#### Daniel Bayless – Pew Biomedical Scholars Award – One page summary

Project title: Impact of aging on neural circuits that encode and retrieve social memories

Social relationships are essential for our physical and mental well-being. They are also essential for the existence of our communities and for social progress. Social relationships depend upon forming and maintaining social memories unique to each person. Brain imaging studies and lesions in humans have revealed that the formation of new social memories depends upon a brain region called the hippocampus<sup>1,2</sup>. Studies in mice have further elucidated our understanding of the neurobiology of social memory. In particular, these studies have shown that the dorsal CA2 (dCA2) and ventral CA1 (vCA1) subregions of the hippocampus are critical for social memories<sup>3</sup>. dCA2 neurons receive, process, and relay social memory information to the vCA1, where this information is stored and relayed to brain centers that generate social behaviors<sup>4–7</sup>.

Inhibition of vCA1 neurons disrupts both the formation and retrieval of social memories<sup>8</sup>. Indeed, some vCA1 neurons are selectively activated by familiar social partners, and increased activation of these neurons enhances social memory performance<sup>8</sup>. However, only ~10% of vCA1 neurons respond to familiar social partners<sup>8</sup>, and no markers have been identified that would enable researchers to study these neurons in isolation. We hypothesize that one such marker could be expression of estrogen receptor a (ERa), which is encoded by the gene *Esr1*. Female mice exhibit better social memory over longer delays than do male mice<sup>9,10</sup>. For there to be a sex difference in social memory performance, then some neurons that encode social memories are likely responsive to sex hormones (e.g., express ERa). ERa is expressed in a subset of vCA1 neurons<sup>11,12</sup>, and we aim to study these neurons in isolation to determine their functional significance.

In the past 20 years, the number of research articles studying social memory in rodents has steadily increased (5 in 2000  $\rightarrow$  21 in 2010  $\rightarrow$  54 in 2020)<sup>13</sup>. In 2021, there were 86 published studies on social memory in rats or mice<sup>13</sup>. This increase in social memory research reflects the increased interest and successful insights that are being provided by these studies. However, only 2 of the 86 studies in 2021 examined social memory in aged mice, and the majority of these studies did not include female subjects<sup>13</sup>. Therefore, there is a gap in our growing knowledge of the neurobiology of social memory. This proposal aims to fill that gap by studying how the aging process alters the neural circuits that encode and retrieve social memories in males and females. We will do this by selectively discerning the activity (**Specific Aim 1, SA1**) and function (**SA2**) of *Esr1*-expressing vCA1 (vCA1<sup>Esr1</sup>) neurons during social memory performance in young and aged mice. In addition, we will characterize potential changes in the strength of vCA1<sup>Esr1</sup> connectivity during aging (**SA3**).

#### SA1: Resolve activity of single vCA1<sup>Esr1</sup> neurons during social memory performance in young and aged mice.

We hypothesize that vCA1<sup>Esr1</sup> neurons are active during social memory formation and retrieval. To obtain detailed insight into their activity, we will image vCA1<sup>Esr1</sup> activity by expressing the Ca<sup>2+</sup> indicator, jGCaMP8f, in a Cre-dependent manner in vCA1<sup>Esr1</sup> neurons of Esr1<sup>Cre</sup> mice. jGCaMP8f sensitively reports changes in Ca<sup>2+</sup> concentration as fluorescence changes that correlate with neural activity. We will resolve the activity of individual vCA1<sup>Esr1</sup> neurons using miniscope imaging. This imaging technique enables the tracking of single neuron activity across timepoints, providing valuable information about changes in vCA1<sup>Esr1</sup> activity during aging as well as potential sex differences in vCA1<sup>Esr1</sup> activity in males and females.

## SA2: Determine the function of vCA1<sup>Esr1</sup> neurons during social memory performance in young and aged mice.

We hypothesize that vCA1<sup>Esr1</sup> neurons encode information that is necessary for and sufficient to enhance social memory. To manipulate vCA1<sup>Esr1</sup> activity during social memory assays, we will express optogenetic opsins in a Cre-dependent manner in vCA1<sup>Esr1</sup> neurons of Esr1<sup>Cre</sup> mice. In **SA2A**, we will use the inhibitory opsin halorhodopsin (eNpHR3.0) to test the requirement of vCA1<sup>Esr1</sup> neurons for the formation and/or retrieval of social memories. In **SA2B**, we will use the excitatory opsin channelrhodopsin-2 (ChR2) to test whether activation of vCA1<sup>Esr1</sup> neurons can enhance social memories.

**SA3:** Analyze potential changes in strength of synaptic inputs and outputs of vCA1<sup>Esr1</sup> neurons in young and aged mice. We hypothesize that social memory deficits observed with aging result from decreased synaptic connectivity of vCA1<sup>Esr1</sup> neurons with age. To measure the strength of synaptic inputs and outputs, we will express Cre-dependent retrograde and anterograde tracers selectively in vCA1<sup>Esr1</sup> neurons of Esr1<sup>Cre</sup> mice. In **SA3A**, we will use monosynaptic rabies to map and measure the upstream inputs of vCA1<sup>Esr1</sup> neurons. In **SA3B**, we will express synaptophysin-fused mRuby in vCA1<sup>Esr1</sup> neurons, which will allow us to selectively quantify synaptic puncta in downstream projection targets.

#### Conclusions and significance

Breakdowns in social memory can be devastating, both for the individuals and their loved ones. The proposed studies aim to increase our understanding of the neurobiology of social memory formation and retrieval in the hopes that this knowledge can be used to help maintain or enhance social memories in humans. All three Specific Aims are independent and can be completed in the four-year period of the award. These studies will provide valuable insights into how aging alters the activity, function, and connectivity of neurons that encode and retrieve social memories. They will also provide details about these neural processes in both males and females, and they have potential to identify a marker (*Esr1* expression) that labels social memory neurons in the vCA1. Identification of such a marker will be needed to develop targeted treatments in humans aimed at increasing social memory performance without altering other cognitive abilities.

