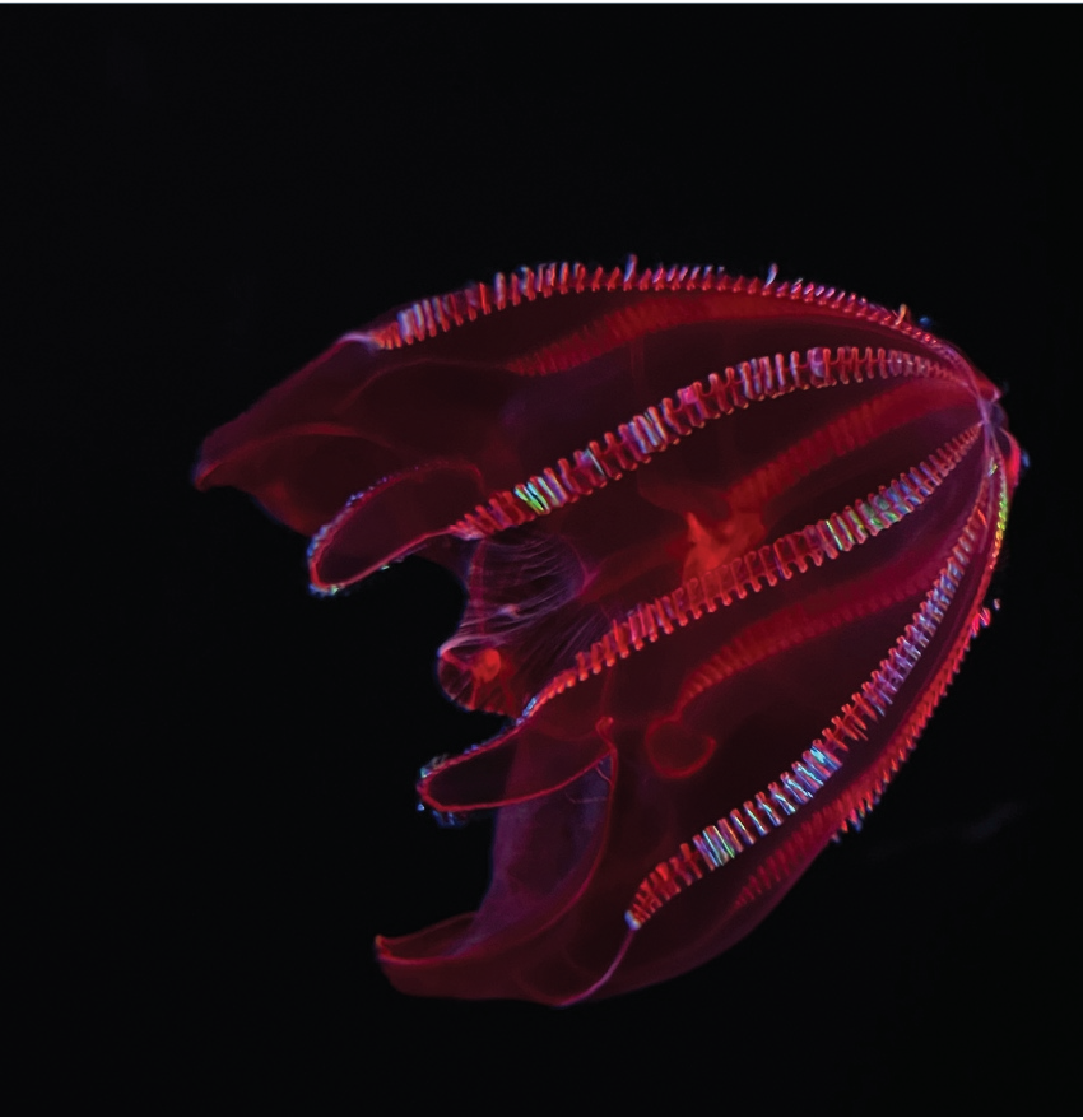
Berkeley College of Letters & Science

SPRING 2024

DIVISION OF BIOLOGICAL SCIENCES



Letter from the Dean

Dear Friend,

I will conclude leading the Division of Biological Sciences in June. It has been my great honor to serve as dean since 2016 — a highlight of my 45 years on this faculty.

Berkeley is an extraordinary place for biological research. A public university to me is where the frontiers of research are expanded by a hunger for uncovering the unknown, and where education enables us to appreciate where we have been and where we are heading. Our morning star has always been fostering basic, curiosity-driven research that often leads to unanticipated discoveries. It's a necessary prerequisite to developing transformative technologies that impact our lives, such as cancer immunotherapy and CRISPR genome editing, which emerged from Berkeley biology labs.

