OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Ochoa, Lorenzo Francisco

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-9880-1900

Position Title: Postdoctoral Fellow

Organization and Location: Massachusetts Institute of Technology , Cambridge, Massachusetts, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Università degli Studi di Palermo, Sicily , Not Applicable, N/A, Italy	Doctor of Philosophy (PHD)	08/2019	06/2022	Neuroscience
University of Texas Medical Branch , Galveston , Texas, United States	Doctor of Philosophy (PHD)	08/2017	08/2023	Biomedical Sciences/Neuroscience
University of Texas at El Paso , El Paso, Texas, United States	Bachelor of Science (BS)	08/2008	12/2012	Biochemistry/Biology

Appointments and Positions

2024 - present Postdoctoral Fellow , Massachusetts Institute of Technology , Cambridge, Massachusetts, United States
2023 - 2024 Postdoctoral Associate, Massachusetts Institute of Technology , Cambridge, Massachusetts, United States

Products

Products Closely Related to the Proposed Project

1. Solomon OD, Villarreal P, Domingo ND, Ochoa L, Vanegas D, Cardona SM, Cardona AE, Stephens R, Vargas G. Dynamic intravital imaging reveals reactive vessel-associated microglia play a protective role in cerebral malaria coagulopathy. Sci Rep. 2023 Nov 9;13(1):19526. PubMed Central PMCID: PMC10636186.
2. Ochoa LF, Kholodnykh A, Villarreal P, Tian B, Pal R, Freiberg AN, Brasier AR, Motamedi M, Vargas G. Imaging of Murine Whole Lung Fibrosis by Large Scale 3D Microscopy aided by Tissue Optical Clearing. Sci Rep. 2018 Sep 6;8(1):13348. PubMed Central PMCID: PMC6127188.
3. Tian B, Patrikeev I, Ochoa L, Vargas G, Belanger KK, Litvinov J, Boldogh I, Ameredes BT, Motamedi M, Brasier AR. NF-κB Mediates Mesenchymal Transition, Remodeling, and Pulmonary Fibrosis in Response to Chronic Inflammation by Viral RNA Patterns. Am J Respir Cell Mol Biol. 2017 Apr;56(4):506-520. PubMed Central PMCID: PMC5449514.
4. Ha Y, Ochoa LF, Solomon O, Shi S, Villarreal PP, Li S, Buscho S, Vargas G, Zhang W. Light-Sheet Microscopy of the Optic Nerve Reveals Axonal Degeneration and Microglial Activation in NMDA-Induced Retinal Injury. EC Ophthalmol. 2021 Nov;12(11):23-31. PubMed Central PMCID: PMC9450914.
5. Nelson J, Ochoa L, Villareal P, Dunn T, Wu P, Vargas G, Freiberg AN. Powassan Virus Induces Structural Changes in Human Neuronal Cells In Vitro and Murine Neurons In Vivo. Pathogens. 2022 Oct 21;11(10) PubMed Central PMCID: PMC9609669.

Other Significant Products Highlighting Contributions to Science

1. Wilson KD, Ochoa LF, Solomon OD, Pal R, Cardona SM, Carpio VH, Keiser PH, Cardona AE, Vargas G, Stephens R. Elimination of intravascular thrombi prevents early mortality and reduces gliosis in hyper-inflammatory experimental cerebral malaria. J Neuroinflammation. 2018 Jun 4;15(1):173. PubMed Central PMCID: PMC5987620.
2. Wilson KD, Stutz SJ, Ochoa LF, Valbuena GA, Cravens PD, Dineley KT, Vargas G, Stephens R. Behavioural and neurological symptoms accompanied by cellular neuroinflammation in IL-10-deficient mice infected with Plasmodium chabaudi. Malar J. 2016 Aug 24;15(1):428. PubMed Central PMCID: PMC4995805.
3. Luisi JD, Lin JL, Ochoa LF, McAuley RJ, Tanner MG, Alfarawati O, Wright CW, Vargas G, Motamedi M, Ameredes BT. Semi-automated micro-computed tomography lung segmentation and analysis in mouse models. MethodsX. 2023;10:102198. PubMed Central PMCID: PMC10154963.
4. Tian B, Liu Z, Litvinov J, Maroto R, Jamaluddin M, Rytting E, Patrikeev I, Ochoa L, Vargas G, Motamedi M, Ameredes BT,