#### References

- 1. Cipolotti, L., and Bird, C.M. (2006). Amnesia and the hippocampus. Curr Opin Neurol *19*, 593–598. 10.1097/01.wco.0000247608.42320.f9.
- 2. Eichenbaum, H. (2013). What H.M. taught us. J Cogn Neurosci 25, 14–21. 10.1162/jocn\_a\_00285.
- 3. Watarai, A., Tao, K., Wang, M.-Y., and Okuyama, T. (2021). Distinct functions of ventral CA1 and dorsal CA2 in social memory. Curr Opin Neurobiol *68*, 29–35. 10.1016/j.conb.2020.12.008.
- 4. Smith, A.S., Williams Avram, S.K., Cymerblit-Sabba, A., Song, J., and Young, W.S. (2016). Targeted activation of the hippocampal CA2 area strongly enhances social memory. Mol Psychiatry *21*, 1137–1144. 10.1038/mp.2015.189.
- 5. Meira, T., Leroy, F., Buss, E.W., Oliva, A., Park, J., and Siegelbaum, S.A. (2018). A hippocampal circuit linking dorsal CA2 to ventral CA1 critical for social memory dynamics. Nat Commun *9*, 4163. 10.1038/s41467-018-06501-w.
- 6. Rao, R.P., von Heimendahl, M., Bahr, V., and Brecht, M. (2019). Neuronal Responses to Conspecifics in the Ventral CA1. Cell Rep *27*, 3460-3472.e3. 10.1016/j.celrep.2019.05.081.
- Gergues, M.M., Han, K.J., Choi, H.S., Brown, B., Clausing, K.J., Turner, V.S., Vainchtein, I.D., Molofsky, A.V., and Kheirbek, M.A. (2020). Circuit and molecular architecture of a ventral hippocampal network. Nat Neurosci 23, 1444– 1452. 10.1038/s41593-020-0705-8.
- 8. Okuyama, T., Kitamura, T., Roy, D.S., Itohara, S., and Tonegawa, S. (2016). Ventral CA1 neurons store social memory. Science *353*, 1536–1541. 10.1126/science.aaf7003.
- 9. Bluthé, R.M., and Dantzer, R. (1990). Social recognition does not involve vasopressinergic neurotransmission in female rats. Brain Res *535*, 301–304. 10.1016/0006-8993(90)91613-I.
- 10. Markham, J.A., and Juraska, J.M. (2007). Social recognition memory: influence of age, sex, and ovarian hormonal status. Physiol Behav *92*, 881–888. 10.1016/j.physbeh.2007.06.020.
- 11. McEwen, B., Akama, K., Alves, S., Brake, W.G., Bulloch, K., Lee, S., Li, C., Yuen, G., and Milner, T.A. (2001). Tracking the estrogen receptor in neurons: implications for estrogen-induced synapse formation. Proc Natl Acad Sci U S A *98*, 7093–7100. 10.1073/pnas.121146898.
- 12. Shughrue, P.J., and Merchenthaler, I. (2000). Evidence for novel estrogen binding sites in the rat hippocampus. Neuroscience *99*, 605–612. 10.1016/s0306-4522(00)00242-6.
- Cum, M., Santiago Pérez, J.A., Wangia, E., Lopez, N., Wright, E.S., Iwata, R.L., Li, A., Chambers, A.R., and Padilla-Coreano, N. (2024). A systematic review and meta-analysis of how social memory is studied. Sci Rep 14, 2221. 10.1038/s41598-024-52277-z.

## Daniel W. Bayless, Ph.D.

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## SCHOLARLY PROFILE

The research mission of the Bayless Lab is to increase our understanding of the neural circuits that underlie social behavior and the factors that alter these neural circuits. Our experiments focus on how past experiences and sex hormones shape and modulate these neural circuits. The neural circuits that underlie innate social behaviors, such as social approach, mating, and aggression, are intermingled among circuits that regulate unrelated neural processes and behaviors. To isolate and selectively study neural circuits that encode and generate fundamental elements of social behaviors, we use advanced molecular genetic techniques in mice.

### **ACADEMIC POSITIONS**

2023 – Present Assistant Professor	The Salk Institute	Molecular Neurobiology
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2019 – 2023	Basic Life Research Scientist	<u>Stanford University</u> Advisor: Dr. Nirao Shah	Neurobiology
2016 – 2019	Postdoctoral Fellow	<u>Stanford University</u> Advisor: Dr. Nirao Shah	Neurobiology
2014 – 2016	Postdoctoral Fellow	<u>University of California, San</u> <u>Francisco</u> Advisor: Dr. Nirao Shah	Neurobiology
2012 – 2014	Ph.D.	<u>Tulane University</u> Advisor: Dr. Jill Daniel	Behavioral Neuroscience
2009 – 2012	M.S.	<u>Tulane University</u> Advisor: Dr. Jill Daniel	Behavioral Neuroscience
2004 - 2008	B.A.	University of Oklahoma	Psychology

## EDUCATION AND TRAINING

### PUBLICATIONS

- 1. **Bayless D.W.**, Davis C.O., Yang R., Wei Y., Carvalho V.M., Knoedler J.K., Yang T., Livingston, O., Lomvardas A., Martins G.J., Vicente A.M., Ding J.B., Luo L., Shah N.M. A neural circuit for male sexual behavior and reward. <u>Cell</u>, 186, 3862-3881 (2023) (<u>link to pdf</u>)
- Yang T., Bayless D.W., Wei Y., Landayan D.S., Marcelo I., Wang Y., DeNardo L.A., Luo L., Druckmann S., Shah N.M. Hypothalamic neurons that mirror aggression. <u>Cell</u>, 186: 1-17 (2023). (<u>link to pdf</u>)
- Knoedler J.R., Inoue S., Bayless D.W., Yang T., Tantry A., Davis C.O., Leung N.Y., Parthasarathy S., Wang G.D., Alvarado, M., Rizvi A.H., Fenno L.E., Ramakrishnan C., Deisseroth K., Shah N.M. A functional cellular framework for sex and estrous cycle-dependent gene expression and behavior. <u>Cell</u>, 185: 654-671 (2022). (<u>link to pdf</u>)

- Darling J.S., Bayless D.W., Dartez L.R., Taylor J.H., Mehrotra A., Smith W.L., Daniel J.M. Sex differences in impulsivity in adult rats are mediated by organizational actions of neonatal gonadal hormones and not by hormones acting at puberty or in adulthood. <u>Behavioural Brain</u> <u>Research</u>, 395: 112843 (2020). (link to pdf)
- Bayless D.W., Yang T., Mason M.M., Susanto A.A.T., Lobdell A., Shah N.M. Limbic neurons shape sex recognition and social behavior in sexually naïve males. <u>Cell</u>, 176: 1190-1205 (2019). (<u>link to pdf</u>)
- Bayless D.W., Shah N.M. Genetic dissection of neural circuits underlying sexually dimorphic social behaviours. Invited Review in Themed Issue, "Multifaceted origins of sex differences in the brain", <u>Phil. Trans. R. Soc. B</u>, 371: 20150109 (2016). (<u>link to pdf</u>)
- 7. **Bayless D.W.**, Daniel J.M. Sex differences in myelination within and strength of projections from the orbital frontal cortex to the dorsal striatum in adult rats: Implications for sex differences in inhibitory control. <u>Neuroscience</u>, 300: 286-296 (2015). (link to pdf)
- 8. **Bayless D.W.**, Perez M.C., Daniel J.M. Comparison of the validity of the use of the spontaneously hypertensive rat as a model of attention deficit hyperactivity disorder in males and females. <u>Behavioural Brain Research</u>, 286: 85-92 (2015). (link to pdf)
- Bayless D.W., Darling J.S., Daniel J.M. Mechanisms by which neonatal testosterone exposure mediates sex differences in impulsivity in prepubertal rats. <u>Hormones and Behavior</u>, 64(5), 764-769 (2013). (<u>link to pdf</u>)
- 10. **Bayless D.W.**, Darling J.S., Stout W.J., Daniel J.M. Sex differences in attentional processes in adult rats as measured by performance on the 5-choice serial reaction time task. <u>Behavioural Brain Research</u>, 235, 48-54 (2012). (<u>link to pdf</u>)