As dean, I have worked to expand opportunity for broader participation in basic research. Advancing diversity, equity, inclusion, and belonging is critical both to the success and preeminence of our research enterprise. In 2018, I helped develop the Life Sciences Initiative to advance faculty diversity at all UC campuses by creating a template for more inclusive outreach to and recruitment of young scholars.

I am gratified to have launched the STEM Excellence through Equity and Diversity (SEED) Scholars Honors Program that has so far recruited four cohorts of talented high school students to pursue scientific and technical studies at Berkeley.

Guiding the future evolution of the biosciences at Berkeley has been another priority. I'm pleased that we have established, for example, a master's program in biotechnology, a new departmental division focused on molecular therapeutics, and, most recently, a dedicated Department of Neuroscience.

I will leave my post confident in the collective strength and wisdom of our biological sciences community to maintain excellence in our education and research for the foreseeable future. Finally, I thank the division's staff for their invaluable advice and support throughout my appointment, and I thank you for continuing your interest in and support of the life sciences at Berkeley. Fiat Lux!

Warmest Regards,

Michael Botchan, Ph.D.
Dean of Biological Sciences

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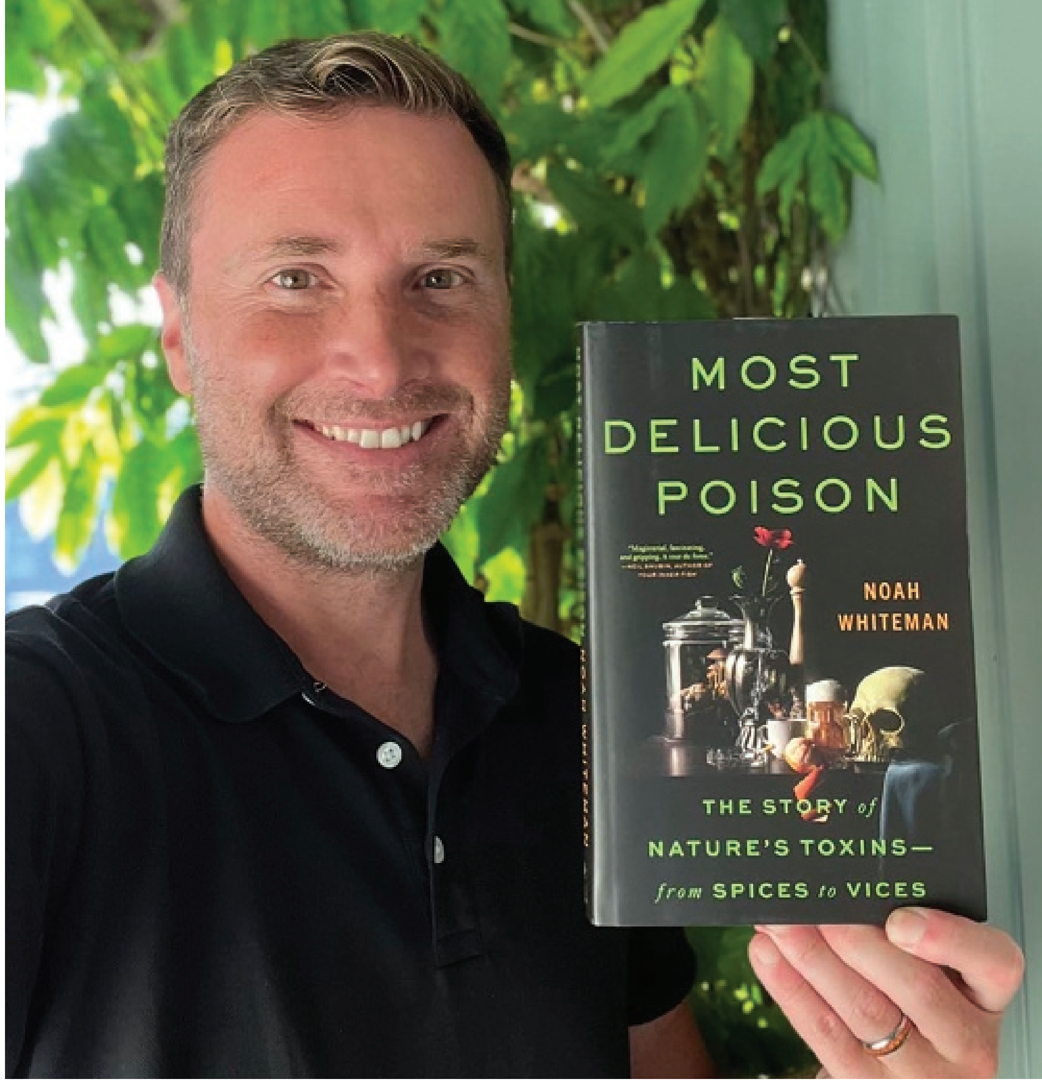
COVER PHOTO: First discovered in 1979, the bloody-belly comb jelly (*Lampocteis cruentiventer*) lives at ocean depths. Research by Berkeley biologist Daniel Rokhsar concluded comb jellies also reside deep on the tree of life and originated earlier than all other animals. (See page 8.) Photo credit: Shutterstock

