

COLLEGE OF SCIENCE DEPARTMENT OF BIOCHEMISTRY AND BIOPHYSICS

# CATALYST

When basic research unlocks new cures

SPRING 2020



Oregon State  
University

# CATALYST

## Spring 2020

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**On the cover** — Confocal image from Franco Lab (see p. 9) of human glioblastoma U87 cells forming a “tumoroid,” stained for nitrated Hsp90 (red) and mitochondrial cytochrome c oxidase (green). Image taken by Kyle Nguyen.



# From the head

**Elisar Barbar**  
Department Head



**Greetings faculty, students, alumni and friends!** At the start of a new decade, I am honored to take on the leadership of our active, engaging and thriving department. We are committed to changing lives.

I was raised with the belief that education is the road to opportunity and a better life. My childhood and teenage years were shaped by a war caused by ethnic and religious conflict, where I learned to improvise, survive and even thrive in the worst of situations. This has shaped how I approach life, how I approach science, and how I take on responsibilities and deliver.

I am both a champion and a product of diversity. As a woman in a field dominated by men, as an immigrant and daughter of immigrants, I have a talent and desire to work with people of all backgrounds to foster their growth and independence. I bring a fresh perspective to leadership.

For the past 16 years at OSU, I have been fortunate to lead a lab of motivated undergraduate and graduate students who exemplify the true meaning of our lab's motto: "Take risks, insist, and persist." They have helped develop paradigm-shifting discoveries and elevate the lab's reputation to the level we now enjoy. Students in my lab take full advantage of our department's unlimited access to cutting-edge technology including nuclear magnetic resonance instrumentation, electron microscopy, mass spectrometry, X-ray crystallography and fluorescence microscopy.

Under Andy Karplus' skillful leadership, the year has brought remarkable achievements! Congratulations to Ryan Mehl for receiving the Milton Harris Award for Basic Research, and to David Hendrix for being promoted to associate professor and receiving the 2019 University Mentoring and Professional Development Award.

Significant new research funding is allowing us to develop transformative cures for Alzheimer's disease and neurofibromatosis, study gene silencing in chromatin networks, and determine molecular mechanisms for deafness. As always, our undergraduates are making us proud, receiving a Fulbright scholarship, two National Science Foundation Graduate Research Fellowships, and two Goldwater scholarships – all prestigious national awards.

Lastly, this year we have the exciting opportunity to hire two tenure-track positions. These will be in the broad areas of cell and molecular biology and in structural biology. Spread the word.

I look forward to working together to develop the next generation of leaders to solve national and global problems. Your gifts make a difference. Stay in touch and come visit when you are in the area!

## UPCOMING EVENTS

TBD	<i>Kensal Van Holde Symposium</i>	Corvallis
June 22-26, 2020	<i>Computational Biology Summer Camp</i>	Corvallis
July 22-28, 2021	<i>Genetic Code Expansion Workshop</i>	Corvallis

All spring and summer events have been cancelled or postponed due to the coronavirus as we all stay home to save lives.

# Best and brightest

## OUR TALENTED FACULTY



Kate Shay

Mareike Möller

John Ridenour and family

Grace Galles

### Newly onboard

**Kate Shay** joined the department as an instructor and advisor in September 2019. She earned a B.S. in biology from Scripps College in Claremont, California and a Ph.D. in genetics and cell biology from Washington State University, where she researched oncogenes that initiate leukemia and lymphoma. As a research associate at OSU's Linus Pauling Institute, she conducted studies on the molecular mechanisms of aging. Shay loves teaching and helping students to pursue career goals and cultivate lifelong learning in the sciences.

**John Ridenour** and **Mareike Möller** joined the department in 2019 as postdocs in the Freitag Lab.

Ridenour, an Oklahoma native, received an M.S. in plant pathology and a Ph.D. in plant sciences at the University of Arkansas, where he studied the circadian biology of a plant pathogenic fungus. Supported by the National Institute of Food and Agriculture, he

will study how chromatin-mediated gene silencing regulates fungal pathogenesis. John, his wife, Tabby, and their two children are enjoying adventures across Oregon.

Möller received her master's degree in molecular and cellular biology from the University of Marburg, Germany in 2014 and her Ph.D. from the University of Kiel and the Max Planck Institute for Evolutionary Biology in 2018. Her main research focus is how chromatin structure and DNA methylation influence genome stability in plant pathogenic fungi. Her current research at OSU is supported by a German Science Foundation fellowship.