#### AWARDS

2022 Nominee for 2022 Stanford Postdoc JEDI (Justice, Equity, Diversity, and Inclusion) Champion Award 2021 Honorable Mention for Stanford.Berkeley.UCSF Next Generation Faculty Symposium 2013 First Place, Outstanding Graduate Research Award, Tulane University Science and Engineering Research Day 2011 Tulane University Flowerree Summer Research Fund Award 2008 Graduated with Special Distinction from the University of Oklahoma 2007 Psi Chi Honor Society 2006 National Society of Collegiate Scholars 2006 Phi Kappa Phi Honor Society 2005 Alpha Lambda Delta Honor Society 2005 R. Boyd Gunning Scholar, Top 1% of Freshman Class, University of Oklahoma

### **RESEARCH SUPPORT**

### <u>Completed</u>

1. Pilot Funding for Autism Research12/19/2022 – 08/14/2023Autism Research Working Group at Stanford University12/19/2022 – 08/14/2023Functional significance of ASD-linked gene expression in a sexually dimorphic subcortical nucleusFunding: \$21,700Role: Principal Investigator

2. NIH T32 Postdoctoral Training Grant T32 HD007263, Mellon (PI) National Institute of Child Health & Human Development Integrated Training in Reproductive Sciences Genetic imaging and manipulation of sexually dimorphic neurons durin Role: Trainee	12/01/2014 – 11/30/2015 ing reproductive behaviors
<u>3. State of Louisiana Board of Regents Graduate Fellowship</u> LEQSF (2009-2014)-GF-13, Daniel (PI) Role: Trainee	08/01/2009 – 05/15/2014
<u>4. Tulane University Flowerree Research Award</u> <i>Effect of Neonatal Hormone Exposure on Impulsivity in Prepubertal R</i> Role: Principal Investigator	06/01/2011 – 08/20/2011 Pats

#### **TEACHING AND MENTORSHIP**

#### Teaching Philosophy

Educating and mentoring students and trainees is one of the most influential and long-lasting impacts that a research scientist can have. Scientific knowledge is continually built upon the discoveries that came before it. Therefore, it is paramount to provide an excellent education and learning environment for students and trainees, so that the next generation of scientists is fully equipped to advance the scientific knowledge of today and so that those who choose career paths outside of research remain true advocates for trusting and funding scientific research. I have worked as a high school science teacher and as a graduate teaching assistant leading group discussions, lectures, and experiments. In addition, I am passionate about actively promoting diversity and equity in science, and I foster an environment of belonging and respect in the classroom and lab. I am the first person in my family's history to earn a doctorate degree, so I understand the value of sharing my experiences with and teaching and mentoring the next generation of teachers, policymakers, and scientists.

#### Classroom Instruction

2013-14	Teaching assistant, Undergraduate Neuroscience Lab, NSCI 6515: Biopsychology Laboratory, Tulane University, New Orleans, LA (Lead Instructor: Dr. Thomas Hebert)
2012-14	Teaching assistant, High School Neuroscience Summer Program, NSCI 1015: Basic Neuroscience with Laboratory, Tulane University, New Orleans, (Lead Instructor: Dr. Thomas Hebert)
2008-09	Substitute teacher, Norman Public Schools, Norman, OK (Supervisor: Robbi Mullinax)

#### Scientific Research Mentorship

2023-present	Pom Jantarachanatanthiti, Salk Institute Research Assistant
2022	Oscar Livingston, (High School Student), Stanford Summer Research Internship
2021-23	Leonardi Gozali, (Stanford Grad Student), Stanford Biology Program
2019	Chelsea Nnebe, (Stanford M.D./Ph.D. Student), Stanford School of Medicine
2018-19	Victoria Flagg, (Stanford Master's Student), Stanford Neurosciences Program
2018-23	Chung-ha Davis, (Stanford Grad Student), Stanford Neurosciences Program
2018-19	Ilana Zucker-Scharff, (Stanford Grad Student), Stanford Neurosciences Program

- 2017-18 Corey Fernandez, (*Stanford Grad Student*), Stanford Neurosciences Program
- 2018 Lexi Lobdell, (Mount Holyoke Undergrad), Stanford Summer Research Internship
- 2017-18 Albert Susanto, (UC Berkeley Undergrad), Stanford Research Assistant
- 2015-17 Matthew Mason, (UC Berkeley Undergrad), UCSF/Stanford Research Technician
- 2015 Gabriel Chan, (UCLA Undergrad), UCSF Summer Research Internship
- 2013-14 Jacob Rosenblum, (*Tulane Undergrad*), Tulane Research Assistant
- 2012-14 Maria Perez, (Tulane Undergrad), Tulane Research Assistant
- 2010-13 Jeffrey Darling, (*Tulane Undergrad*), Tulane Research Assistant

### INVITED TALKS AND SEMINARS

- 1. <u>Stanford Autism Working Group Seminar Series</u>, Stanford, CA, March 2, 2023, "Neural circuits for innate but flexible social behavior."
- 2. <u>UC-Santa Cruz NeuroClub Seminar Series</u>, Santa Cruz, CA, May 11, 2021, "Sex on the brain: Neuropeptidergic modulation of sex recognition and mating behavior."
- 3. <u>Eco-Evo Lunch Seminar Series</u>, Virtual Zoom talks given by early career ecology and evolution scientists, November 17, 2020, "Sex on the brain: Sexually differentiated regulation of sex recognition and mating behavior."
- 4. <u>Max-Planck Institute Munich Winter Conference on Stress</u>, Garmisch-Partenkirchen, Germany, March 17, 2019, "Neural pathway for innate sex recognition."
- 5. <u>Stanford Center for Molecular Neuroscience in Health and Disease</u> Member Meeting, Stanford, CA, July 19, 2018, "A neural substrate for sex recognition."
- 6. <u>Stanford Neurobiology Lab Evening</u>, Stanford, CA, November 30, 2017, "Neurobiology of social interactions."
- 7. <u>UCSF Center for Reproductive Sciences Workshop</u>, San Francisco, CA, February 5, 2016, "Genetic dissection of the neural circuits underlying reproductive behavior in mice."
- 8. <u>Tulane Graduate Studies Student Association Colloquium Series</u>, New Orleans, LA, November 6, 2013, "Sex differences in impulsivity: Role of neonatal testosterone exposure."
- 9. <u>Tulane University Psychology Colloquium Series</u>, New Orleans, LA, March 2, 2012, "Sex differences in attention and impulsivity in prepubertal and adult rats."

