

## Daniel Bayless – Edward Mallinckrodt, Jr. Foundation Grant – 1-page LOI for Salk ApCom

### **Project title:** Dissecting the discrete neural pathways that alleviate social anxiety

The Edward Mallinckrodt, Jr. Foundation supports “early-stage biomedical investigators engaged in basic and translational research that has the potential to make fundamental advances in biomedical science”. Our proposed studies will do so by identifying the molecular and circuit-level mechanisms that promote resilience to social stress. Our central hypothesis is that neurons in an understudied region of the amygdala, the basomedial amygdala (BMA), are a key node in a circuit that actively buffers social stress and promotes social behavior.

Humans are constantly exposed to social stress in environments such as schools and workplaces, where evaluation by others is unavoidable. Social anxiety disorder (SAD) is a debilitating condition characterized by an excessive fear of negative social evaluation and avoidance of social interactions. Its prevalence is substantial and rising, with approximately 12% of individuals in the United States experiencing SAD at some point in their lifetime. Prior studies have identified brain regions involved in stress processing, including the amygdala. However, the neural circuits that actively promote resilience, enabling individuals to adapt to and overcome social stress, remain largely undefined. Notably, SAD exhibits a sex bias, with women showing approximately 1.4-fold higher prevalence than men. Despite this disparity, the neurobiological basis of these sex differences remains poorly understood. Thus, there is a critical gap in our understanding of 1) how the brain regulates adaptive responses to social challenges and 2) what underlies the sex difference in social anxiety.

In preliminary experiments, we discovered that, in males, chemogenetic activation of aromatase (Aro)-expressing neurons in the BMA ( $BMA^{Aro}$ ) promotes social approach behavior toward males but not toward females (Fig. 1). Since the approach toward conspecific males is inherently anxiety-provoking in male mice, this suggests that  $BMA^{Aro}$  neurons may actively mediate social stress and promote approach behavior under socially challenging conditions. Our preliminary data also demonstrate that  $BMA^{Aro}$  neurons are more abundant in females than in males (Fig. 2). Together, these findings support the hypothesis that  $BMA^{Aro}$  cells regulate social stress-induced avoidance in a sex-dependent manner. We propose to test this with three specific aims.

### **Aim 1: Determine if activation of $BMA^{Aro}$ neurons alleviates social anxiety following chronic social defeat**

We will first establish a chronic social defeat stress paradigm to define the behavioral dynamics underlying the emergence of social avoidance in male and female mice. Then, we will use *in vivo* calcium imaging during social interactions to determine the neural activity profile of  $BMA^{Aro}$  neurons before, during, and after social defeat (Aim 1A). Finally, we will determine if chemogenetic activation of  $BMA^{Aro}$  neurons is sufficient to alleviate social avoidance behavior following social defeat in both males and females (Aim 1B).

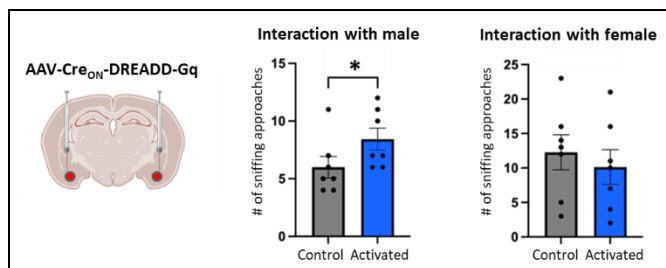
### **Aim 2: Dissect the circuit mechanisms through which $BMA^{Aro}$ neurons regulate social anxiety**

First, we will map  $BMA^{Aro}$  projection targets using anterograde tracing approaches to identify downstream regions implicated in social anxiety (Aim 2A). Then, we will use optogenetic terminal activation of specific  $BMA^{Aro}$  projections to isolate their function in alleviating social anxiety (Aim 2B). Based on our preliminary data, we observe a promising projection from  $BMA^{Aro}$  neurons to the zona incerta (ZI). These experiments will determine how specific  $BMA^{Aro}$  circuits modulate social behavior and anxiety-related responses.

