DIVISION OF BIOLOGICAL SCIENCES

Photo: Johnny Gan Chong

To read an interview with Dean Richard Harland, go to: https://ls.berkeley.edu/news/biological-sciences-have-new-leader-richard-harland-read-his-first-interview-dean.

If you need any of these materials in an alternative format, including electronic, large print, or braille, please contact Melanie VandenBerghe at mevanden@berkeley.edu to make a request. Please allow 7-10 days in cases of brailled material requests.

COVER PHOTO: The endangered mountain gorilla is one of the primate species studied by incoming faculty member Tierra Smiley Evans, a wildlife veterinarian and expert on emerging zoonotic diseases. (See page 6.) Photo credit: Courtesy of Tierra Smiley Evans

Letter from the Dean

Dear Friend,

At the end of June, our esteemed dean and colleague, Michael Botchan, began his well-deserved retirement. As senior associate dean, I worked closely with Mike for many years in service of the Division of Biological Sciences. Now, as dean, I am committed to partnering with our leadership team to ensure our steadfast support of our excellent students, faculty, staff, and community of alums and friends.

My immediate priorities align with former dean Botchan's: better use of our lab space, more support for our graduate students, and improved representation of people of all backgrounds. Though we are a complex, high-performing institution, our formula for success is quite simple. We recruit the best people, provide stellar facilities, purchase cutting-edge equipment, and provide an environment where everyone can thrive.

Of course, all that is easier said than done, and we wouldn't be able to prosper as a division without supporters like you. I am delighted to provide you with a look at the fascinating research and compelling scientists arising from our division. No matter where you landed after college, I hope you agree with me that no place compares to UC Berkeley.

As biologists, we know that life on Earth is always changing, and our division must adapt as well to remain at the top of our field. This year, our new Department of Neuroscience will accept undergraduate majors for the first time. Also of note, our new Division of Molecular Therapeutics is launching innovative initiatives to accelerate drug discovery. We are investing in breakthrough research into CRISPR-based treatments for genetic diseases, psychedelic therapeutics for brain disorders, and ancient DNA's revelations about the origins of life. We do all this while maintaining our focus on the greater good, which drives our research enterprise.

I hope the stories we are sharing in this newsletter make you as proud as I am of UC Berkeley's excellence. Thank you for your ongoing support of our world-class research and education.

Fiat Lux,

Richard Harland
Dean of Biological Sciences
C.H. Li Distinguished Professor of Molecular and Cell Biology

Empowering Neuroscience's NEXT GENERATION

WITH NEW INNOVATIONS AND INSIGHTS INTO the human body and its complex and interrelated organ systems emerging all the time, now is an opportune moment for deeper understanding of ourselves. Yet one piece of our biological puzzle remains, in many ways, enigmatic: the human brain. With an initial $200,000 gift, and a promise of future philanthropy, Rick and Carole Horwitz '69 aim to seed the next generation of neuroscience researchers, by supporting talented undergraduate neuroscience students as they perform research in the laboratories of top faculty experts and pursue answers to the brain's mysteries. Their gift establishes the Stent Neuroscience Research Scholars and Faculty Scholars Fund to help bring a new generation of highly talented researchers into the field of neuroscience.

The couple has deep roots at Cal. Carole graduated from Berkeley, and Rick was a postdoctoral researcher in magnetic resonance from 1970–1973 in the lab of Melvin Calvin and Mel Klein. Rick went on to become the inaugural executive director of the Allen Institute for Cell Science.

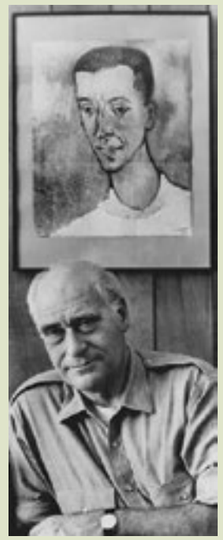
"We both feel a deep affinity for Berkeley given our experiences there and how they shaped not only who we are and what we learned but the trajectories of our lives," said the couple, "so we felt compelled to pay that influence forward for tomorrow's leaders."