### PRESENTATIONS

- 1. **Bayless D.W.**, Flagg V.G., Shah N.M. A sexually dimorphic neuronal circuit for innate sex/mate recognition in mice. *Poster Presentation*, <u>Cold Spring Harbor Laboratory, Neuronal Circuits Meeting</u>; Cold Spring Harbor, NY (2020).
- Bayless D.W., Shah N.M. Genetic imaging and manipulation of sexually dimorphic neurons during reproductive behaviors. *Poster Presentation*, <u>Center for Reproductive Sciences</u>, <u>UCSF</u> <u>Annual Retreat</u>; San Francisco, CA (2015).
- 3. **Bayless D.W.**, Daniel J.M. Sex differences in the strength of projections from the orbital frontal cortex to the dorsal striatum in adult rats: Implications for sex differences in inhibitory control. *Poster Presentation*, <u>Society for Neuroscience Annual Meeting</u>; Washington, DC (2014).

- 4. **Bayless D.W.**, Noonan M.M., Fitzpatrick M.E., Daniel J.M. (2013). Mechanism by which neonatal testosterone exposure mediates sex differences in impulsivity in prepubertal rats. *Poster Presentation*, <u>Society for Neuroscience Annual Meeting</u>; San Diego, CA (2013).
- 5. **Bayless D.W.**, Daniel J.M. Sex differences in myelination in the adult rat orbital frontal cortex and striatum: Implications for sex differences in inhibitory control. *Poster Presentation*, <u>Society</u> for Behavioral Neuroendocrinology Annual Meeting; Atlanta, GA (2013).
- Bayless D.W., Noonan M.M., Fitzpatrick M.E., Daniel J.M. Mechanism by which neonatal testosterone exposure mediates sex differences in impulsivity in prepubertal rats. *Poster Presentation*, <u>Organization for the Study of Sex Differences Annual Meeting</u>; Weehawken, NJ (2013).
- 7. **Bayless D.W.**, Darling J.S., Rosenblum, J.D., Daniel J.M. Effect of gonadectomy on attentional processes in adult male rats on the 5-choice serial reaction time task. *Poster Presentation*, <u>Society for Neuroscience Annual Meeting</u>; New Orleans, LA (2012).
- Bayless D.W., Darling J.S., Koster A.J., Daniel J.M. Sex differences in impulsive choice in prepubescent and adult rats. *Poster Presentation*, <u>Society for Neuroscience Annual Meeting</u>; Washington, DC (2011).
- Bayless D.W., Perez M.C., Daniel J.M. Sex differences in attentional processes in the spontaneously hypertensive rat, a rodent model of attention-deficit/hyperactivity disorder. *Poster Presentation*, <u>Organization for Study of Sex Differences Annual Meeting</u>; Oklahoma City, OK (2011).
- Bayless D.W., Stout W.J., Darling J.S., Daniel J.M. Effect of biological sex on attentional processes in adult rats. *Poster Presentation*, <u>Society for Neuroscience Annual Meeting</u>; San Diego, CA (2010).

### PROFESSIONAL SERVICE AND MEMBERSHIPS

- 2023-present Ad hoc peer reviewer, eLife
- 2021-2022 Creator/editor, Stanford Neurobiology Community monthly newsletter
- 2021 Co-coordinator, Stanford Neurobiology Anti-Oppression Summer Reading Group, 8 bi-weekly meetings focused on discussion/praxis related to oppression in STEM.
- 2020-2023 Coordinator, Stanford Neurobiology "Research in Progress" series, bi-weekly talks given by post-docs and grad students in the Neurobiology Department
- 2020-2023 Founding member, Diversity, Equity, Inclusion, and Belonging Committee for the Stanford Neurosciences Ph.D. Program
- 2020-2023 Founding member, Diversity, Equity, and Inclusion Committee for the Stanford Neurobiology Department
- 2013-14 Coordinator, Tulane Uptown Neuroscience Meetings, monthly presentations given by neuroscience labs at Tulane University
- 2011-present Member, Organization for the Study of Sex Differences
- 2010-present Member, Society for Behavioral Neuroendocrinology
- 2009-present Member, Society for Neuroscience
- 2009-14 Member, Greater New Orleans Society for Neuroscience

## PATENTS

1. <u>Methods to Elicit Desire to Mate and Mating Behavior.</u> US Patent Application No. 63/292,986. Filed 12/22/2022. Inventors: Daniel Bayless, Chung-ha Davis, Sayaka Inoue, Joseph Knoedler, and Nirao Shah.

## REFERENCES

#### Nirao Shah, M.D., Ph.D.

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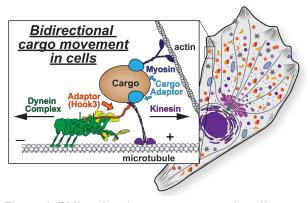
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# Gary Dohanich, Ph.D.

Professor Dept. of Psychology Tulane University 3047 Percival Stern Hall New Orleans, LA 70118 (504) 862-3307 dohanich@tulane.edu Letter of Intent

#### **PEW Biomedical Scholar**

**OVERVIEW:** Cells must coordinate the transport of hundreds of different cellular cargoes (organelles, vesicles, viruses, and macromolecules) to support essential functions, including cell survival, maturation, and growth. Disruption of transport processes is linked to numerous neurodevelopmental diseases and cancers. Cargoes are transported by molecular motors (dynein, kinesins, and myosins) along the polarized cytoskeletal tracks (microtubules or actin filaments) (Figure 1). Most cargoes move bidirectionally by switching directions or jumping to a different track. Switching tracks could allow cargo handoff between microtubule or actin-based motors, yet the mechanism of this is unknown. Similarly, motors that move in one direction Figure 1. Bidirectional cargo movement in cells.



and on the same track (dynein and kinesin) must coordinate

bidirectional cargo movement, but how these motors communicate with each other is largely unknown.

Cytoplasmic dynein-1 (dynein) is the predominant minus-end directed microtubule motor that transports dozens of distinct cargoes. I previously discovered and reconstituted the first example of a human physiological scaffold system where the dynein adaptor Hook3 directly and simultaneously interacts with dynein and kinesin<sup>1</sup>. To understand the importance of this complex in cellular transport, I characterized the molecular connections that dynein makes with multiple cargoes, including early endosomes, which are linked to dynein via Hook3<sup>2</sup>. As molecular motors and transport processes are highly dynamic, I used structural biology combined with timeresolved approaches to identify novel dynein conformations and showed that dynein's ATPase activity is critical for its activation (manuscript in preparation and<sup>3</sup>). These discoveries provide a path to build a physiologically relevant bidirectional system to study how bidirectional cargo transport is regulated in cells.