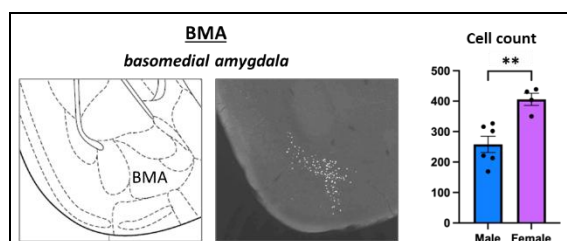
### **Aim 3: Define the molecular mechanisms underlying the function of $BMA^{Aro}$ neurons during social behavior**

To identify the molecular mechanisms underlying these effects, we will perform a selective adult knockout of Aro in BMA neurons via AAV-Cre delivery in  $Aro^{Fllox}$  mice and assess behavioral consequences on social interaction and approach (Aim 3A). Finally, we will perform snRNAseq of BMA neurons to define the molecular identity of  $BMA^{Aro}$  neurons and identify candidate genes/pathways mediating their role in social anxiety (Aim 3B).

**Overview:** This proposal is innovative in its focus on the understudied BMA and the inclusion of female social defeat models. Current treatments for SAD are limited to psychotherapy and antidepressant medications, which are not universally effective and do not directly target specific mechanisms. Defining the mechanisms that promote resilience to social stress has the potential to enable transformative, fundamental therapies for SAD.



**Fig. 1:**  $BMA^{Aro}$  activation promotes social approach under anxiety-provoking conditions (e.g., encounters with an unfamiliar intruder male) but not other conditions (e.g., encounters with an unfamiliar female).



**Fig. 2:**  $BMA^{Aro}$  cell number is greater in females

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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 sex hormones, genes associated with human disorders, and aging shape and modulate these neural circuits. The brain circuits that underlie innate social behaviors, such as social approach, aggression, social memory, and anxiety 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	<b>Assistant Professor</b>	<u>The Salk Institute</u>	Molecular Neurobiology
2024 – Present	<b>Adjunct Assistant Professor</b>	<u>University of California, San Diego</u>	Department of Neurobiology

**EDUCATION AND TRAINING**

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

**PUBLICATIONS**

- Jantarachanatanthiti P., **Bayless D.W.** The rhythm of sequential behavioral transitions: Neuro-modulatory dynamics and male sexual behavior. *Preview, Neuron*, 113, 1124-1126 (2025) ([link to pdf](#))
- 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. *Cell*, 186, 3862-3881 (2023) ([link to pdf](#))
- 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. *Cell*, 186: 1-17 (2023). ([link to pdf](#))
- 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. *Cell*, 185: 654-671 (2022). ([link to pdf](#))

5. 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. *Behavioural Brain Research*, 395: 112843 (2020). ([link to pdf](#))
6. **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. *Cell*, 176: 1190-1205 (2019). ([link to pdf](#))
7. **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"*, *Phil. Trans. R. Soc. B*, 371: 20150109 (2016). ([link to pdf](#))
8. **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. *Neuroscience*, 300: 286-296 (2015). ([link to pdf](#))
9. **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. *Behavioural Brain Research*, 286: 85-92 (2015). ([link to pdf](#))
10. **Bayless D.W.**, Darling J.S., Daniel J.M. Mechanisms by which neonatal testosterone exposure mediates sex differences in impulsivity in prepubertal rats. *Hormones and Behavior*, 64(5), 764-769 (2013). ([link to pdf](#))
11. **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. *Behavioural Brain Research*, 235, 48-54 (2012). ([link to pdf](#))

## AWARDS

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|------|--|
| 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

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### Current

#### 1. Whitehall Foundation Grant

01/01/2026 – 12/31/2028

*Illuminating the role of neuro-estrogens in social behavior*

Funding: \$300,000

Role: Principal Investigator

2. Brain Research Foundation Seed Grant

06/01/2024 – 05/31/2026

Grant Number: *BRFSG-2024-02*

*Understanding the Impact of ASD-linked Genes on Subcortical Processing of Social Cues*