Zhou J, Brasier AR. Efficacy of Novel Highly Specific Bromodomain-Containing Protein 4 Inhibitors in Innate Inflammation-Driven Airway Remodeling. Am J Respir Cell Mol Biol. 2019 Jan;60(1):68-83. PubMed Central PMCID: PMC6348724.

5. Nazari H, Ivannikov M, Ochoa L, Vargas G, Motamedi M. Microsurgical Dissection and Tissue Clearing for High Resolution Intact Whole Retina and Vitreous Imaging. J Vis Exp. 2021 Mar 11; PubMed PMID: 33779596.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Ochoa, Lorenzo Francisco

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-9880-1900

Position Title: Postdoctoral Fellow

Organization and Location: Massachusetts Institute of Technology , Cambridge, Massachusetts, United States

Personal Statement

As a Picower Postdoctoral Fellow at MIT in the Chung Lab, I integrate tissue transformation engineering, multiscale microscopy, and quantitative computation to map brain-wide circuit vulnerabilities that precede cognitive decline. My long-term goal is to become an independent R1 investigator leading an interdisciplinary laboratory that connects neuromodulatory circuit biology with scalable 3D imaging and spatial multi-omics to define early mechanisms of neurodegeneration and identify actionable intervention points.

My research trajectory has been shaped by breadth of training across multiple disciplines. I have pursued and applied methods spanning neuroscience and biomedical engineering, with additional experience in toxicology, infectious disease biology, and disease-focused questions in respiratory illness, alongside the development and application of computational approaches for large-scale imaging datasets. This diversity has taught me to move fluently between experimental design, technology development, and biological interpretation, selecting the level of analysis required by the question rather than forcing the question to fit a single method. It also reinforced a systems-level view of neurodegeneration: circuit vulnerability is rarely explained by one cell type or pathway in isolation, but instead emerges from interactions among neurons, glia, and the local tissue environment across space and time.

In my current postdoctoral work, I focus on early vulnerability in the locus coeruleus (LC), a neuromodulatory hub essential for brain-wide homeostasis and implicated early across multiple neurodegenerative conditions. I am developing a tract-resolved framework to understand why some LC projections degenerate early while others remain comparatively resilient, and how this selective vulnerability is associated with maladaptive glial programs and circuit dysfunction. This direction motivates my K99/R00 proposal, which couples projection-resolved 3D structural mapping with spatial transcriptomic profiling to link connectivity loss and axonal injury features to local cell-type and cell-state programs in a shared anatomical context. To expand my toolkit for independence, I am also receiving complementary training in chemical engineering through my primary mentor, Alzheimer's disease biology through my co-mentor, and computational biology through my advisor.

The K99/R00 mechanism is essential to my transition to independence. During the mentored K99 phase, I will strengthen two areas that are critical for my independent career: (i) rigorous computational strategies for spatial transcriptomic analysis and multimodal integration, and (ii) hypothesis-driven experimental design in complex tissue that supports clear inference while remaining feasible and reproducible. These skills will enable an independent R00 program that generalizes tract-resolved vulnerability principles across neurodegenerative contexts and advances toward interventions that preserve circuit function.

I am equally committed to mentorship and broadening access to research training. Having benefited from structured mentorship that made research careers tangible and accessible, I have prioritized mentoring and outreach throughout my training. In my independent laboratory, I plan to institutionalize rigorous and supportive training practices that emphasize reproducibility, scientific ownership, and the development of diverse trainees into confident, independent scientists.