TOXIC Temptations

GENETICIST AND EVOLUTIONARY BIOLOGIST Noah Whiteman wears many hats on campus. He holds appointments as a professor in the departments of Integrative Biology and Molecular & Cell Biology. He recently became faculty director of the Essig Museum of Entomology. Other research affiliations include the University and Jepson Herbaria, the Museum of Vertebrate Zoology, the Helen Wills Neuroscience Institute, and the Center for Computational Biology.



Author and Professor Noah Whiteman with his book

In October, Whiteman added the hat of being an author. His book *Most Delicious Poison: The Story of Nature's Toxins — From Spices to Vices* takes readers on an interdisciplinary tour through the risky realm of plant, fungal, and animal biotoxins and their use and abuse by people. Whiteman taught a first-year seminar on the subject this spring.

The book is an intellectual extension of research in the Whiteman Lab, which focuses on what he calls "the ancient battle between plants and the animals that eat them." For instance, experiments with CRISPR-edited fruit flies revealed how the monarch butterfly resists and repurposes toxins made by milkweed, their preferred plant food and host. Consumed by caterpillars, the toxins shield adult butterflies from predatory birds during their epic migration through North America.

Although not trained as a chemist, Whiteman is clearly intrigued by nature's chemical ingenuity. *Most Delicious Poison* covers a fair amount of organic chemistry, and artwork by Julie Johnson incorporates the chemical structures of various toxins. Whiteman's wide-ranging curiosity leads him into anthropology, botany, history, and other fields of inquiry to illuminate our complicated relationships with natural toxins. Among many excursions, he explores the chemicals contained in several spices (capsaicin, cinnamon, nutmeg, and pepper), narcotics (cocaine, methamphetamine, opium), psychedelics (ayahuasca, psilocybin), medicines (aspirin, digoxin, scopalomine) and, of course, caffeine.

A takeaway lesson from the book, writes Whiteman, is that, "Plants have evolved to produce diverse chemicals that manipulate animal brains and brawn to their own ends, whether to keep us away or to draw us in. In turn, we have turned the tables ourselves and can tap into these chemicals as medicines and for other purposes."

While we have benefitted from this co-evolutionary arms race, our reliance, and sometimes overreliance, on these toxins also means we must balance along "a knife's edge between healing and harm." A recurring example in *Most Delicious Poison* involves Whiteman's father. An amateur naturalist, his passion for natural history propelled his son's academic pursuits. But he succumbed to alcohol use disorder as Noah's butterfly research achieved breakthrough results. Through writing this book, Whiteman sought to reconcile his personal and professional journeys.

"The moral of this story," Whiteman says, "is that plants evolved this stuff not for us but because they want to live, too."

Paving the Way for Future Ph.D.s

Douglas Fambrough

DOUG FAMBROUGH, YOU MIGHT SAY, WAS BORN INTO BIOLOGY. RAISED by a biophysicist father and high school biology teacher mother, he was immersed in the living world at all levels. So, it was natural that he studied biology in college.

Fambrough noticed that several of his Cornell professors shared the same credential: a Berkeley Ph.D. That drew his attention to Berkeley's unparalleled group of researchers in fruitfly genetics, including Corey Goodman and Gerry Rubin. During a campus visit, he was also drawn to the open, collaborative lab culture. It became an easy decision; Berkeley was where Fambrough would earn his own doctoral degree.

"Corey's lab was a hotbed of world-class work on an interesting problem — developmental neurobiology — using cutting-edge *Drosophila* genetic tools. I loved the intensity," Fambrough recalls.