GOALS: The goal of my research is to identify how opposite-polarity motors and motors that travel on different tracks regulate bidirectional transport in cells and how disruption of these processes leads to disease.

We will determine how motor complexes assemble to allow for cargo transport. I hypothesize that bidirectionality can be regulated by the composition of complexes and/ or the order of complex assembly, especially in cases where the same adaptor links different motors. Using time-resolved CryoEM and the components of the bidirectional system I previously reconstituted<sup>1</sup>, we will capture the assembly of activated dynein complexes in the presence of ATP to account for the contribution of ATPase activity to dynein activation. Our long-term goal is to enable the incorporation of increasing complexity to ultimately reconstitute and characterize bidirectional cargo complexes using time-resolved CryoEM. Complementary approaches will be in vitro reconstitutions combined with TIRF microscopy and live-cell imaging, allowing us to test structure-driven functional hypotheses.

We will determine the mechanism of cargo handoff at the intersections of actin and microtubule tracks. I hypothesize that cargo handoff can be mediated by proteins that link different cellular tracks. Microtubule plus ends and actin tracks are linked by a large protein called Microtubule and Actin Cross-Linking Factor 1(MACF1). This crosslinker with an ATPase function is proposed to also bridge tracks to Golgi-derived vesicles, providing a possible cross-section for the cargo handoff between motors. We will purify MACF1 and reconstitute the bidirectional cargo movement in the presence of MACF1, microtubule and actin tracks, and the different motors. Using TIRF microscopy and CryoEM we will decipher the role of MACF1 in bidirectional transport. We will also apply time-resolved CryoEM to understand how the ATPase function of MACF1 contributes to its ability to crosslink cytoskeletal tracks and aid in cargo handoff.

Outlook and Significance: Our research will use innovative approaches to determine how intracellular cargoes are delivered to their proper cellular destinations in space and time. We will fill the gaps in our understanding of basic transport processes and the contribution of these processes to disease progression.

### **References (\*co-first authors)**

- 1. Kendrick, A.A., Dickey, A.M., Redwine, W.B., Tran, P.T., Vaites, L.P., Dzieciatkowska, M., Harper, J.W., Reck-Peterson, S.L., 2019. Hook3 is a scaffold for the opposite-polarity microtubule-based motors cytoplasmic dynein-1 and KIF1C. J Cell Biol 218, 2982–3001.
- 2. Christensen\*, J.R., Kendrick\*, A.A., Truong, J.B., Aguilar-Maldonado, A., Adani, V., Dzieciatkowska, M., Reck-Peterson, S.L., 2021. Cytoplasmic dynein-1 cargo diversity is mediated by the combinatorial assembly of FTS-Hook-FHIP complexes. eLife 10, e74538.
- 3. Karasmanis\*, E.P., Reimer\*, J.M., Kendrick\*, A.A., Nguyen, K.H.V., Rodriguez, J.A., Truong, J.B., Lahiri, I., Reck-Peterson, S.L., Leschziner, A.E., 2023. Lis1 relieves cytoplasmic dynein-1 autoinhibition by acting as a molecular wedge. Nat Struct Mol Biol 1-8.

# AGNIESZKA (AGA) KENDRICK, Ph.D.

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Professional positions	
Assistant Professor   Salk Institute for Biological Studies	2023 – present
Education and Training	
<b>University of California San Diego and Howard Hughes Medical Institute</b>   Department of Cellular and Molecular Medicine   Postdoctoral Fellow, Advisor: Samara Reck-Peterson, Ph.D.	2016 - 2023
<b>University of Colorado Denver</b>   Ph.D., Structural Biology and Biochemistry Ph.D. Graduate Student, Advisor: Elan Z. Eisenmesser, Ph.D.	2016
<b>University of Colorado Denver</b>   M.S., Chemistry M.S. Graduate Student, Advisors: Karen R. Jonscher, Ph.D. and Douglas F. Dyckes, Ph.D.	2010
University of Wroclaw   B.S., Chemistry	2005
Fellowships and Grants	
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
Equity, Diversity, and Inclusion	
DISCOVER – <u>D</u> iverse <u>I</u> nclusive <u>S</u> cientific <u>C</u> ommunity <u>O</u> ffering a <u>V</u> ision for an <u>E</u> cosystem <u>R</u> eimagined program reviewer   The Salk Institute	2024
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
Chemistry tutor to Afghan and Libyan refugees	2010 - 2014
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

# **Professional Service**

ASCB subgroup co-organizer: "Not just Cellular railroads: microtubules as cargoes and	2021
signaling centers" Chair of Structural Biology and Biochemistry Program Student Committee   University of	2013 - 2014
Colorado Denver	
Co-Chair of bi-annual symposium: Translating Structural Biology to Medicine   University of Colorado Denver	2013

## **Publications**

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

#### Research

- Karasmanis EP\*, Reimer JM\*, <u>Kendrick AA\*</u>, Kendrick HVN, 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.
- 2. Christensen JR\*, <u>Kendrick AA\*</u>, Truong JB, Aquilar-Maldonado A, Adani V, Dzieciatkowska M, Reck-Peterson SL. Cytoplasmic dynein-1 cargo diversity is mediated by the combinatorial assembly of FTS-Hook-FHIP complexes. eLife. 2021 Dec 9;10:e74538.
- 3. <u>Kendrick AA</u>, Dickey AM, Redwine WB, Tran PT, Pontano Vaites L, Dzieciatkowska M, Harper JW, Reck-Peterson SL. Hook3 is a scaffold for the opposite-polarity microtubule-based motors cytoplasmic dynein-1 and KIF1C. *J Cell Bio*. 2019; 218(9):2982-3001. F1000 recommended: Kapitein L: F1000Prime, 30 Jul 2019; 10.3410/f.736211626.793563078
- 4. <u>Kendrick AA</u>, Schafer J, Dzieciatkowska M, Nemkov T, D'allessandro A, Neelakantan, D, Ford HL, Pearson CG, Weekes CD, Hansen KC, Eisenmesser EZ. CD147: a small molecule transporter ancillary protein at the crossroad of multiple hallmarks of cancer and metabolic reprogramming. *Oncotarget*. 2017; 8(4): 6742-6762.
- 5. Ying-Chi C, Rahkola JT, <u>Kendrick AA</u>, Holliday MJ, Janoff EN, Eisenmesser EZ. *Streptococcus pneumoniae* IgA1 protease: A metalloprotease that can catalyze in a split manner. *Protein Sci.* 2016; 26(3): 600-610.
- 6. Saeedi BJ, Kao DJ, Kiitsenberg DA, Dobrinskih E, Schwisow KD, Masterson JC. <u>Kendrick AA</u>, Kelly CJ, Bayless AJ, Kominsky DJ, Campbell EL, Kuhn KA, Furuta GT, Colgan SP, Glover LE. HIF-dependent regulation of claudin-1 is central to intestinal epithelial tight junction integrity. *Mol Bio Cell*. 2015; 26(12): 2252-62.
- Kendrick AA, Holliday MJ, Isern NG, Zhang F, Camilloni C, Huynh C, Vendruscolo M, Armstrong G, Eisenmesser EZ. The dynamics of interleukin-8 and its interaction with human CXC receptor I peptide. *Protein Sci.* 2014; 23(4): 464-80.
- 8. Glover LE, Bowers BE, Saeedi B, Ehrentraut SF, Campbell EL, Bayless AJ, Dobrinskikh E, <u>Kendrick AA</u>, Kelly CJ, Burgess A, Miller L, Kominsky DJ, Jedlicka P, Colgan SP. Control of creatine metabolism by HIF is an endogenous mechanism of barrier regulation in colitis. *Proc Natl Acad Sci*. 2013; 110(49): 19820-5.
- Redzic JS, <u>Kendrick AA</u>, Bahmed K, Dahl KD, Pearson CG, Robinson WA, Robinson SE, Graner MW, Eisenmesser EZ. Extracellular vesicles secreted from cancer cell lines stimulate secretion of MMP-9, IL-6, TGF-β1 and EMMPRIN. *PLoS One.* 2013; 8(8): e71225.
- Kendrick AA\*, Choudhury M\*, Rahman SM, McCurdy CE, Friederich M, Van Hove JL, Watson PA, Birdsey N, Bao J, Gius D, Sack MN, Jing E, Kahn CR, Friedman JE, Jonscher KR. Fatty liver is associated with reduced SIRT3 activity and mitochondrial protein hyperacetylation. *Biochem J.* 2011; 433(3): 505-14. *Biochem J* most cited paper of the year (2011).