**Grace Galles**, a research assistant in Chris Ahern's lab at the University of Iowa, is a visiting trainee at OSU's Unnatural Protein Facility through April 2020.

### Moving on up

**Elisar Barbar** is our department's new head (see p. 12).

**Zhen Yu** was promoted to senior faculty research assistant of biochemistry and biophysics.

**David Hendrix** was promoted to associate professor of biochemistry and biophysics and electrical engineering and computer science and granted indefinite tenure.

### Well-deserved recognition

**Ryan Mehl** won the Milton Harris Award for Basic Research from the College of Science in recognition of his impactful, internationally recognized basic research in the area of genetic code expansion – using engineered protein synthesis machinery to incorporate novel chemical groups into proteins at pre-specified places.

**David Hendrix** received the 2019 University Mentoring and Professional Development Award, which recognizes those who excel in supporting and encouraging OSU employees. Hendrix is a dedicated mentor to the five



graduate students who work in his lab. His deeply supportive and encouraging mentorship style has attracted a highly diverse team and created a home where students thrive professionally and are supported emotionally. **Hendrix donated the full amount of his award to the OSU STEM Academy to support scholarships for the Computational Biology Camp.**

**Stephanie Ramos**, our STEM Leaders program coordinator, was awarded the student-selected Phi Beta Kappa Best Mentor Award for 2019.

## New major, multiyear grants

**Colin Johnson** and Joe Baio (Chemical, Biological, and Environmental Engineering) have received a National Science Foundation (NSF) three-year \$450K grant to identify the molecular mechanisms that mediate cell membrane repair. Their work will focus on new spectroscopic and other studies of dysferlin structure and function.

**Ryan Mehl, Rick Cooley** and **Weihong Qiu**, along with Chris Cebra and Shay Bracha from the OSU Carlson College of Veterinary Medicine School, received a College of Science

Research and Innovation Seed Program (SciRIS) stage two grant to develop their “Chemically Functionalized Nanobodies” project.

**Victor Hsu** along with Chris Beaudry (Department of Chemistry), Siva Kolluri (Department of Environmental and Molecular Toxicology) also received a SciRIS stage two grant to develop their project titled “Homoharringtonine: Chemical Synthesis and Evaluation of Designed Analogs.”

**Elisar Barbar** won a supplementary NSF grant to continue collaborative work with Nico Loening (Lewis and Clark University) on the structural basis of phosphorylation and alternative splicing in dynein regulation.

**Ryan Mehl** is a collaborator on a newly funded National Institutes of Health grant led by Ray Trievel (University of Michigan) for the project “Unnatural Amino Acid Chemistry for Lysine Methyltransferase Substrate Discovery.”

**Tory Hagen** received a National Institute of Aging grant for his proposed work to study “Triphenylphosphonium-glutathione as a protectant against mitochondrial decay in Alzheimer’s Disease.”



## A FOND FAREWELL

At the end of last summer, we honored our distinguished colleague **Bill Baird** and his wife Beth, as Bill stepped into retirement. Since he arrived at OSU in 1997, Bill has held a joint appointment in Biochemistry and Biophysics and the College of Agricultural Science’s Environmental and Molecular Toxicology Department.

Bill’s impactful career began with seven years at the Wistar Institute in Philadelphia, followed by 17 years in the biochemistry department at Purdue University. He established himself as a world leader in understanding the molecular mechanisms by which polyaromatic hydrocarbons (like the benzopyrene found in coal tar, tobacco smoke and grilled meats) promote mutagenesis and cancer. He led the Purdue Cancer Center for 13 years, until 1997 when OSU recruited him to lead our Environmental Health Sciences Center and to teach general biochemistry to non-majors.


Despite suffering a debilitating stroke in 1998, Bill persevered and, with the support of family – especially his wife Beth – and physicians and colleagues, came back and continued an inspirational career, working part time over the last two decades to delve further into the mechanisms by which chemicals induce cancer. Bill was elected in 1999 as a Fellow of the American Association for the Advancement of Science and received recognition for his “his many years of research, kindness and mentoring of students.”



Bill Baird is celebrated by colleagues, friends and family at his retirement party.

# On the move

## STUDENTS GOING ABOVE AND BEYOND



Goldwater scholar Kendra Jackson at work in the Freitag lab.

### Goldwater momentum

Our department has an enviable track record recently of Goldwater Scholars. Last year, biochemistry alumna Delaney Smith ('19) was the only student from an Oregon institution to win a 2018 Goldwater. This year, two biochemistry and molecular biology (BMB) honors seniors, **Kendra Jackson** and **Isabella Karabinas**, won 2019 Goldwater Scholarships.