Their gift honors the late Professor Emeritus of Molecular and Cell Biology Gunther Stent, a pioneer of molecular biology and visionary neuroscientist who worked at the intersection of molecular biology, developmental biology, and neuroscience to understand how the nervous system develops and generates behavior. Stent's time at Berkeley spanned decades and included being a founder and the inaugural chair, from 1987-1992, of the Department of Molecular and Cell Biology. Said Rick, "Stent was an unusually inspiring scholar and teacher who introduced me to the newly emerging field of neuroscience in the early '70s. We are thrilled to name something after him."

The gift will support passionate, talented undergraduates (known as Stent Research Scholars) who are eager to immerse themselves in a research experience in the lab of top Neuroscience Department faculty (known as Stent Faculty Scholars), who will mentor and guide the students' work. Applications for the inaugural year of the program were reviewed in August. The Department of Neuroscience recently named the first two recipients: Stent Research Scholar Emma Bi, who will conduct research with Stent Faculty Scholar Yang Dan, and Stent Research Scholar Michael Tanios, who will be mentored by Stent Faculty Scholar Stephan Lammel.

Professor and department chair Dan Feldman, who holds the Coates Family Endowed Chair in Neuroscience, also expressed gratitude and excitement for this new initiative. "Our undergraduate students are some of the most brilliant learners anywhere and are eager to leave their mark on neuroscience," said Feldman. "Rick and Carole's gift will allow us to give undergraduates an opportunity to engage with high-level topics and research practices, an invaluable piece of their academic journey as they continue on to grad school or into the professional sphere."

Gunther Stent



CRISPR's Curious Origin Makes the Case for BASIC RESEARCH

SIX THOUSAND MILES FROM THE SLEEK BERKELEY HEADQUARTERS OF THE Innovative Genomics Institute lie the Spanish salt marshes where, in 1992, Francisco Mojica identified repeating DNA sequences he later named CRISPR. Mojica was a microbiologist interested in how the marsh's peculiar, single-celled microorganisms could grow in high salinity. From those humble origins, CRISPR (short for clustered regularly interspaced short palindromic repeats) ignited a globetrotting journey of scientific discovery that led to Nobel Prizes and a biotech revolution.

Mojica was not the first person to notice these repeating sequences; Yoshizumi Ishino observed them in 1986 in the bacteria *E. coli*. However, Mojica was one of the most persistent CRISPR pioneers. Scientists ridiculed his findings. Government agencies denied his grant applications. Prominent journals rejected his submissions. But Mojica kept searching for answers.

Jennifer Doudna with CRISPR-Cas9 model

In 2005, Mojica and other scientists realized that the spacer sequences between the repeated ones resembled virus sequences, which soon led to an exciting hypothesis: CRISPR was an adaptive immune system that works similarly to RNA interference, or RNAi.

The CRISPR experiments caught the eye of Jillian Banfield, a UC Berkeley professor who marveled at the possibilities and hoped to collaborate with another principal investigator. She typed "RNAi and UC Berkeley" into Google and wrote to the person who appeared in the first result: Jennifer Doudna.

"At the time, neither of us were thinking about the applications of these systems," said Banfield. "We were just amazed to think that bacteria may have an interference system that was somewhat analogous to that of humans."

"All I knew at the beginning was that CRISPR was interesting, and we simply didn't know enough about how it worked in nature," said Doudna. "It was pure curiosity-driven research, with no notion that it would later develop into a practical tool. It was only by collaborating with Emmanuelle Charpentier to study how CRISPR-Cas9 functioned that we were able to discover that it was something that could be harnessed and reprogrammed to cut DNA at specific places. That was an incredible realization."