### Commentary

- 1. <u>Kendrick AA</u><sup>#</sup> and Christensen JR<sup>#</sup>. Bidirectional lysosome transport: a balancing act between ARL8 effectors. *Nat Commun.* 2022; 13, 5261.
- Humpries BA, Hwang PY, <u>Kendrick AA</u>, Kulkarni RP, Pozzar RA, San Martin R. Overstretched and overlooked: solving challenges faced by early-career investigators after the pandemic. *Trends in Cancer.* 2021 Oct;7(10):879-882.

#### **Manuscripts in preparation**

**Kendrick AA.** Leschziner EM, and Reck-Peterson SL. CryoEM captures snapshots of dynein's activation pathway. – I investigated how dynein's mechanochemical cycle is regulated by its regulator, Lis1. Using time-resolved CryoEM I identified multiple conformations of dynein bound to Lis1 or dynein alone (16 unique structures, including 7 unique structures from one dataset), allowing me to map the different steps of dynein's activation in real time. My data shows that Lis1 alters dynein's mechanochemical cycle by transitioning dynein into an activated state more efficiently. I propose a new model for how Lis1 relieves dynein's autoinhibition and promotes conformations that are compatible with motility.

## **Independent Reviewer**

Nature Communications Journal of Cell Biology

## **Invited Talks**

Molecular Mechanisms of Motors Driving Cellular Movements   2024 Gordon Research Conference	2024
Cell Biology & Physiology Seminar  Davis, CA	2023
UC Davis Biophysics Seminar  Washington University in St. Louis	2023
Biophysical Society   2023 Annual Meeting	2023
American Society for Cell Biology   2022 Annual Meeting Microsymposium	2022
American Society for Cell Biology   2021 Annual Meeting Subgroup	2021
International Dynein Meeting	2021
Leading Edge Symposium	2020, 2022
American Society for Cell Biology   2018 Annual Meeting Minisymposium	2018
Colorado Biological Mass Spectrometry Society Meeting	2009
Teaching and Mentorship	
Teaching	
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	
Kendrick Nguyen   Graduate student   Leschziner lab	2022 – present
Joey Truong   Undergraduate student   Reck-Peterson lab	2019 - 2022
<i>Currently:</i> PhD student, UC Davis	
Donte A. Stevens   Graduate student   Reck-Peterson lab	2018 – present
Andrea Dickey   MD/PhD student   Reck-Peterson lab	2018 - 2022
<i>Currently</i> : Finishing MD, UC San Diego	
Vinit Adani   Undergraduate student   Reck-Peterson lab	2018 - 2019
<i>Currently</i> : PhD student, UC Riverside	
Phuoc Tien Tran   Research Assistant   Reck-Peterson lab	2016 - 2018
<i>Currently</i> : PhD student, Harvard University	
Johnathon Shafer   Research Assistant   Eisenmesser lab	2014 - 2016
Currently PhD student UC Denver	

*Currently*: PhD student, UC Denver

#### **Biologically Inspired Membrane Tension Sensors for In Situ Force Imaging**

Membrane tension – the physical stress of the cell membrane – is a fundamental property that regulates the behavior and interactions of cells. Cellular processes as diverse as motility, endocytosis, and differentiation, can be controlled through changes in membrane tension. It is therefore not surprising that membrane tension plays a central role in many complex processes such as immune cell interactions, cancer progression, and in mechanosensation in the periphery. In immune biology, T cells exert mechanical force leading to an increase in membrane tension that potentiates the killing of target cells. In cancer biology, tissue mechanics have long been a known modulator of tumor growth, progression, and metastasis, and the interaction of cancer cells with the surrounding tissue by necessity happens at the membrane. Nowhere in biology is perhaps the importance of membrane tension clearer than in our ability to sense mechanical touch. This intimate sense is mediated by touch-sensitive neurons in the periphery, and the mechanotransducing molecule was found to be a membrane tension-sensitive ion channel from the Piezo family of proteins. With the landmark discovery of these Piezo proteins, it soon became clear that membrane tension sensing is the underlying property measured in many interoceptive senses including proprioception, blood pressure sensing, urination control, and respiration.

With membrane tension being such a potent biological driver, not unlike the membrane electric potential, there is a strong need for methods to reveal its magnitude and distribution in biological systems. However, our ability to quantify and map membrane tension in living systems remains very limited. Membrane tension sensors such as conformation-sensitive dyes and fluorescent proteins give only qualitative readouts and are highly sensitive to chemical perturbations. Currently, the only quantitative method requires direct perturbation of the cell membrane tension in living systems, similar to how it is possible to spatially map electrical activity in tissue using for instance voltage-sensitive fluorescent dyes, then we would be able to determine how mechanical forces distribute in living systems, and how these forces drive biological function.