Funding: \$80,000

Role: Principal Investigator

Completed

1. Pilot Funding for Autism Research

12/19/2022 – 08/14/2023

Autism Research Working Group at Stanford University

*Functional significance of ASD-linked gene expression in a sexually dimorphic subcortical nucleus*

Funding: \$21,700

Role: Principal Investigator

2. NIH T32 Postdoctoral Training Grant

12/01/2014 – 11/30/2015

Grant Number: *T32 HD007263, Mellon (PI)*

National Institute of Child Health & Human Development

Integrated Training in Reproductive Sciences

*Genetic imaging and manipulation of sexually dimorphic neurons during reproductive behaviors*

Role: Trainee

3. State of Louisiana Board of Regents Graduate Fellowship

08/01/2009 – 05/15/2014

Grant Number: *LEQSF (2009-2014)-GF-13, Daniel (PI)*

Role: Trainee

4. Tulane University Flowerree Research Award

06/01/2011 – 08/20/2011

*Effect of Neonatal Hormone Exposure on Impulsivity in Prepubertal Rats*

Role: Principal Investigator

**TEACHING AND MENTORSHIP**

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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, graduate teaching assistant, and undergraduate course lecturer.

Classroom Instruction

2025-present Organizer and lecturer, Core course for UCSD Neurosciences PhD Program

*NEU 200B: Systems Neurobiology*

University of California, San Diego

2025-present Facilitator and lecturer, Chalk talk workshop

*Salk's Annual Chalk Talk Workshop Course*

Salk Institute for Biological Studies

2026-present Lecturer, Course for UCSD Biological Sciences PhD Program

*BGGN 248: Cellular and Molecular Mechanisms in Neural Development and Regeneration*

Guest lecture: *Neural circuits that guide social behavior*

University of California, San Diego

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, LA  
(Lead Instructor: Dr. Thomas Hebert)
- 2008-09 Substitute teacher, Norman Public Schools, Norman, OK  
(Supervisor: Robbi Mullinax)

### **Scientific Research Mentorship**

#### As an assistant professor at the Salk Institute:

- 2026-present Dr. Amir Alayoubi, (*Postdoctoral Fellow*)
- 2024-present Lisa Tatsumi, (*PhD Student, UCSD Biology Program*)
- 2024-present Caliope Marin, (*PhD Student, UCSD Biology Program*)
- 2024-25 Sarah Gharagozlou, (*High School Student*)
- 2024-25 Elina Thode, (*High School Student*)
- 2024-present Alisa Kudo, (*UCSD Undergrad*)
- 2024-present Annika Torres, (*UCSD Undergrad*)
- 2024-present Ashrika Paudyal, (*UCSD Undergrad*)
- 2024-present Dr. Subhalakshmi Guha, (*Postdoctoral Fellow*)
- 2024-present Dr. Seungjoon Lee, (*Postdoctoral Fellow*)
- 2024-24 Leanne Lehmann, (*Rotating PhD Student, UCSD Neuroscience Program*)
- 2023-24 Joycelyn Yiu, (*Rotating PhD Student, UCSD Bioengineering Program*)
- 2023-present Pom Jantarachanathiti, (*Research Assistant I*)

#### As a postdoctoral researcher in Nirao Shah's lab at Stanford University and UCSF:

- 2022-22 Oscar Livingston, (*High School Student*)
- 2021-23 Leonardi Gozali, (*PhD Student, Stanford Biology Program*)
- 2019-19 Chelsea Nnebe, (*M.D./Ph.D. Student, Stanford School of Medicine*)
- 2018-19 Victoria Flagg, (*Master's Student, Stanford Neurosciences Program*)
- 2018-23 Chung-ha Davis, (*PhD Student, Stanford Neurosciences Program*)
- 2018-19 Ilana Zucker-Scharff, (*PhD Student, Stanford Neurosciences Program*)
- 2017-18 Corey Fernandez, (*PhD Student, Stanford Neurosciences Program*)
- 2018-18 Lexi Lobdell, (*Mount Holyoke Undergrad*)
- 2017-18 Albert Susanto, (*UC Berkeley Undergrad*)
- 2015-17 Matthew Mason, (*UC Berkeley Undergrad*)
- 2015-15 Gabriel Chan, (*UCLA Undergrad*)