That revelation led Doudna to receive the 2020 Nobel Prize in Chemistry and launch the Innovative Genomics Institute (IGI) in 2015. IGI works to build genome editing tools, fight climate change, and cure diseases. Doudna still collaborates with Banfield, who serves as IGI's director of microbiology, and both remain on Berkeley's faculty.

Nobody could have predicted how this scientific expedition would unfold, not even the researchers themselves. Their breakthroughs were guided by a spirit of inquiry into how natural systems work. To Richard Harland, the dean of UC Berkeley's Division of Biological Sciences, that pursuit of knowledge is the point.

"The outcome of basic science is unpredictable," said Harland. "Sometimes, basic science will discover new principles and mechanisms that can be harnessed for the public good. Applications will come later, and their impact is not always obvious at the start.

Salines de Santa Pola, Spain, where CRISPR sequences of DNA were discovered in 1992

In this case, the impact of guided DNA editing was immediate. However, the goal of understanding how life in all its glorious variety works is what drives so many researchers at Berkeley, and it's why we have excelled in the sciences for decades."

In addition to the studies of early CRISPR pioneers, Doudna said that the work she does today could not happen without other fundamental research findings, including Sanger sequencing, polymerase chain reaction (PCR) techniques, and understanding the structure of DNA. Each research paper acts as a building block for the scientist who follows.

"Translational research doesn't exist without basic science. It's like trying to build a house without a foundation," said Doudna.

"With CRISPR, I never set out to discover a genome-editing tool," she continued. "So many discoveries throughout history have the same story. If we don't support curiosity-driven research, then we won't develop the next fundamental discovery that can be applied to real-world problems."

ADDITIONAL FOUNDATIONAL BERKELEY FINDINGS

- Telomerase: In 1984, Elizabeth Blackburn and Carol Greider identified telomerase, an enzyme that promotes cell division and growth, pointing to potential treatments for cancer and aging.
- Brain census: In 2021, Berkeley neuroscientists helped map brain cell types in the primary motor cortex, part of a national effort on the scale of the Human Genome Project to learn how neural networks work.
- Evolutionary origins: In 2023, Daniel Rokhsar's team used a novel approach based on chromosome structure to identify comb jellies as the first lineage to branch off from the animal tree.

TRACKING THREATS from Emerging Diseases

MPOX. AVIAN FLU. SARS-COV-2. RECENT HEADLINES ABOUT VIRUSES THAT evolved in animals and pose risks to people underscore how our health is intertwined with that of wildlife and their habitat. "Most of these diseases that cause serious infections in humans originally came from animals," said wildlife veterinarian Tierra Smiley Evans. This fact motivates her to seek a deep understanding of that interconnection and the conditions whereby an infectious disease transfers from another species to us.

Tierra Smiley Evans in the field

For the past 15 years, Smiley Evans has pursued viral pathogens from a base at UC Davis's One Health Institute, where she is a research faculty member and chief veterinary and scientific officer with Gorilla Doctors. In January, she joins the UC Berkeley faculty in a new joint appointment with the Department of Integrative Biology and the School of Public Health, focusing on emerging diseases in wildlife, or zoonoses, that could pose broader threats.

"It just seemed like such a perfect fit," said Smiley Evans about the opportunity and its dual responsibilities. "I've always felt that my research has really bridged those two areas [of wildlife biology and public health]."

While completing her D.V.M. degree at Tufts University's School of Veterinary Medicine, Smiley Evans spent summers on disease-related research projects in Nepal and then Rwanda. There, she began her relationship with Gorilla Doctors, a partnership between the Mountain Gorilla Veterinary Project, Inc. and the Karen C. Drayer Wildlife Health Center at UC Davis. The group provides personalized health care for mountain gorillas and Grauer's gorillas in Rwanda, Uganda, and Democratic Republic of Congo.

Smiley Evans leapt at an opportunity to earn her Ph.D. at UC Davis while working with Gorilla Doctors and studying her favorite animal. As part of those studies, she developed a clever method to monitor the health of individual apes and monkeys by collecting chewed leaves or fruit they had dropped while foraging, and showing that traces of saliva on these samples could be used to detect viral infections and help identify individuals.