**Jackson**, an Oregon native, plans to pursue an M.D./Ph.D. in molecular biology or genetics towards her dream of becoming a physician scientist. Jackson's dream began when she was five years old and witnessed her younger sister's miraculous recovery from acute lymphoblastic leukemia thanks to a new FDA-approved drug. "It really drove home that it wasn't just the physicians and the treatment that were helping my sister and other patients – it was the research behind all of it," Jackson explains.

In Freitag's lab, Jackson is investigating the mechanism by which PRC2, a

specific protein complex important to mammalian development, is recruited to genes for silencing gene expression.

Jackson was recognized with the Goldwater Honorable Mention in 2018. She has received the department's CRIPPS Undergraduate Research Experience award to support her summer research and OSU's Drucilla Shepard Smith Award for academic excellence.

Last summer she traveled to Panama with Global Brigades, an international nonprofit that partners with local doctors to run free health clinics in impoverished communities. In her spare time, she competes in many distance-running events, including the annual 199-mile Hood to Coast Relay.

**Karabinas**, a Mexican-American originally from Southern California, also aspires to pursue an M.D./Ph.D degree towards the goal of conducting laboratory and clinical research in neuroscience as a practicing physician and university-level teacher. A Gateways to the Laboratory internship last summer took Karabinas to a lab

in Weill Cornell Medical College in New York City, where she worked on projects related to neurobiology and behavioral neuroscience in the areas of stress and depression. In Alvaro Estevez's lab at OSU, Karabinas studies the role of a protein essential for cellular survival in the development of neurodegenerative diseases.

Karabinas has won multiple awards, including the Zonta Club of Corvallis STEM Scholarship, Phi Beta Kappa Honor Society membership, the





Southern Oregon Latino Scholarship and the national Hispanic Scholarship Fund award. Most notably, she received the Abby Rockefeller Mauzé Scholar award, which is awarded to interns for outstanding achievements in the Weill Cornell/Rockefeller/Sloan-Kettering Tri-Institutional M.D.-Ph.D. Gateways to the Laboratory Program.

A well-rounded scholar, Karabinas has long pursued the arts as well as science. She has played the piano for 10 years and loves to take courses outside her major, most recently in Middle Eastern literature and medical anthropology.

## Shooting for stars and hoops

**Cooper Lee Stateler** ('19), a first-generation BMB major who grew up near Coos Bay, Oregon, was one of only 30 in his high-school graduating class. He set his sights on college in elementary school, when teachers noticed his potential and encouraged him to pursue higher education despite some family struggles. "I was definitely raised by the village."

Inspired by his teachers as well as his dad, who worked overtime at the local plywood mill and imbued him with a strong work ethic, Cooper studied hard and won a Ford Family Foundation Scholarship, which meets up to 90% of the unmet college costs for financially strapped students. With the financial means to go anywhere, Cooper chose Oregon State after a campus tour guide mentioned that the College of Science medical school admittance rate was much higher than the national average. "If I could do well here, I could go anywhere. It was a no-brainer."

Cooper worked in the Hagen Lab on human clinical trials to test the validity of vitamins for the elderly. The lab



Cooper Lee Stateler '19, top left, enjoys the Oregon Coast with friends.

work became routine, but the time spent elbow-to-elbow with Hagen did not. "I think the world of him," said Cooper. "He's very pro student success, resilient and," Cooper grinned, "extremely smart."

Cooper took on other challenges, too. He volunteered for TRIO Student Support Services to help students from at-risk populations succeed. He played on OSU's intramural basketball league and, his senior year, served as a scout for the Oregon State women's basketball program. Helping the Beavers prepare for their national-level league games "was a tremendous part of my experience here!"

Graduating with an acceptance to Pacific University's Optometry School in his pocket, Cooper is still drawn to his original dream of medical school.

## Making us proud

**Diego J. Rodriguez**, an honors senior double-majoring in BMB and psychology, received the 2019 Marion B. Sewer Distinguished Scholarship from the American Society for Biochemistry and Molecular Biology and, from the Honors College, the Joe Hendricks Scholarship for Academic Excellence and the DeLoach Work

Scholarship for his research in Afua Nyarko's lab on how the WW domain and C2 (WWC) family of proteins selectively bind to proline-rich proteins. Last summer, he interned at the Massachusetts Institute of Technology.

