

NIH BIOGRAPHICAL SKETCH

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NAME: Mitchell, Kasey Lee

eRA COMMONS USER NAME (credential, e.g., agency login): KaseyMitchell

POSITION TITLE: Graduate Student Research Assistant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Berkeley	BA	08/2014	12/2017	Integrative Biology
University of Wisconsin - Madison	PHD	08/2023	05/2028 (Expected)	Endocrinology and Reproductive Physiology

A. Personal Statement

I graduated from UC Berkeley a semester early in December 2017. I had wanted to become a marine biologist since I was a little kid, so the work and research experience I gathered for the next six years was with the goal of going to graduate school and getting my Ph.D. in marine biology, specifically in the field of shark biology. I became a diligent, reliable, and extremely hard-working lab manager. In 2022, when I was applying for graduate programs for the third try, I became interested in fields such as endocrinology and physiology with the hope that my extensive experience in marine biology and stem cell biology could fuse and make for novel research. I joined Dr. Wei Xu's lab at UW-Madison in January 2024 and am looking forward to developing novel cancer therapies for both female and male breast cancer. During my time here, I am also pursuing a certificate in Strategic Innovation, and am taking supplemental coursework to develop my skills in business entrepreneurship, patent law, and technological innovation strategies. It is with this hope that upon graduating with my Ph.D. I am in a position to confidently launch my own biotech startup or serve as a consultant for local biotech companies.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 – Present	Graduate Research Assistant, University of Wisconsin - Madison
2019 – 2023	Lab Assistant II, Scripps Institution of Oceanography, UC San Diego
2018 – 2019	Researcher at Ab Initio Biotherapeutics, LLC

Honors

2022	Poster Presenter, Sharks International Conference, Valencia, Spain
2014-2017	George Miller Band Scholarship
2017	Berkeley Study Abroad Scholarship
2016	Herb Towler Leadership Award

2016
2013

Summer Undergraduate Research Fellowship
University of California, Berkeley - Cal Summer Experience Scholarship

C. Contributions to Science

Undergraduate Research: During the summer of 2016, I pursued a SURF Fellowship in the lab of Prof. Tanja Dominko at the Worcester Polytechnic Institute. Under the mentorship of then-graduate student, David Dolivo, I investigated the role of L-tryptophan and its metabolite kynurenine in the expression of pro-regenerative wound healing response in human dermal fibroblasts. I performed cell culture, immunocytochemistry, and spectrophotometric analyses of IDO activity. I not only gained proficiency in mammalian cell culture techniques and honed my interpersonal skills, asserting myself as a reliable and diligent lab member. This experience opened my eyes to the potential of using analogs and inhibitors to interrogate molecular pathways in studying complex molecular mechanisms. As an undergraduate, I also volunteered for the White Shark Diving Company in Gansbaai, South Africa, during my study abroad program in Spring of 2017. Under the direction of Mary Rowlinson, MS, I used dorsal fin identification software to aid in local shark population studies, communicated shark conservation strategies to local visitors and fishermen, and collected climate data. I participated in the necropsy of the largest female great white shark to wash ashore in Gansbaai - a moment pivotal to the country's conservation management strategies and course-altering in my development as an aspiring marine biologist.

Research as a Lab Assistant: Immediately after graduating from UC Berkeley in December 2017, I joined the team as a research scientist at Ab Initio Biotherapeutics Inc., a biotechnology startup in South San Francisco. In this role, I was responsible for several projects. These included extracting and purifying G-protein coupled receptor (GPCRs) proteins from baculovirus-infected SP6 insect cells. I was also responsible for the extraction, purification, and basic functional testing of antibodies and nanobodies as drug candidates against these GPCRs. Immediately after Ab Initio was sold, I became a lab technician in Prof. Amro Hamdoun's lab at Scripps Institution of Oceanography. The position allowed me to combine my skills from the biotech industry with lab procedures unique to a marine biology setting. As Prof. Hamdoun's lab manager for four years, I designed and operated our new mammalian cell culture room. In the design phase, I managed all aspects of space configuration, equipment, and supplies procurement, as well as organized and optimized all protocols necessary for a functional stem cell laboratory. As part of my work in Prof. Hamdoun's lab, I helped establish unique sea urchin culturing conditions for ABCB1 CRISPR knockout lines of *Lytechinus pictus* – the first sea urchin knockout line in the country. During this four-year commitment, I gained expertise in not only sea urchin animal husbandry but in algal culturing, water condition chemistry, and team management strategies. Our team effort was published in 2022 in *Development*, titled "Generation of a homozygous mutant drug transporter (ABCB1) knockout line in the sea urchin *Lytechinus pictus*".