An outbreak of Ebola virus is a constant concern among those who care for gorillas. Smiley Evans said, "They're susceptible to it, just like we are." She strives to understand Ebola's ecology, including pinpointing the main wildlife host — bats being a prime suspect — and determining the diversity of other viral spillover hosts among forest mammals that humans also encounter. Ensuring healthy populations of people living in proximity to gorillas is another important aspect of this work.

Her career has also taken Smiley Evans to Myanmar, where she conducted postdoctoral research among loggers using elephants to harvest teak trees and who hunt wildlife for subsistence and commercial uses. She has returned to the country to study coronaviruses in local bat populations and assess whether the activities of people living at the forest's edge put them at heightened risk of disease spillover.

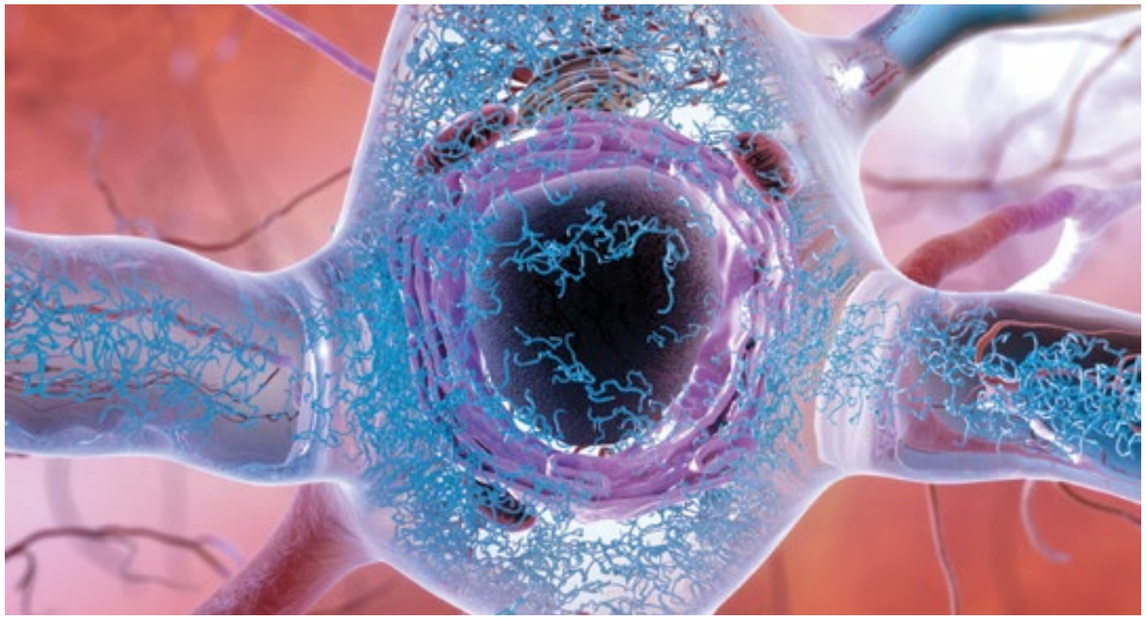
"Myanmar's a very challenging but fascinating place to work," she said, "because it's one of the last huge strongholds of forest biodiversity in Asia." Smiley Evans demonstrated this recently with an encouraging discovery. The skywalker gibbon was first described in 2017 with a known population of just 150 individuals in Yunnan, China. By recording dawn duets between male and female gibbons, photographing several individuals, and obtaining gibbon DNA from a chewed plant specimen, Smiley Evans and her colleagues confirmed the endangered ape's existence — and greater abundance — in Myanmar. Most of the Myanmar gibbons live outside protected areas, providing an opportunity for forest conservation.