Here, I propose to develop biologically inspired membrane tension sensors that will enable accurate mapping of mechanical forces in living systems. The central innovation in my approach draws on the ingenious mechanism of tension sensing by Piezo proteins. These membrane proteins achieve an exquisite sensitivity to changes in membrane tension by curving its membrane footprint into a dome-like shape (Figure 1A-B). This structural dome amplifies the structural deformation caused by changes in membrane tension, turning small changes in membrane tension into large changes in protein structure, which in turn control the gating of a central ion conducting pore.

I will repurpose naturally tension-sensitive Piezo proteins and turn them into genetically encoded membrane tension sensors with a fluorescent *in situ* readout (Figure 1C). I will then determine the interplay between membrane tension and gene expression by combining the new membrane tension tools with my lab's capabilities in spatial transcriptome profiling. My new technology will enable tissue-wide imaging of cell membrane tension in parallel with spatial mapping of cell structure and gene expression. With these advances, I aim to contribute to the advent of a new era of mechanobiology where we can directly observe how mechanical forces shape biological function across scales and across systems, from cancer to immune biology to neuroscience.

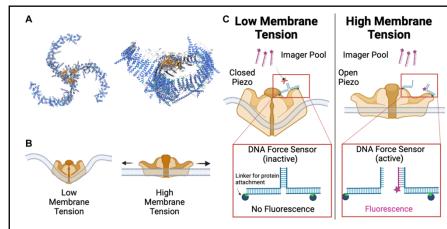


Figure 1. Repurposing Piezo as a scaffold for a membrane tension sensor with fluorescent **readout.** (A) Top and side views of the Piezo2 protein, the membrane tension sensor that mediate the sense of touch. PDB:6KG7. (B) By imparting their curved shape onto the membrane, Piezo proteins amplify the structural changes caused by a change in membrane tension. Increases in tension cause the Piezo structure to flatten. I will leverage this mechanism to develop sensitive and quantitative membrane tension sensors with fluorescent readouts. (C) My sensor design consists of a DNA force sensor with a programmable unfolding force, crosslinking the center ("cap") and periphery ("blade") of a Piezo protein. A sufficiently strong increase in

membrane tension will then flatten the Piezo protein and break open the DNA force sensor. This opening exposes a DNA binding sequence that can be detected using standard Fluorescence *In Situ* Hybridization (FISH), or DNA-PAINT. The latter option will enable detection and localization of activated sensors in live cells, through the transient binding of fluorescent oligos in solution.

## Pallav Kosuri, PhD

10010 N. Torrey Pines Rd, La Jolla CA 92037 | pkosuri@salk.edu | kosurilab.com l +1 (917) 379 9724

#### **PROFESSIONAL APPOINTMENTS**

Hearst Foundation Assistant Professor, 2021-present Salk Institute for Biological Studies, La Jolla, CA

Assistant Adjunct Professor, Department of Molecular Biology, Division of Biological Sciences, 2021-present University of California San Diego, La Jolla, CA

**Postdoctoral Fellow**, Department of Chemistry and Chemical Biology, Department of Physics, 2013-2020 Harvard University, Cambridge, MA <u>Advisor</u>: Xiaowei Zhuang, Professor of Chemistry and Chemical Biology, Professor of Physics <u>Research focus</u>: Development of DNA self-assembly methods for single molecule imaging

#### EDUCATION

**Ph.D. in Biochemistry and Molecular Biophysics**, *with distinction*, 2012 Columbia University, New York, NY <u>Advisor</u>: Julio M. Fernandez, Professor of Biological Sciences <u>Thesis</u>: Mechanochemical methods for single molecule biochemistry

#### B.S./M.Sc. in Engineering Physics, 2005

Royal Institute of Technology (KTH), Stockholm, Sweden Thesis research at European Organization for Nuclear Research (CERN), Meyrin, Switzerland <u>Advisors</u>: Lars-Erik Berg (Professor, KTH), Valentin N. Fedosseev (Senior scientist, CERN) <u>Thesis</u>: Operation and development of a Resonant Ionization Laser Ion Source

#### PUBLICATIONS

#### SELECTED PUBLICATIONS

Rotation tracking of genome-processing enzymes using DNA origami rotors <u>Kosuri P</u>\*, Altheimer BD\*, Dai M, Yin P, Zhuang X (\**co-first authors*) **Nature** 572:136-40 (2019)

S-glutathionylation of cryptic cysteines enhances titin elasticity by blocking protein folding Alegre-Cebollada J\*, <u>Kosuri P</u>\*, Giganti D, Eckels E, Rivas-Pardo JA, Hamdani N, Warren CM, Solaro RJ, Linke WA, Fernandez JM (\**co-first authors*) **Cell** 156:1235-46 (2014) *cover story* 

Protein folding drives disulfide formation <u>Kosuri P</u>, Alegre-Cebollada J, Feng J, Kaplan A, Ingles-Prieto A, Badilla C, Stockwell BR, Sanchez-Ruiz JM, Holmgren A, Fernandez JM **Cell** 151:794-806 (2012)

#### Additional Publications

Tetra-gel enables superior accuracy in combined super-resolution imaging and expansion microscopy Lee H, Yu CC, Boyden ES, Zhuang X, <u>Kosuri P</u> **Scientific Reports** 11:16944 (2021)

Work done by titin protein folding assists muscle contraction Rivas-Pardo JA, Eckels EC, Popa I, <u>Kosuri P</u>, Linke WA, Fernandez JM **Cell Reports** 14:1339-1347 (2016) Predicting readmission of heart failure patients using automated follow-up calls Inouye S, Bouras V, Shouldis E, Johnstone A, Silverzweig Z, <u>Kosuri P</u>\* (\**corresponding author*) **BMC Medical Informatics and Decision Making** 15:22 (2015)

Picomolar amyloid-β peptides enhance spontaneous astrocyte calcium transients Lee L, <u>Kosuri P</u>, Arancio O **Journal of Alzheimer's Disease** 38:49-62 (2014)

Force dependency of biochemical reactions measured by single-molecule force-clamp spectroscopy Popa I\*, <u>Kosuri P</u>\*, Alegre-Cebollada J, Garcia-Manyes S, Fernandez JM (\**co-first authors*) **Nature Protocols** 8:1261-76 (2013)

Direct observation of disulfide isomerization in a single protein Alegre-Cebollada J, <u>Kosuri P</u>, Rivas-Pardo JA, Fernandez JM **Nature Chemistry** 3:882-7 (2011)

Protease power strokes force proteins to unfold Alegre-Cebollada J, <u>Kosuri P</u>, Fernandez JM **Cell** 145:339-40 (2011) *preview* 

Single-molecule paleoenzymology probes the chemistry of resurrected enzymes Perez-Jimenez R, Ingles-Prieto A, Zhao Z, Sanchez-Romero I, Alegre-Cebollada J, <u>Kosuri P</u>, Garcia-Manyes S, Kappock TJ, Tanokura M, Holmgren A, Sanchez-Ruiz JM, Gaucher EA, Fernandez JM **Nature Structural & Molecular Biology** 18:592-6 (2011)