In February 2020, just before the Covid-19 outbreak, I spent 14 days in Prof. Amander Clarke's lab at UCLA, learning all aspects of embryonic stem cell culture, cryopreservation, expansion, and differentiation into primordial germ-like cells (PGCs). Progress during the following two years was frequently interrupted. However, I resumed ESC- and PGC-based experiments and continued to characterize mRNA, protein expression, and activity of ABC transporters using in situ hybridization, immunocytochemistry, and efflux assays as readouts of the ability of PGCs to protect themselves from effects of organic pollutants and maintain genomic and epigenomic integrity.

In May 2022, I co-authored a research proposal in a collaboration between our laboratory, Prof. Chris Lowe at California State University Long Beach, Prof. Tanja Dominko at WPI, Dr.

Ketchum at the University of Mexico, La Paz, Baja California, and the NOAA Observer Program for development of cell culture resources for studying cartilaginous fishes. Today, there are no available shark or ray cell lines. The proposal received encouraging reviews, and the work following tested several culture conditions and environmental variables, resulting in several established and continuing primary cell cultures from sevengill sharks, leopard sharks, and round stingray tissue samples. I presented my research findings in a poster at the Sharks International conference in Valencia, Spain, in October 2022, entitled "Developing elasmobranch somatic cell lines – A new research resource".

Publications:

1. Vyas H, Schrankel CS, Espinoza JA, Mitchell KL, Nesbit KT, Jackson E, Chang N, Lee Y, Warner J, Reitzel A, Lyons DC, Hamdoun A. Generation of a homozygous mutant drug transporter (ABCB1) knockout line in the sea urchin *Lytechinus pictus*. Development. 2022 Jun 1;149(11):dev200644. doi: 10.1242/dev.200644. Epub 2022 Jun 6. PMID: 35666622; PMCID:PMC9245184

Presentations:

1. Kasey L. Mitchell, Yoon Lee, Evan Tjeerdema, Tanja Dominko, Christopher G. Lowe, Martin Tresguerres, Amro Hamdoun (2022). Developing elasmobranch somatic cell lines: a new research resource. Sharks International Conference. Valencia, Spain, October 2022.
2. Evan Tjeerdema¹, Himanshu Vyas, Jose Espinosa, Catherine Schrankel, Kasey L. Mitchell, Katherine Nesbit, Elliot Jackson, Nathan Chang, Yoon Lee, and Amro Hamdoun (2022). Generation and propagation of an ABCB1a knockout line in the sea urchin *Lytechinus pictus*. Annual meeting of the Society of Environmental Toxicology and Chemistry. San Diego, California May 2022.

Graduate Research:

Project 1: Developing novel DipG analogues as a therapy for HR+/HER2+ breast cancer

HR+/HER2+ positive breast cancer accounts for 13% of all BC cases. Current drug therapies are often unable to bind to mutated forms of these receptors, and intricate crosstalk between the receptors establishes the need to target both receptors instead of just one. There is thus a critical need to develop a drug treatment capable of targeting both WT and mutant ER and HER2. Heat shock protein 90 (HSP90) is a molecular chaperone of ER and HER2, which promotes the ligand-binding conformations of these receptors. It has also been shown that tumors show elevated expression of HSP90 and HSP70. Dipsosaurus G (DipG), a naturally derived plant product discovered by Dr. Xu's lab, has been found to bind to HSP90. DipG has been shown to promote ER/HER2 degradation by stabilizing the HSP90-E3 ubiquitin ligase-ER/HER2 complex, thus degrading ER and HER2. My project aims to identify DipG analogues that have a stronger binding affinity to HSP90 (as well as other potential heat shock proteins) that could effectively promote ER/HER2 degradation at low concentrations.

Project 2: Effects of exogenous E2 and P4 on tumor development in male rats (Male Breast Cancer)

Male breast cancer (MBC) accounts for 1% of all breast cancer cases. Despite all the research explored in female breast cancer, there is not much known about MBC. Specifically, there is a knowledge gap of how estrogen and progesterone play a role in tumor formation and cancer progression in males. My project aims to elucidate how pregnancy-levels of estrogen and progesterone in male ACI and Enhx rat strains contribute to the development of mammary (or other tissue) tumor growth. I would like to isolate cells from these tumors and develop cell lines

that would be publicly available. I would also like to explore how androgens, such as testosterone, may play a protective role in MBC formation. This research would help fill a substantial knowledge gap in the increasingly important field of male breast cancer.