This year, she's analyzing the first phase of research as a principal investigator with the EpiCenter for Emerging Infectious Disease Intelligence, part of a National Institutes of Health-funded network of 10 centers studying global zoonotic hotspots. The EpiCenter focuses on emerging diseases in Peru and Uganda, with Smiley Evans leading the African effort in disease surveillance among people, primates, and other wildlife along a gradient from pristine to more disturbed forest, in order to explore whether different environments affect disease transmission.

In her new role, Smiley Evans looks forward to teaching Berkeley students the skills to conduct research in limited-resource field labs and to collaborate productively with international partners. She will maintain her Davis affiliations and hopes to strengthen ties between the two universities, such as developing an academic pathway for Berkeley undergraduates to prepare for studying veterinary medicine at Davis's esteemed school.

Mountain gorillas in Volcanoes National Park, Rwanda

STRESSED CELLS Linked to Brain Disease



An illustration of a brain cell in a person with Alzheimer's disease, showing the accumulation and clumping of tau proteins (blue squiggles) in the cytoplasm of brain cells. Protein clumps, also known as aggregates, are thought to lead to cell death and dementia. New research suggests that such clumps may not cause brain cell death directly, but rather throw the cell's response to stress off balance so that it never gets turned off.

Courtesy of the National Institute on Aging, National Institutes of Health

MANY NEURODEGENERATIVE DISEASES, SUCH AS ALZHEIMER'S AND Parkinson's diseases, are characterized by the accumulation of protein clumps, or aggregates, in the brain. This correlation led scientists to assume that the clumps kill brain cells. The search for treatments that break up and remove these tangled proteins has had little success, however.

But a new discovery by UC Berkeley researchers suggests that it's the body's failure to turn off brain cells' stress response that kills the cells. In a study published in the journal *Nature*, the researchers reported that cells that mimic early-onset dementia can be saved by delivering a drug that forces the stress response to shut down.

The finding could offer clinicians another option for treating neurodegenerative diseases caused by mutations in the protein that switches off the cellular stress response. In addition, lead researcher Michael Rapé noted that other neurodegenerative diseases — including Mohr-Tranebjærg syndrome, childhood ataxia, and Leigh syndrome — are also characterized by stress responses in overdrive and have symptoms similar to those of early-onset dementia.

The researchers found that stress responses need to be turned off once a brain cell has successfully addressed a difficult situation. Rapé explained this finding in simple terms: You not only need to clean up your room, but also turn out the light before going to bed. If you don't turn off the light, you can't fall asleep.

In their paper, Rapé and his colleagues describe a very large protein complex they discovered and called SIFI (SIlencing Factor of the Integrated stress response). This machine serves two purposes: It cleans up aggregates and, afterward, turns off the stress response signaling triggered by the aggregated proteins.

"When there are aggregates around, SIFI is diverted from the stress response, and the signaling continues," said Rapé, head of the new Division of Molecular Therapeutics in the Department of Molecular and Cell Biology. "SIFI tries to clean up the mess first, so when you have an aggregate in the cell, the light is always on. If the light is always on, stress signaling is always on, and the cell will die."

"That's a problem," continued Rapé, "but that means that you can treat these dozen or so neurodegenerative diseases that keep their stress responses on with an inhibitor that turns off the light. You don't have to worry about completely getting rid of large aggregates, which changes how we think about treating neurodegenerative diseases and, most importantly, makes this doable."

Rapé studies the role of ubiquitin — a ubiquitous protein in the body that targets proteins for degradation — in regulating normal and disease processes in humans. In 2017, he discovered that a protein called UBR4 assembles a specific ubiquitin signal that was required for the elimination of proteins that tend to aggregate inside cells.

Only later did other researchers find that mutations in UBR4 are found in some inherited types of neurodegeneration. This discovery led Rapé, graduate student Andrew Ingersoll, and postdoctoral fellows Diane Haakonsen, Michael Heider, and Samuel Witus — all of UC Berkeley — to team up with colleagues at Stanford University to find out how UBR4 causes these diseases.