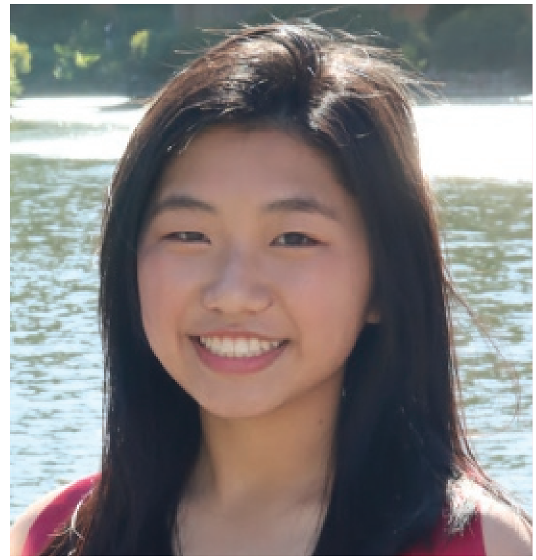
Now, he has established The Douglas M. Fambrough III, Ph.D. 1996 Fellowship to support a graduate student in the Department of Molecular & Cell Biology (MCB). In addition to the eponymous fellowship, Fambrough supports the department's needs with an unrestricted annual gift. He says, "I want MCB to remain the thriving community it was for me and continues to be."

Berkeley and the Bay Area kindled Fambrough's interest in biotech entrepreneurship. He learned by observing mentors Goodman and Rubin create their company, Exelixis. Following a postdoc with Eric Lander at MIT, working on the groundbreaking Human Genome Project, Fambrough took a position at Boston venture capital firm Oxford Bioscience Partners. He spent the next decade investigating and investing in innovative life science companies.

One of those venture capital investments was Sirna Therapeutics, which was pioneering the use of newly discovered RNA interference (RNAi) technology for drug discovery. As a natural mechanism by which the body blocks protein production by genes, RNAi struck Fambrough as the perfect tool to turn knowledge gleaned from sequencing the human genome into potential disease treatments.

Sirna was acquired by Merck in 2006, and the following year Fambrough co-founded second-generation RNAi company Dicerna Pharmaceuticals, later becoming its president and CEO. With a vision "To maximize the impact of RNAi on medicine," Dicerna sought to optimize this technology and enable simple and safe delivery of disease therapies. When Novo Nordisk acquired the company in 2021, Dicerna had 17 drug development programs underway, both wholly owned and collaborative efforts with big pharma firms. Dicerna's most advanced product, targeting a rare kidney disease, recently received FDA approval for use in patients — a milestone that few biotech companies achieve.

Should the first Fambrough Fellow lean toward entrepreneurship, Doug Fambrough's advice is to pursue top-notch science but not neglect mastering the business side of biotech.



Inspiring Student Scholars

Daphne Situ ’25

DAPHNE WAS AWARDED THE JESSICA WAXMAN Nagle Life Science Scholarship, which supports an undergraduate woman in the Robinson Life Science, Business, and Entrepreneurship (LSBE) program. “As the first in my family to attend a four-year university,” Daphne says, “the scholarship has empowered me to be the best version of myself when approaching my academics.”

Students in LSBE earn two bachelor’s degrees — one in molecular and cell biology and one in business administration.

After arriving at Berkeley, Daphne was uncertain where to direct her interest in biology, but this program has exceeded expectations. Daphne says, “Learning both subjects simultaneously has opened my eyes to a different understanding of the applications of science outside of academia.” She appreciates LSBE’s emphasis on biotechnology and ample opportunities to engage with fellow students, faculty, and staff.

Daphne currently envisions a career in the biotech industry but also enjoys pursuing basic research. Having participated last spring in the Harland Lab’s Research Preparation and Resilience Program, a bench skills bootcamp, Daphne returned to that lab to continue studying neural development in the frog *Xenopus*.

Inspired by meeting Jessica Nagle and learning about the donor’s passion to elevate women in STEM fields, Daphne aspires someday to support another student’s educational journey.

Simran Bawa

TO PURSUE HER RESEARCH IN THE LAB OF Professor of Integrative Biology Caroline Williams, Simran earned a coveted fellowship as a Shurl and Kay Curci Foundation Ph.D. Scholar, which provides funding for new graduate students.

“Being a Curci Scholar,” says Simran, “has led me to be more proactive in my research.” For example, she was able to prepare and present a poster about her past two years’ of data at the recent annual meeting of the Society for Integrative and Comparative Biology.

Simran had already spent a year as staff manager of the Williams Lab, learning all about its research focus on how insects develop and respond to environmental change. While assisting summer field work with grasshoppers in Colorado’s Rocky Mountains, she says, “I fell in love with the system and my team” — and applied for graduate school last year.

