Neurons resemble high-functioning cities with no room for traffic jams. Their survival relies on the precise transport of vesicles, RNA granules, and organelles along a complex, multi-lane highway of microtubules and actin filaments. This highway supports bidirectional cargo flow, enabling neurons to grow, communicate, and adapt. At the core of neural communication are synapses, dynamic hubs where information is transmitted and memories form. Actin scaffolds the synapse for vesicle docking, receptor trafficking, and rapid shape change, while microtubules deliver cargo along long axons to and from the soma[1,2]. Together, microtubules and actin safeguard the flow of information essential for synaptic health, and their failure is a hallmark of neurodegeneration. **But in a system where transport determines cell fate, who directs the traffic?**

Cellular cargo transport is powered by unidirectional molecular motors, microtubule-based dynein and kinesins, and actin-based myosins, yet cargoes move bidirectionally, frequently switching directions or moving to a different track. Directional switches are not random. They are tightly regulated and essential for processes such as mitochondrial quality control and synaptic communication[3,4]. While it is well-established that actin and microtubules are functionally and physically linked, and disrupting these connections or the tracks themselves leads to many diseases, including Amyotrophic Lateral Sclerosis (ALS), Alzheimer's disease (AD), and age-related cognitive decline, mechanisms that control track switching are unknown[1].

I previously discovered a new mechanism of microtubule-based bidirectional transport, in which opposite polarity motors, dynein and kinesin, directly link to each other via a shared adaptor[5]. This finding highlights the importance of motor communication and raises a broader question of whether such coordination exists at a larger scale**. In this proposal, we will investigate a new facet of bidirectionality: how microtubule-actin connections coordinate intracellular transport.** By integrating structural biology with cellular assays in induced neurons (iNs) from young, aged, and AD patients, which retain age-related features[6] we aim to uncover fundamental principles of neuronal transport along the lifespan and how age-linked transport decline contributes to disease.

Transport of mitochondria and synaptic vesicles, two essential bidirectional cargoes that depend on both actin- and microtubule-based transport, declines with age[4,9,10]. Mitochondria, which provide energy and calcium balance for the synapse, primarily use microtubules for long-range axonal movement and actin for local positioning, while synaptic vesicles use actin-based transport at the periphery and switch to microtubule-based movement within the axon interior[11,12]. Although most long-range transport is microtubule-driven, microtubules do not reach the cell membrane. Instead, their plus ends are linked to actin via crosslinking proteins, providing sites where molecular motors accumulate[7,8]. These sites could facilitate cargo capture such as mitochondria and synaptic vesicles that enter or exit synaptic regions, but the precise mechanisms of this is unknown. Disruption in either cytoskeletal system impairs synaptic trafficking, however, the mechanisms coordinating the cytoskeletal tracks, the cargo handoff between these tracks, and how they change with age, remain poorly understood.

Our central hypothesis is that cellular cues coordinate cargo handoff between microtubule and actin networks, but with age these cues change, leading to synaptic dysfunction and neurodegeneration. To dissect this complex regulation and define healthy aging vs. disease-linked cellular changes, we will pursue two projects. **Project 1** will utilize young, aged, and AD iNs to investigate how aging affects cargo transport along actin and microtubule tracks in and out of the synapse, and how these changes impact synaptic communication. By combing confocal live-cell imaging of mitochondria and synaptic vesicles with cryo-electron tomography, we will define both the dynamics and native organization of transport machinery across aging and disease. **Project 2** will elucidate how the accumulation of motors at microtubule-actin intersections coordinates cargo handoff between different transport modalities. Using single-molecule reconstitution of cellular cargo transport and time-resolved cryo-EM, we will capture the dynamic processes that govern cytoskeletal coordination and define how their distribution contributes to neuronal dysfunction.

Impact: This work addresses a fundamental and largely unexplored problem: how cells coordinate cargo transport across different cytoskeletal systems. By defining these transitions and how they fail with age, we will uncover early drivers of cargo mislocalization and synaptic decline. These insights will establish a new framework for understanding intracellular transport and may reveal new targets for early interventions.

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16. G.-H. Wu, *et al.*, *Nat Commun* **14**, 692 (2023).
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Professional positions

Assistant Professor | Salk Institute for Biological Studies	2023 – present
Assistant Adjunct Professor | Cell & Developmental Biology | University of California San Diego	2025 – present
Postdoctoral Fellow | University of California San Diego and Howard Hughes Medical Institute | Department of Cellular and Molecular Medicine | Advisor: Samara Reck-Peterson, Ph.D.	2016 – 2023

Education

Ph.D., Structural Biology and Biochemistry | University of Colorado Denver Advisor: Elan Z. Eisenmesser, Ph.D.	2010 – 2016
M.S., Chemistry | University of Colorado Denver Advisors: Karen R. Jonscher, Ph.D. and Douglas F. Dyckes, Ph.D.	2007 – 2010
B.S., Chemistry | University of Wroclaw	2002– 2005

Fellowships

American Cancer Society Postdoctoral Fellowship	2018 – 2021
NIH F32 Ruth L. Kirschstein Postdoctoral Fellowship - NIGMS	2018
NIH F31 Ruth L. Kirschstein Predoctoral Fellowship - NCI	2013 – 2016