They found that UBR4 is actually part of the much larger protein complex, SIFI, which is needed when a cell can't sort proteins into its mitochondria. Such proteins that end up at the wrong location in cells tend to clump.

The core substrates of the SIFI complex are two proteins, one of which senses when proteins don't make it into mitochondria. That protein detects that something is wrong, and it then activates a kinase that shuts down most new protein synthesis, giving the cell time to correct the protein locations.

The fact that a drug can turn off the response and rescue brain cells bodes well for the development of treatments for potentially many neurodegenerative diseases. Already, another stress response inhibitor, a drug called ISRIB discovered at UCSF in 2013, has been shown to improve memory in mice and reduce age-related cognitive decline.

"That means there is the prospect that by manipulating stress silencing, you might target other neurodegenerative diseases, as well," Rapé said. "At the very least, it's another way we could help patients with these diseases. In the best possible way, I think it will change how we treat neurodegenerative diseases."

Rapé, already a co-founder of two startups, Nurix Therapeutics Inc. and Lyterian Therapeutics, is now looking to develop therapies to silence the stress response while maintaining the cell's cleanup of protein aggregates.

Michael Rapé

Student Scholars
GAIN CRUCIAL SUPPORT

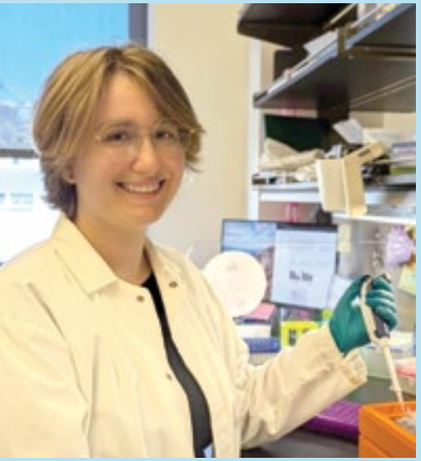
Dawson Chung ’26

DAWSON CHUNG APPRECIATES THE opportunity to contribute to Dean and Professor Richard Harland’s research team. The senior, majoring in molecular and cell biology, came to Berkeley after attending Chabot College in his hometown of Hayward, California.

Thanks to the generosity of Rebecca and Ronald Harris-Warrick, Chung participated in the Morgan and Marjorie R. Harris Scholars Program. After gaining research skills, he was one of three young scholars placed in Berkeley laboratories as Harris Fellows this summer.

“It is hard to explain how much this opportunity to work in a research lab means to me,” Chung said. “I came in as a transfer student with practically no research experience. Through the research preparation program, I was able to build connections and get some research experience that would allow me to join a research lab.”

Chung continues to assist in Harland’s laboratory, which studies early vertebrate development at the molecular level, by applying the techniques he learned to working with frog embryonic tissues. He credits Harris Fellows mentor and postdoctoral student Marta Truchado-Garcia with helping him become a productive team member. Chung has enjoyed biology since high school, but being a Harris Fellow boosted his confidence and has motivated him to pursue a graduate degree and possible academic career.



Sam Rider

MOLECULAR AND CELL BIOLOGY PH.D. STUDENT Sam Rider developed a passion for viruses during her first year at Berkeley. Rider is the inaugural recipient of the Dr. Saul and Gordon Kit Fellowship for promising graduate students pursuing animal virology. Gordon Kit created the fellowship in memory of his father, Saul, who earned his bachelor’s in biochemistry in 1948 and his Ph.D. in 1951 from Berkeley.

“I greatly admire and am grateful for Gordon’s support of our work as virologists,” Rider said. “Science is so exciting to witness in real time, and I would deeply value the chance to show Gordon our lab and the work we do.”

In Professor Britt Glaunsinger’s laboratory, Rider studies gammaherpesviruses to learn how increases in RNA decay decrease host transcription. The lab’s research could advance understanding of how the RNA life cycle controls cellular fate, leading to antiviral and viral therapeutic outcomes. After graduation, she plans to pursue a career in academia and scientific policy advising.