Simran’s dissertation work will bring her back to the Rockies to investigate how climate change comparatively affects the energetics of *Melanoplus boulderensis*, an endemic grasshopper, and wider-ranging species *M. sanguinipes*, which live at different elevations. With the aid of museum specimens, Simran aims to forecast how increasing temperatures could constrain the future physiology of each species.

Nuñez Lab Advances CRISPR and Community

JAMES NUÑEZ IS A RISING STAR IN EPIGENETICS, WHICH STUDIES HOW small chemical modifications on DNA are associated with human health and disease. Nuñez, an assistant professor in UC Berkeley's Department of Molecular & Cell Biology, shows so much promise that the Howard Hughes Medical Institute and Chan Zuckerberg Biohub — two of the largest biomedical funders in the country — contributed to his lab's launch.

Yet despite all his professional accomplishments, Nuñez is blown away by his students at Berkeley. Even his undergraduates have done amazing things by the time they arrive on campus.

"I could not have gotten into here as an undergraduate," says Nuñez, laughing. "The talent pool among our students is unbelievable."

Nuñez kindled his interest in biology at the University of Colorado, Denver and successfully applied to Berkeley as a Ph.D. candidate. He landed in Jennifer Doudna's lab in 2012, months before she co-published her landmark paper on CRISPR that eventually earned her a Nobel Prize. Scientists can now make precise cuts in the DNA sequence using the gene-editing tool, leading to breakthrough treatments for diseases ranging from sickle-cell anemia to COVID-19.

Rather than directly modifying genes, epigeneticists like Nuñez alter the chemical environment to cause genes to react in specific ways, a safer strategy that is less likely to result in cell death, according to some researchers. As a postdoctoral scientist at UCSF, Nuñez co-invented CRISPRoff, a tool that can turn off genes causing health issues without needing to change a cell's DNA sequence. If CRISPR is a pair of molecular scissors, CRISPRoff is a light switch.

Nuñez used CRISPRoff to demonstrate it is possible to reduce the potency of a gene associated with Alzheimer's. In addition, scientists are looking into epigenetic methods to lower cholesterol and reverse aging. One promising area Nuñez is monitoring would allow the immune system to prolong its fight against cancer by switching off genes that cause our T-cells to become tired during their fight against tumors.

Since joining Berkeley's faculty in 2021, Nuñez has gained a new perspective on his admittance as a doctoral student.

"One of the best things about Berkeley is that the graduate students here are passionate about making an impact in our world," says Nuñez. "Now that I've been on the admissions process for incoming Ph.D. students, I understand how hard it is to get into this place."

Nowadays, Nuñez receives visits from established colleagues seeking advice. Nuñez understands the value of collaboration from his experience with group lab experiments. Rithu Pattali, a graduate student with a joint appointment in the Nuñez and Doudna labs, sees a lot of similarities between the two professors.

"They've achieved a lot in their careers, and they're both so humble and easy to talk to," says Pattali. "Both of them care a lot about their students' development."

Assistant Professor James Nuñez, at right, and lab members

The Nuñez Lab bucks the demographic trend of many scientific research labs, in that it has achieved gender parity and a majority of its researchers are people of color. Nuñez credits these traits to deliberately recruiting people with different backgrounds and approaches.

"Part of why my lab has been so vibrant is because of our diversity," says Nuñez. "It's become an open, safe space where people can ask what some people may consider dumb questions. We minimize any of that hesitation where people are learning. They're not going to be judged."

Others have noticed. Pattali said the lab is an increasingly popular destination for graduate student rotations. Even students from other labs come to socialize and talk about science on the Nuñez Lab's couches.