Honors

2025	Koch Institute Image Awards , Massachusetts Institute of Technology
2024	Picower Postdoctoral Fellow, Massachusetts Institute of Technology
2023	NIH Outstanding Scholars in Neuroscience Award Program (OSNAP), National Institute of Health
2022	Betty J. Williams Scholarship, University of Texas Medical Branch
2022	Neuroscience Graduate Program Summer 2022 Merit Award, University of Texas Medical Branch
2021	Malcom S. Brodwick Memorial Scholarship, University of Texas Medical Branch
2020	Arthur V. Simmang Scholarship, University of Texas Medical Branch
2019	Arthur V. Simmang Scholarship, University of Texas Medical Branch
2019	Eva Yznaga Seger, MD Presidential Scholarship, University of Texas Medical Branch

2018 - 2023	NIH T32 pre-doctoral fellow in the Environmental Toxicology (ETox) training program, University of Texas Medical Branch
2013 - 2014	NIH Postbaccalaureate Research Education Program (PREP) R25, University of Texas Medical Branch
2012	Cum Laude Honors Graduate, University of Texas at El Paso
2010 - 2012	Dean's List, University of Texas at El Paso
2010 - 2011	NIH Bridges to the Baccalaureate Program (B2B) R25, University of Texas Medical Branch

Contributions to Science

1. Quantitative multiscale imaging and tissue transformation to enable 3D pathology readouts: My work has focused on translating advanced imaging and tissue processing methods into quantitative 3D measurements of complex biological phenotypes. In multiple organ systems, I developed and applied protocols for intact or thick-tissue preparation, optical clearing, and multiscale microscopy to preserve spatial context and enable analyses not possible with conventional 2D histology. This includes 3D characterization of human placental membrane microarchitecture (Richardson et al., 2017) and development of methods for eye/optic nerve investigation (Ha, Ochoa et al., 2021; Nazari et al., 2021), establishing a methodological foundation that I now apply to circuit-scale questions in neurodegeneration.

2. Imaging-enabled understanding of inflammatory pathology in infectious disease models: A second major contribution has been applying in vivo and cleared-tissue imaging to define how immune and glial responses shape tissue pathology during infection. In collaborative work on cerebral malaria, I established and implemented in vivo thinned-skull cranial window approaches and integrated these with ex vivo large-scale imaging enabled by optical clearing to assess the gliovascular unit and associated cellular events (Wilson et al., 2016; Wilson et al., 2018; Solomon et al., accepted Sept 2023). I also adapted and applied thick-tissue clearing, labeling, and large-scale microscopy approaches to high-containment viral infection models, contributing to studies including a published manuscript (Nelson et al., 2022). Together, these projects strengthened my expertise in quantitative imaging of neuroimmune interactions across scales.

3. Large-organ imaging of respiratory disease pathology and fibrosis progression: I contributed to defining respiratory disease pathology using multiscale imaging strategies that link tissue-level remodeling to quantitative structural features. In idiopathic pulmonary fibrosis studies, I performed whole-lung optical clearing and used multiphoton microscopy and second harmonic generation imaging to capture fibrotic architecture in intact lung tissue (Ochoa et al., 2018; Tian et al., 2017; Tian et al., 2018). This work supported continued collaborations aimed at characterizing lung pathology in respiratory syncytial virus infection and related inflammatory disease settings. These experiences reinforced my ability to bring advanced tissue imaging pipelines into disease-focused collaborations with clear, quantitative deliverables.

4. Circuit-scale vulnerability in neurodegeneration through projection-resolved mapping and multimodal integration: My current postdoctoral research is centered on understanding tract-selective circuit vulnerability in neurodegeneration, with a focus on early dysfunction in the locus coeruleus (LC) and its downstream impact on glial states and circuit integrity. Building on my background in scalable tissue processing and quantitative imaging, I am developing a framework that combines large-volume 3D mapping of projection integrity and axonal injury features with spatially resolved molecular profiling and computational integration. This program is being executed within the U01 AD–LC collaborative effort, where I have progressed from project co-lead to lead and have presented progress directly to NIH program staff as part of ongoing milestone and strategy discussions. A manuscript describing these findings is in active preparation and expected imminently, alongside continued data generation to strengthen mechanistic interpretation.

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