Originally from Colorado and Texas, Rider earned bachelor’s degrees in molecular biology and philosophy at the University of Wisconsin, Madison. Time spent playing with a magnifying glass with her grandfather sparked her scientific interest. She said, “I was intrigued by how much I could see even at that small magnification.”

SCIENCE UP CLOSE:
Immersive Field Trips at UC Berkeley

IN THE DIVISION OF BIOLOGICAL SCIENCES, we know that the best way to appreciate and understand science is through firsthand experience. That’s why, over the past few years, we’ve hosted field trips that immerse our community in the vibrant world of research. From the lab to the field, these events foster deeper connections between our alums and friends and the university.

For many of our biologists, nature is their laboratory. The Biological Sciences development team decided that, while we could tell you about their science, why not show you? As Associate Professor of Integrative Biology Seth Finnegan put it, “A drawer of museum specimens can be very interesting, but seeing those fossils in the context of the sedimentary rocks recording the environment in which they lived is much richer experience.”

In June 2023, Professor Finnegan and Integrative Biology Professor Juan Liu a fossil-hunting trip at Capitola Beach, guiding a group of Berkeley alums anc friends through slippery and lush tide teeming with marine life and ancient r Participants discovered the excitemer identifying fossils like shark teeth and bones, learning about the geological c of these archaic creatures.

Our field trips have also brought scier fans to Berkeley’s campus, granting th access to biology labs and walking the through the work that happens there. October 2023, Integrative Biology Prc Noah Whiteman hosted folks in his lat where he studies evolutionary biology and the dual nature of plant toxins and medicines. He taught participants about the local bay laurel tree and its healing properties, leaving the lab to forage for the tree’s nuts on campus, and then demonstrating how to roast and prepare them for eating.

Most recently, in September 2024, we teamed up with the Department of Earth & Planetary Science (EPS) and the Department of Environmental Science, Policy, and Management for a trip to Mount Diablo State Park, titled “Tarantulas and Tectonics.” EPS Professor Francis Macdonald and Ph.D. students in entomology led a unique exploration of nature and Earth history.

geography and geophysics of the iconic landscape. As sunset approached, guests were able to observe the tarantulas native to the area, as their mating season was in full swing. This trip was a prime example of the myriad ways in which Berkeley scientists use California as their laboratory, and served as a wonderful opportunity to open the door to scientific discovery for our community of supporters.

As we plan future field trips, we have an eye on the California redwoods, Point Reyes tide pools, sunflower blooms in Davis, and even the La Brea Tar Pits. The possibilities are expansive, and we look forward to continuing to explore and explain the natural world with you, our alums and friends, through the lens of biological

Tarantula encountered c
Photo cr

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Basic Science Lights the Way Goes Live

This fall we hosted our ninth consecutive season of "Basic Science Lights the Way," continuing to bring our community of alums and friends together over Zoom to learn about foundational research happening on campus. Our virtual lineup this season covered topics from California's ancient fossil record to fluid dynamics to the connections between music, physics, and neuroscience. The appeal of this series keeps expanding, and we reached a milestone this semester by hosting our first live session.

During Homecoming weekend, "Basic Science LIVE! It's Getting Hot in Here: Insights on a Warming World" brought together series alums Bill Boos, Caroline Williams, David Romps, and Dipti Nayak for an on-campus discussion about climate change — specifically the effects of a warming world on microbial systems, plants, animals, and humans. Our faculty represented the departments of Earth & Planetary Science, Integrative Biology, and Molecular & Cell Biology, and shared perspectives from their respective fields. The hour-long moderated discussion was an insightful success, allowing the audience to ask questions and addressing some of the most pressing environmental issues of our time. We look forward to continuing to bring this series in front of new audiences.

You can watch recordings of all Basic Science Lights the Way events, and sign up for future events, at basicscience.berkeley.edu

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