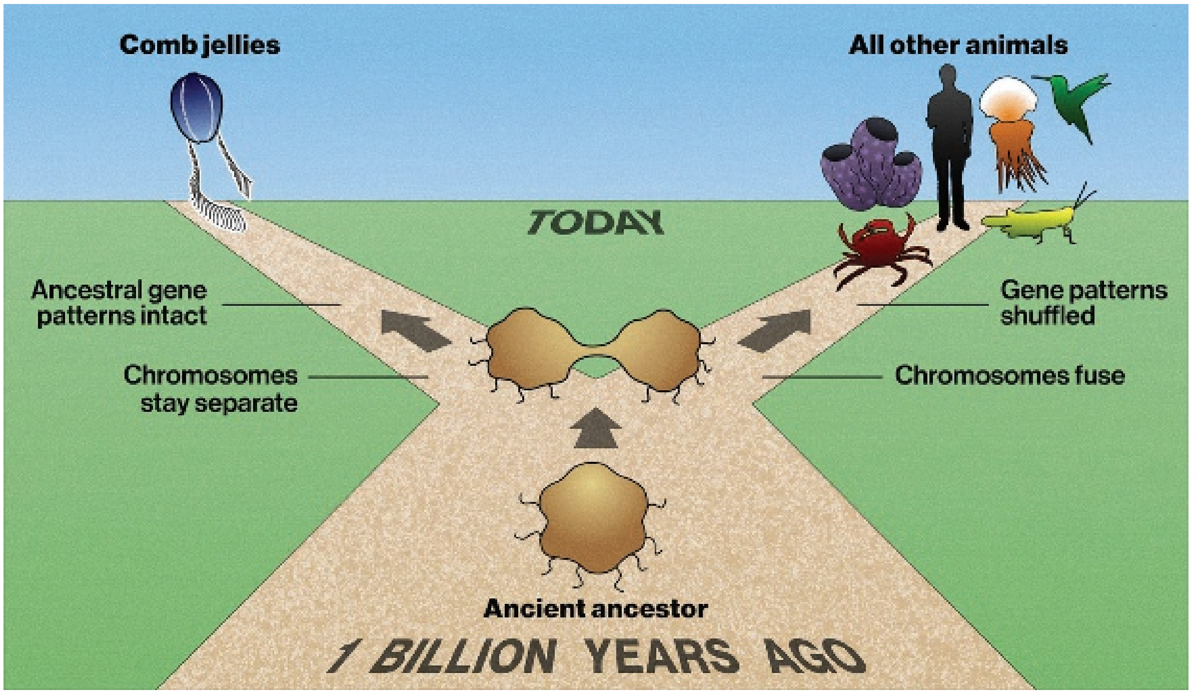
"A lot of people come to our lab; a lot of those people are people of color," says Izaiah Ornelas, a graduate student whose interest in epigenetics was sparked by observing differences with his twin brother. "It's a space where we feel really comfortable."

With his prominence in the CRISPR world, Nuñez had many options for faculty positions. Nuñez was on the job market during the height of the pandemic, which allowed him to think seriously about what he truly wanted out of academia.

"What it ended up being was community," says Nuñez. "I really enjoyed my time at Berkeley as a student. I felt like people here were generally happy with the research they were doing, and every lab here is a leader in their field."

Nunez smiled as he considered his time as a faculty member. "Everyone wants you to succeed. This is really an incredible place to be."

A Twist to Early Animal Evolution



Around 700 million years ago, comb jellies split from the evolutionary branch with all other animals.
Credit: Madeline Go/ MBARI

DANIEL ROKHSAR ABIDES BY A QUOTE FROM science fiction author Ted Chiang: "The past has left its traces on the world, and we only have to know how to read them." A professor in the departments of Molecular & Cell Biology and Physics, Rokhsar's research combines computational genomic analysis with comparative developmental biology to infer how animals evolved approximately 700 million years ago.

As he puts it, "There was a time in the oceans where there was nothing we would recognize as an animal. And then, millions of years later, there were animals. How did that transition happen?"

In an April 2023 issue of *Nature*, Rokhsar and colleagues from two universities and the Monterey Bay Aquarium Research Institute revealed a partial answer, and resolved an enduring academic debate, by analyzing ancient genetic traces among diverse animal groups.

The research team took on a chicken-and-egg conundrum concerning which of two candidates originated prior to other animals on the tree of life. Did sponges or distant jellyfish relatives known as ctenophores, or comb jellies, come first?

Previous studies relying on DNA sequences reached inconsistent results as to which was the probable ancestor. Superficially, sponges seem the logical choice, since they lack nerves and muscles and settle into a sessile life after their larval stage. Free-swimming comb jellies, in contrast, propel themselves by beating comb-like rows of cilia.

Because DNA sequences can change so much through time, Rokhsar and colleagues tried a different approach: zooming out to the scale of chromosomes, the cellular structures that contain sequences of genes and change at a slower rate. Genes tend to remain linked to the same chromosomes over vast stretches of time and among distantly related organisms.

"If I want to look at these very deep moments in time, I have to look very broadly across a huge swath of organisms, and be able to figure out what it is that they share," says Rokhsar. "Then, I can use that to triangulate back to what their common ancestor was like."