Single-molecule force spectroscopy approach to enzymatic catalysis Alegre-Cebollada J, Perez-Jimenez R, <u>Kosuri P</u>, Fernandez JM **Journal of Biological Chemistry** 285:18961-6 (2010)

Kalman filter estimates of the contour length of an unfolding protein in single-molecule force spectroscopy experiments Fernandez VI, <u>Kosuri P</u>, Parot P, Fernandez JM **Review of Scientific Instruments** 80:113104 (2009)

Partially folded equilibrium intermediate of the villin headpiece HP67 defined by 13C relaxation dispersion O'Connell NE, Grey MJ, Tang Y, <u>Kosuri P</u>, Miloushev VZ, Raleigh DP, Palmer AG **Journal of Biomolecular NMR** 45:85-98 (2009)

Diversity of chemical mechanisms in thioredoxin catalysis revealed by single-molecule force spectroscopy Perez-Jimenez R, Li J, <u>Kosuri P</u>, Berne BJ, Fernandez JM **Nature Structural & Molecular Biology** 16:890-6 (2009)

Force-clamp spectroscopy detects residue co-evolution in enzyme catalysis Perez-Jimenez R, Wiita AP, Rodriguez-Larrea D, <u>Kosuri P</u>, Gavira JA, Sanchez-Ruiz JM, Fernandez JM **Journal of Biological Chemistry** 283:27121-9 (2008)

Coupling of ribosomal L1 stalk and tRNA dynamics during translation elongation Fei J, <u>Kosuri P</u>, MacDougall DD, Gonzalez RL **Molecular Cell** 30:348-59 (2008)

Development of a RILIS ionisation scheme for gold at ISOLDE, CERN Marsh BA, Fedosseev VN, <u>Kosuri P</u> **Hyperfine Interactions** 171:109-16 (2006)

## PATENTS

Force-clamp spectrometer with functionalized cantilever tip, US 9,880,088 (Licensed to: *Luigs & Neumann GmbH*) Fernandez JM, Perez-Jimenez R, <u>Kosuri P</u>

Ancestral proteins, EP 2,593,472 (Licensed to: *Evolgene Genomics SL*) Fernandez JM, Perez-Jimenez R, Gaucher E, <u>Kosuri P</u>

#### INVITED SEMINAR TALKS (SELECTED)

Lewis-Sigler Institute, Princeton University, Princeton, NJ, 2024 Foundations of Nanoscience, Snowbird, UT, 2023 Johns Hopkins University School of Medicine, Dept. of Molecular Biology and Genetics, Baltimore, MD, 2023 UC Irvine, Department of Developmental and Cell Biology, Irvine, CA, 2023 Biophysical Society Annual Meeting, San Diego, CA, 2023 Aspen Center for Physics: Single Molecule Biophysics Meeting, Aspen, CO, 2023 Karolinska Institutet, Department of Medical Biochemistry and Biophysics, Stockholm, Sweden, 2022 Okanagan Biophysics Conference, University of British Columbia, Kelowna, BC, 2022 Frontiers in Biophysics Conference, Simon Fraser University, Vancouver, BC, 2022 (*keynote*) Swiss Society of Biomaterials & Regenerative Medicine, ETH Zürich, Switzerland, 2022 (*keynote*) Boston Protein Design and Modeling Seminar Series, Harvard Medical School, Boston, MA, 2021 Genetics, Bioinformatics and Systems Biology Colloquium, UC San Diego, San Diego, CA, 2020 Physics of Living Systems, Harvard University, Cambridge, MA, 2014 Bauer Forum, Center for Systems Biology, Harvard University, Cambridge, MA, 2014 The New York Academy of Sciences, New York, NY, 2012

### **TEACHING & ADVISING EXPERIENCE**

<u>Chromatin Structure & Dynamics BGGN 283 / BIMM 194</u> (Undergraduate and Graduate Level), UC San Diego <u>Cellular Physiology of Disease</u> (Undergraduate and Graduate Level), Columbia University <u>Molecular Biophysics</u> (Graduate Level), Columbia University <u>Experimental Biophysics</u> (Graduate Level), Tel Aviv University, Israel

#### AWARDS

W.M. Keck Foundation Award
Beckman Young Investigator Award
Titus M. Coan Prize for Excellence in Basic Research
Columbia University Distinction Award for doctoral defense
Columbia Technology Ventures Validation Fund Award
Henrik Göransson Sandviken Foundation Scholarship
Fulbright Scholarship

## FUNDING

Salk Innovation Grant (100K) (2023-2024)

NIH R01 (1.45M) (Co-investigator) (2023-2028)

Beckman Young Investigator Award (600K) (2022-2026)

W.M. Keck Foundation Award (1.3M) (Co-investigator) (2024-2026)

## **OTHER SERVICE & EXPERIENCE**

#### COMMITTEES

- <u>Program Director</u>, Physical Cell Biology, Biophysical Society, 2022-2023
- <u>Elected Representative</u>, Academic Council, Salk Institute for Biological Studies, 2022-present
- Director, Engagement & Wellbeing Initiative, Salk Institute for Biological Studies, 2021-present
- Board Member, Harvard University Institutional Review Board (IRB), 2018-2020
- President, Graduate Student Organization, Columbia University Medical Center, 2007-2008

#### EDUCATIONAL OUTREACH

• Group Leader, Mentor, Harvard Health Professions Recruitment & Exposure Program (HPREP), 2013-2015

### **OTHER PROFESSIONAL APPOINTMENTS**

- InSITE Fellow, Startup & Venture Capital fellowship at Columbia Business School, 2011-2015
- <u>Research Fellow</u>, Columbia Technology Ventures, Technology Transfer, 2010-2013

#### MEMBERSHIP IN PROFESSIONAL SOCIETIES

- American Heart Association (AHA), 2021-present
- International Society for Nanoscale Science, Computation and Engineering (ISNSCE), 2018-present
- Biophysical Society (BPS), 2008-present

#### **GRANT REVIEWER (SELECTED)**

- German Research Foundation (DFG)
- City University of New York (CUNY)
- University of Wisconsin-Milwaukee (UWM)

#### **REVIEWER FOR RESEARCH JOURNALS (SELECTED)**

- Nature
- Nature Physics
- Nature Methods

#### **CURRENT TRAINEES**

- Yuening Liu, PhD (Postdoctoral fellow)
- Amanda Wacker (PhD student, Biological Sciences)
- Ryan Fantasia (PhD student, Biological Sciences)
- Delisa Ramos (PhD student, Biological Sciences)
- Jocelyn Olvera (PhD student, Biological Sciences; co-mentored by Dmitry Lyumkis)
- Jerry Wu (Undergraduate student, Bioengineering)
- Annabelle Coles (Research Technician, Undergraduate student, Bioinformatics)