene expression profile of input-recipient neurons. This approach enables a comprehensive understanding of both the circuitry and the molecular characteristics of the neurons involved. Furthermore, this approach holds promise in identifying key drug-targetable neuronal populations that play a role in regulating sleep-wakefulness and sleep-related disorders, such as narcolepsy, hyperarousal, and sleep apnea. By deciphering the molecular underpinnings of these circuits, we can potentially develop targeted therapeutic interventions for these conditions.

In my recent research, through the combination of CRACM recordings with single-cell RT-PCR, I revealed that the lateral hypothalamic GABAergic neurons promote wakefulness by directly inhibiting galaninergic neurons in the ventrolateral preoptic area (VLPO), which play a crucial role in promoting sleep (Venner, De Luca et al., 2019 - *Current Biology*).

Moreover, I conducted a recent study demonstrating the involvement of orexin/hypocretin neurons in the maintenance of wakefulness. I discovered a polysynaptic circuit where orexin/hypocretin neurons inhibit the VLPO sleep-active galaninergic neurons, through a local GABAergic circuit, thus leading to the rapid arousal of mice from both non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. This study not only enhances our understanding of how the activity of VLPO is regulated by distal and local wake-promoting inputs, such as the orexin/hypocretin input, but also proposes potential neuronal targets for selective pharmacological interventions in patients with disrupted wakefulness, such as narcoleptic patients (De Luca et al., 2022 - *Nature Communications*).

Finally, I conducted a study done in collaboration with Dr. Ramirez-Plascencia in Dr. Saper's group, in which we found that DMH glutamatergic (DMH^{Vglut2}) and GABAergic (DMH^{Vgat}) neurons influence the circadian rhythm of Cort. DMH^{Vglut2} neurons activate corticotropin-releasing hormone (CRH) neurons in the paraventricular nucleus (PVH^{CRH}), while DMH^{Vgat} neurons disinhibit them via GABAergic neurons of the caudal ventral periPVH (cvPVH). Disruption of these pathways reduces the daily Cort peak, demonstrating their role in Cort regulation (Ramirez-Plascencia, De Luca, et al., *Nature* in revision, 2024. *Res Sq [Preprint]*. PMCID: PMC11261983).

Overall, the combination of CRACM, electrophysiology, and single-cell molecular techniques has proven to be a powerful and valuable approach in unraveling the complexities of circuits involved in sleep-wake regulation and holds great promise for advancing our understanding and treatment of sleep disorders. All of this has motivated me to further explore and apply my skills in molecular biology by employing other single-cell-base sequencing technologies such as spatial transcriptomics.

The field of cell type characterization and spatial organization in various tissues, including the brain, still faces significant challenges. While single-cell sequencing analysis has provided a systematic and quantitative approach to identify cell types and their composition, it lacks the ability to capture the spatial organization and cell-cell interactions crucial for tissue function. However, a groundbreaking technology called spatial transcriptomics, specifically multiplexed error-robust in situ hybridization (MERFISH), has emerged as a game-changing approach to address this limitation. In fact, MERFISH provided by *Vizgen* was recognized as the "Method of the Year" in 2020. Spatial transcriptomics, through MERFISH, allows for the direct profiling of intact tissue's transcriptome with subcellular spatial resolution. This transformative technology enables the simultaneous imaging of a large number of nucleic acid targets at a