After sequencing the genomes of a comb jelly, a sponge, and three more primitive single-celled organisms that precede the origin of animals, the team compared the organization of genes on different chromosomes for each to determine which branch of animal life first diverged from a common ancestor. What did they find?

Ancestral gene patterns remained uniquely intact on the lineage leading to comb jellies, whereas a shared shuffling of chromosomes occurred among other animal groups, from sponges to vertebrates. The comb jelly's chromosomes lacked five distinctive genetic rearrangements found in the other animal groups, while retaining genetic linkages to chromosomes observed in the three non-animals. "That implies," says Rokhsar, "that the comb jellies must have been the first branch, contrary to the conventional wisdom, which had sponges branching first."

The Better to **EAT WITH**

IT'S A GOOD HABIT TO CHEW FOOD THOROUGHLY. OUR ABILITY TO DO so arises from an evolutionary move that mammals made millions of years ago. They reduced the number of bones down to one comprising each side of the lower jaw and connecting to the cranium. Two other bones found in the ancestral vertebrate jaw shifted position to form part of the mammalian middle ear.

A recent study by Associate Professor of Integrative Biology (IB) Z. Jack Tseng, IB students Sergio Garcia-Lara and Emily Holmes, and colleagues from three other institutions, examined how mammals benefitted from this singular jaw structure. The team analyzed jaw shape and biomechanics across nearly 1,100 vertebrate genera to find out.

A curator at the UC Museum of Paleontology and an undergraduate alum in IB, Tseng hypothesized that the shift to a single lower jaw bone, the dentary (or mandible in humans), allowed mammal jaws to be more versatile in shape, stiffer, and more biomechanically efficient. The conclusions, however, were more complicated.

Mammal jaws do tend to be stiffer than those of non-mammals and can assume a wider variety of shapes. But they are not more mechanically efficient than other vertebrate jaws when in use. Nor did the shift to a single bone initiate faster evolution among mammals. "Mammal jaws are more diverse in shape, yet more constrained in their biomechanical characteristics, than non-mammals," says Tseng.

For reasons that remain unclear, mammals emphasized jaw stiffness over speed, efficiency, and other features. "Stiffness resists forces from all different directions," says Tseng, and this trait became "a signature of the mammal jaw."

Mandibular stiffness may have been a necessary foundation for the wide array of teeth found among living mammals — tools designed for crushing bone, grinding grass, shearing muscle, and other functions. By facilitating a variety of chewing motions and allowing precise occlusion between teeth, that stiff, single lower jaw helped mammals become eaters of just about anything. And that's something to chew on.

Sergio Garcia Lara compares the lower jaw of a whale and a bat.
Photo: Jack Tseng

Probing Plasticity with Psychedelics

ANDREA GOMEZ STUDIES HOW MOLECULAR signals at synapses in the brain help foster flexible behavior. After coming to Berkeley in January 2020 as an assistant professor of molecular

and cell biology, Gomez was forced to flex and adapt her own research. The pandemic cut off access to a colony of transgenic mice she had used for her postdoctoral studies in Switzerland, so Gomez took her curiosity in a new direction.

Coincidentally, the year 2020 also marked the launch of the Berkeley Center for the Science of Psychedelics. While Gomez's research had not focused on such powerful substances, she knew, as she told a group of alumni and donors during a recent tour of her lab, that "Psychedelics — whether they are produced by fungi, animals, or plants — have been used by Indigenous peoples for thousands of years to engage cognitive connection and open pathways to healing."

Of Laguna Pueblo and Chicana background, Gomez integrates Indigenous research paradigms into how her lab proposes scientific questions and honors the cultures that have studied and stewarded psychedelic substances. In seeking the synaptic mechanisms that underlie plasticity — the capacity for neurons to respond by altering the number of synapses or the strength of their connections — the Gomez Lab conducts experiments to explore how some psychedelics seem to enhance neural plasticity and connectivity. They focus this work in the prefrontal cortex, a brain region central to cognitive flexibility.

Consider that the human brain contains some 86 billion neurons, each of which can have tens of thousands of signal inputs and external connections; how does a neuron determine which connections should be adaptable? "Our neurons are built to be plastic," says Gomez. "[W]e believe that there are plasticity-responding signals in our brain that will induce some components for neural flexibility. We think that psychedelics like psilocybin robustly engage this information in the genome."

Gomez's team currently hypothesizes that psychedelics engage plasticity within the brain of mice similarly to what occurs early in development when excitatory neurons mature before inhibitory ones. Essentially, says Gomez, "what we think we are doing in a psychedelic experience...is that we're turning back time."