#### As a graduate student in Jill Daniel's lab at Tulane University:

- 2013-14 Jacob Rosenblum, (*Tulane Undergrad*)
- 2012-14 Maria Perez, (*Tulane Undergrad*)
- 2010-13 Jeffrey Darling, (*Tulane Undergrad*)

### **INVITED TALKS AND SEMINARS**

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1. UCLA Neuroendocrinology Seminar Series, Los Angeles, CA, May 30, 2025, "Illuminating the neural circuits that generate social behavior."

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

## PRESENTATIONS

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1. **Bayless D.W.**, Flagg V.G., Shah N.M. A sexually dimorphic neuronal circuit for innate sex/mate recognition in mice. *Poster Presentation*, Cold Spring Harbor Laboratory, Neuronal Circuits Meeting; Cold Spring Harbor, NY (2020).
2. **Bayless D.W.**, Shah N.M. Genetic imaging and manipulation of sexually dimorphic neurons during reproductive behaviors. *Poster Presentation*, Center for Reproductive Sciences, UCSF Annual Retreat; 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*, Society for Neuroscience Annual Meeting; 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*, Society for Neuroscience Annual Meeting; 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*, Society for Behavioral Neuroendocrinology Annual Meeting; Atlanta, GA (2013).
6. **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*, Organization for the Study of Sex Differences Annual Meeting; 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*, Society for Neuroscience Annual Meeting; New Orleans, LA (2012).
8. **Bayless D.W.**, Darling J.S., Koster A.J., Daniel J.M. Sex differences in impulsive choice in prepubescent and adult rats. *Poster Presentation*, Society for Neuroscience Annual Meeting; Washington, DC (2011).

9. **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, Organization for Study of Sex Differences Annual Meeting*; Oklahoma City, OK (2011).
10. **Bayless D.W.**, Stout W.J., Darling J.S., Daniel J.M. Effect of biological sex on attentional processes in adult rats. *Poster Presentation, Society for Neuroscience Annual Meeting*; San Diego, CA (2010).

## PROFESSIONAL SERVICE AND MEMBERSHIPS

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- 2026-present Member, “Salk Science at the Seaside” Planning Committee (full day Salk science and networking event)
- 2025-present Faculty representative, Salk Society of Research Fellows (graduate student and postdoc association at Salk)
- 2025-present Member, UCSD Biological Sciences PhD Program Admissions Committee
- 2024 Member, UCSD Neurosciences PhD Program Admissions Committee
- 2024-25 Member, Salk Institute Thursday Seminar Series Committee
- 2024-present Ad hoc scientific consultant, STAT News
- 2023-present Ad hoc peer reviewer, Nature, Neuron, eLife, Cell Reports, Current Biology, Current Opinion in Neurobiology
- 2021-22 Creator/editor, Stanford Neurobiology Community monthly newsletter
- 2021-21 Co-coordinator, Stanford Neurobiology Anti-Oppression Summer Reading Group, 8 bi-weekly meetings focused on discussion/praxis related to oppression in STEM.
- 2020-23 Coordinator, Stanford Neurobiology “Research in Progress” series, bi-weekly talks given by post-docs and grad students in the Neurobiology Department
- 2020-23 Founding member, Diversity, Equity, Inclusion, and Belonging Committee for the Stanford Neurosciences Ph.D. Program
- 2020-23 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

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1. Methods to Elicit Desire to Mate and Mating Behavior. 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**

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**Nirao Shah, M.D., Ph.D.**

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Dept. of Psychiatry  
and Dept. of Neurobiology  
Stanford University  
1201 Welch Rd, Rm P106  
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