genome-scale, providing high accuracy and sensitivity at the subcellular level. It has broad applications in both fundamental biology and medicine. One of the significant advantages of spatial transcriptomics is its ability to map and catalog diverse cell types within complex biological tissues, including brain samples, from both animal and human subjects. By preserving the tissue's spatial context, researchers can gain insights into the organization of cell types within specific regions and their interactions with neighboring cells. This spatial information is crucial for understanding tissue function and it can significantly enhance our understanding of complex biological systems and contribute to the development of more precise and effective therapeutic strategies in the field of precision medicine.
This technology has become an indispensable component in my most recent works (De Luca et al., 2022 - *Nature Communications*; Nardone et al., 2024 - *Nature Communications*) and was also included in my funded NIH grant proposal (1 R03 NS128993-01A1).
My R03 grant proposal, indeed, aims to uncover the functionality of a group of neurons in the preoptic area (POA) that are involved in the promotion of REM sleep. The main hypothesis I am testing is that the neurons expressing neurotensin in the extended part of the VLPO area (eVLPO) represent the REM sleep-active population of the region. To selectively access this population, which has, however, proven to be a challenging proposition due to the absence of a selective marker, I made an interesting finding that the neuropeptide neurotensin is expressed in the galanin neurons within the eVLPO, while it is not expressed by neurons in the VLPO cluster. Interestingly, the fact that the inhibition of the VLPO neurotensin neurons reduces REM sleep shows significant potential for understanding the role of the POA region in REM sleep regulation. Since REM sleep behavior disorder (RBD) and other REM sleep-related disturbances are prodromal feature of several neurodegenerative diseases such as Parkinson's disease, the clinical relevance of this work is very high. After the successful completion of this work, my short-term plan is to develop an R01 application to further investigate the role of these newly identified neurons in REM sleep.
Obstructive Sleep Apnea (OSA) is characterized by recurrent upper airway collapse, causing apnea, hypercapnia, hypoxia, and brief arousals to restore the airway. While arousals prevent prolonged apnea, they disrupt sleep, leading to daytime sleepiness, neurocognitive impairments, hypertension, and increased cardiovascular risk. Understanding the brain circuits that control breathing, and arousal is crucial for managing OSA. Research suggests that FoxP2-expressing neurons in the Kolliker-Fuse and parabrachial nucleus (PB-KF^{FoxP2}) promote respiration, while CGRP-expressing neurons in the external lateral parabrachial nucleus (PB^{CGRP}) regulate hypercapnia-induced arousals. Both may contribute to opioid-induced respiratory depression (OIRD). However, the forebrain (FB) inputs to PB-KF^{FoxP2} neurons, crucial for enhancing ventilation without triggering arousal, remain unclear. My hypothesis is that manipulating specific FB inputs to PB-KF^{FoxP2} neurons will improve ventilatory responses to hypercapnia and hypoxia without causing cortical arousals. As an Early-Stage Investigator in the P01 (renewal), I have submitted my grant proposal to explore the role of specific FB inputs to respiratory neurons in the dorsal pons to enhance ventilatory responses to hypercapnia/hypoxia during cortical arousals.
Animals must maintain the body temperature (Tb) within a narrow range despite varying ambient temperatures. The POA of the hypothalamus is critical for thermoregulation, containing intrinsically warm-sensitive neurons (iWSNs) that detect small Tb changes. My R21 grant proposal focuses on the use of single-cell calcium imaging and Patch-seq to map and genetically profile iWSNs in the POA. This unbiased approach will enhance understanding of thermoregulatory circuits, reveal potential druggable targets, and pave the way for innovative therapies like therapeutic hypothermia.
I am currently devoting 60% of my time to research, which includes collaborating on multiple research projects within the departments of Neurology and Medicine. This dedication to research is a crucial factor driving me towards achieving my long-term career goals.

Teaching

In addition to my research endeavors, as Instructor, I am currently mentoring three postdoctoral fellows and three students. Over the past years, I have also co-mentored and contributed to the knowledge and education of many students through lectures, seminars, and laboratory interactions. Currently, I allocate

40% of my time to teaching and supervision. Going forward, my future goal is to continue educating and mentoring students, including medical students, within the laboratory environment. I derive immense satisfaction from making meaningful contributions to the education and personal growth of individuals within my field and I am dedicated to continuing this important aspect of my work. Indeed, I recently (Fall 2023) embraced a part-time teaching role as Adjunct Faculty (Instructor) at Simmons College (Biol 113-02 General Biology and Lab courses).

Administration

I have had an active role in the administration of the Lab, that occupied 10% of my time. This included tasks such as organizing Lab areas, managing funding resources, and overseeing research management. However, my aspiration and ultimate goal is to transition into a full-time focus on research and teaching. By dedicating myself entirely to these areas, I believe I can maximize my impact and contribute even more significantly to the advancement of knowledge and the education of future generations.

In conclusion, my passion encompasses both research and teaching, and I consider myself extremely fortunate to be part of the dynamic, collaborative, and supportive academic environment at Beth Israel Deaconess Medical Center and Harvard Medical School. Being surrounded by such an atmosphere enables me to thrive and fulfill my professional aspirations while making valuable contributions to scientific knowledge and nurturing the next generation of researchers and scholars.