Beyond the fundamental work to characterize how these molecular pathways become engaged by psychedelics, the Gomez Lab aims to apply what they learn to designing potential therapeutics. Could psychedelic-induced plasticity, for instance, be deployed to counter symptoms of a stroke or neurodegeneration? Says Gomez, "I think that understanding how psychedelics change the brain can give us a window into how we can manipulate the brain in other ways — including how to treat neurological diseases that impact learning and memory."

Additional research in the Gomez Lab focuses on the enteric nervous system (ENS). Sometimes referred to as the body's "second brain," the ENS encompasses about 500 million neurons that line the digestive tract and help to regulate gastric secretion, absorption, and motility. Research in the Gomez Lab is revealing a similar capacity for plasticity in the ENS, when stimulated by psychedelics such as psilocybin.

The effect of psychedelics on gut neurons is more accessible to direct study *in vitro* compared to neurons in the brain, and this nascent arm of her lab's work could shed light on how the two nervous systems communicate and whether they share a mechanism that permits plasticity. As Gomez noted on the Gastronauts podcast, "We know there's a dialogue between the brain and the gut....if you push one, you affect the other."

Maria Cranor at Builders of Berkeley ceremony in 2011

MARIA CRANOR: A PASSION FOR PREHISTORY AND PHILANTHROPY

THE UNIVERSITY LOST A CLOSE FRIEND AND committed advocate with the passing in January 2023 of Maria Cranor, at the age of 76. A pioneering rock climber and outdoor equipment entrepreneur, Cranor re-invented herself mid-career as a physicist and philanthropist.

The San Francisco native and longtime Salt Lake City resident studied anthropology at Berkeley in the late 1960s. Cranor found a passion for the African paleolithic and human evolution in courses taught by renowned archaeologists J. Desmond Clark and Glynn Isaac.

Much later, she honored both professors by endowing graduate fellowships in their names through the Human Evolution Research Center. In 2012, Cranor established the Philip Sandford Boone Chair in Paleontology named for her father, a 1938 Berkeley alumnus.

Boone Chair Charles Marshall, professor of integrative biology, vividly recalls his first meeting with Cranor, who intuitively understood and appreciated his quantitative approach to paleontological research, offering "a flood of insightful questions infused with that raw and incisive enthusiasm." Marshall says, "She knew what true discovery looked like, what it felt and tasted like, and she sought to foster it with that keen intensity."

According to Cranor's niece and alumna Alastair Boone '16, "By her own account, she was transformed by her time at Berkeley, and left the university intellectually challenged, energized, and committed to progressive politics."

From Berkeley, Cranor joined the mostly male ranks of intrepid rock climbers at Yosemite and Joshua Tree. Her graceful, efficient technique inspired other women climbers to excel in the sport. After working for an equipment manufacturer started by legendary mountaineer Yvon Chouinard, Cranor and a colleague co-founded their own outdoor recreation company, Black Diamond Equipment. Black Diamond became a leading manufacturer of rock climbing, mountaineering, and backcountry skiing gear, and Cranor was its vice president of marketing and creative director.

In 1996, at age 50, Cranor returned to academia at the University of Utah, completing dual degrees in physics and psychology. Recalls physicist Ryan Behunin, a friend and fellow Utah undergraduate, "I was always astounded by her breadth of interests, the depth she explored them, and the energy she committed to learning new things." She commenced graduate studies in astrophysics at Utah, then became a lecturer who developed innovative, popular courses, including one on technical communication and scientific judgment.

Cranor maintained close ties to Berkeley, serving on the College of Letters & Science Advisory Board from 2016-2020 and spending four terms on the UC Berkeley Foundation Board of Trustees. In addition to philanthropic support for paleontology, paleoanthropology, and astronomy, Cranor contributed to such student-centered efforts as the Undocumented Student Program and the Basic Needs Center.

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Basic Science Continues to Light the Way

Having completed its eighth consecutive season, the virtual event series "Basic Science Lights the Way" continues to bring large audiences together over Zoom to learn about groundbreaking research at UC Berkeley. Our Spring 2024 offerings included: What Black Holes Reveal About Gravity's Strangest Properties, Berkeley Science Breakthroughs in the News, The Science of Teaching, and From Neanderthals to Plants to Pathogens: Human Co-evolution with Other Organisms.

Featuring some of Berkeley's most renowned scientists, as well as rising-star faculty and researchers, "Basic Science Lights the Way" has something for everyone who believes in the importance of fundamental scientific research. To register for upcoming events or watch videos of all previous sessions, please visit basicscience.berkeley.edu.

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