Honors and Awards

Leading Edge Symposium Fellow	2020
Biophysical Society Travel Award	2016
University of Colorado Graduate School Student Research Excellence Award	2015
C. Werner and Kitty Hirs University of Colorado Graduate School Student Travel Award	2014 – 2016
Protein Society Travel Award	2014
Colorado Biological Mass Spectrometry Society Poster Award	2009
American Society for Biomolecular Facilities Student/Post-Doc Poster Award	2009
University of Colorado Denver Mike Milash Teaching Assistant Award	2009

Publications

***co-first author, #co-corresponding author**

1. de la Gándara Á and **Kendrick AA**. *Capturing enzymes in motion*. eLife. 2025; 14, e108727.
2. Nguyen KVN, Ma W, Karasmanis EP, **Kendrick AA**, Reck-Peterson SL, Leschziner AE. *Cryo-EM captures early intermediate steps in dynein activation by LIS1*. Nat Comm. 2025, Aug 1,16(1):7054
3. **Kendrick AA**#, Nguyen KVN, Karasmanis EP, Reck-Peterson SL, Leschziner AE#. *Multiple steps of dynein activation by Lis1 visualized by cryo-EM.* Nat Struct Mol Biol. 2025, Aug; 32(8):1434-1444
4. Karasmanis EP*, Reimer JM*, **Kendrick AA***, Nguyen KVN, Rodriguez JA, Truong JB, Lahiri I, Reck-Peterson SL, Leschziner AE. *Lis1 relieves cytoplasmic dynein-1 autoinhibition by acting as a molecular wedge.* Nat Struct Mol Biol. 2023 Sep; 30(9):10:1357-1364.

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Professional Service

Co-organizer: International Salk Cell Cycle Meeting	2025
American Society for Cell Biology subgroup co-organizer: "Not just Cellular railroads: microtubules as cargoes and signaling centers" | virtual due to COVID-19 pandemic	2021
Chair of Structural Biology and Biochemistry Program Student Committee | University of Colorado Denver	2013 – 2014
Co-Chair of bi-annual symposium: Translating Structural Biology to Medicine | University of Colorado Denver	2013

Ad-hoc Reviewer

Nature Structural and Molecular Biology, Nature Communications, Nature Chemical Biology, Journal of Cell Biology, Review Commons, eLife

Invited Talks

Molecular Biology Seminar | University of California Davis, CA	2026
International Dynein Meeting | Ann Arbor, MI	2025

Technology Sandbox workshop | University of California San Diego, CA	2025
Molecular Mechanisms of Motors Driving Cellular Movements 2024 Gordon Research Conference | Portland, ME	2024
Cell Biology & Physiology Seminar | University of California Davis, CA	2023
Biophysics Seminar | Washington University in St. Louis, MO	2023
Structural Biology and Biochemistry seminar | University of Colorado Denver, CO	2023
2023 Annual Biophysical Society Meeting | San Diego, CA	2023
American Society for Cell Biology 2022 Annual Meeting Microsymposium | Washington D.C.	2022
American Society for Cell Biology 2021 Annual Meeting Subgroup | virtual due to COVID-19 pandemic	2021
International Dynein Meeting | virtual due to COVID-19 pandemic	2021
Leading Edge Symposium | virtual due to COVID-19 pandemic	2020, 2022
American Society for Cell Biology 2018 Annual Meeting Minisymposium | San Diego, CA	2018
Colorado Biological Mass Spectrometry Society Meeting | Fort Collins, CO	2009

Service

Society for Research Fellows Faculty Liaison | Salk Institute	2024 – present
Cancer Research Training and Education Coordination Member | Salk Institute	2024 – present
Salk Perspectives and Resources Council Member | Salk Institute	2024 – present
Leading Edge Panel co-organizer: "Parenting and Family life in Academia"	2022
Work life (im)balance workshop | American Cancer Society TheoryLab and Apple podcast	2021
Elementary School Science Presentations | Highline Academy Charter School	2010 – 2013

Professional Training

COMPASS | NIH-funded professional development and mentorship course | ten 4-hour/week sessions and 6-month support program	2023
Salk Faculty & Mentors Training series | two 3-hour sessions	2023, 2025

Teaching and Mentorship

Teaching

Chalk Talk workshop organizer | five 2-hour sessions | Salk Cancer Center	2024 – present
Teaching Assistant | Structural Biology and Biochemistry Graduate Program | University of Colorado Denver	2011 – 2016
Chemistry tutor | Varies Agencies and Institutions in Denver	2008 – 2015
Chemistry Instructor | Pre-Collegiate Outreach Program | University of Colorado Denver	2008
Teaching Assistant | Department of Chemistry | University of Colorado Denver	2007 – 2010

Mentorship

Postdoctoral fellows:

Álvaro de la Gándara, Ph.D. | Catarina Foundation fellow	2024 – present
Ankita Chadda, Ph.D. | NINDS T32 and La Mer Healthy Aging fellow	2024 – present
Amanda Wacker, Ph.D.	2026 – present

Graduate students:

Ryan Stoner | UCSD PiBS T32 fellow	2025 – present

Technicians:

Delaney Sanders	2025 – present
Sonia Goyal	2025 – present