**Isabella Karabinas**, a BMB senior (see above), was awarded an Honors College DeLoach Work Scholarship to further her neuroscience research with Alvaro Estevez. She received an Undergraduate Young Investigator Award for her presentation at the 2019 Society for Redox Biology and Medicine (SfRBM) conference in Las Vegas. The SfRBM only gives out one of these awards each year.

**Jeanine Pestoni**, a BMB major, presented her research in Maria Clara Franco's lab (see p. 9) at OSU's tenth Linus Pauling Institute International Conference. Pestoni won the SfRBM 2018 award (see above). The pressure is on for the Fall 2020 meeting!

**Victor "Tori" Puoci**, an honors BMB senior, used a Summer Undergraduate Research Experience grant to produce the science podcast "At This Point," available on the SoundCloud app. Aimed at a general audience, each 15-minute episode unpacks the science behind a student research project and explores its potential impact on society, with topics

ranging from a blood-testing device that can be used in remote areas to tide pool predators to human brain serotonin levels. “People should have access to understanding how cool science is,” says Puoci, who is adding to his major a certificate in Scientific, Technical, and Professional Communication.

## Summer Research

**We are grateful to donors for supporting undergraduate summer research, which accelerates students’ progress towards future science careers.**

The Cripps Undergraduate Research Experience (CURE) fellowships provide unique, paid research opportunities in biochemistry and biophysics.

Congratulations to 2019 CURE fellows **Maja Engler, Seth Pinckney, Isabella Karabinas, Asra Noor, Dorice Goune Goufack, Mihir Palan, Brooke Galyon, Carolyn Lazaroff, Juno Valerio, Jacob North** and **Audrey Korte.**

The Summer Undergraduate Research Experience (SURE) offers stimulating, paid summer research experiences. Congratulations to 2019 SURE winners **Taylor Kuntz, Ilana Gottfried Lee, Rina Mullendore, Kendra Jackson,**

**Kitty Liu, Rebecca France, Luz Jovita Dimas-Munoz** and **Haelyn Epp.**

## Joel Peterson Undergraduate Travel Award Winners 2019-20

**Thanks to the generosity of alumnus Joel Peterson (see p. 14), many of our undergraduates attended professional conferences this year.**

**Jenna Beyer** —American Society of Biochemistry and Molecular Biology Annual Meeting, Orlando, Florida.

**Delaney Smith** —American Society for Microbiology Microbe Conference, San Francisco, California.

**Isabella Karabinas** —Society for Free Radical Biology and Medicine Annual Conference, Las Vegas, Nevada.

**Allen Aguirre-Burke** — 33rd Annual Hispanic Association of Colleges and Universities National Conference, Chicago, Illinois.

**Joaquin Rodriguez Galvan, Diego Rodriguez,** and **Antony Jozic** — American Society of Biochemistry and Molecular Biology Annual Meeting, San Diego, California.

## Welcome new graduate students!

**Brittany Lasher**, a Pacific Northwest native, earned her M.S. at Johns Hopkins University in Baltimore, studying molecular dynamics simulation involving transmembrane proteins. With a background in chemical engineering, she worked on novel gel materials that mimic skin at the University of Washington.

**Rachel Franklin** graduated from the University of California, Davis with a degree in chemistry. In an honors undergraduate research program, she studied the genetics and proteomics of hair color, and the toxicology of copper to human skin cells. With a special interest in analytical instrumentation, Rachel hopes to expand her knowledge of protein biochemistry.

**Alex Eddins** hails from Hawaii and earned his B.S. at Southern Oregon University in Ashland. He worked on generating a dominant negative inhibitor of c-Jun, and on various National Science Foundation (NSF) Radiation Effects Research Foundation projects on plant-oomycete interactions. His interest is in negligible senescence, specifically the genetics of non-aging organisms.

**Tilottama Chatterjee** earned her B.S. and M.S. in India. Her thesis was a comparison and correlation of serum and placental levels of angiotensin in preeclampsia. She is widely interested in molecular mechanisms that govern biological systems, with an emphasis on signaling and stress.

**Kyle Nguyen** earned a B.S. in biology from Washington State University – Vancouver, where he researched the evolution of legume-rhizobia mutualists and the effects of environmental contaminants on the



New undergraduate students, fall 2019.



mammalian reproductive system. As an undergraduate, he wrote an NSF Graduate Research Fellowship Program proposal on NRF2 homeostasis. His interests lie in aging and the mammalian stress response.

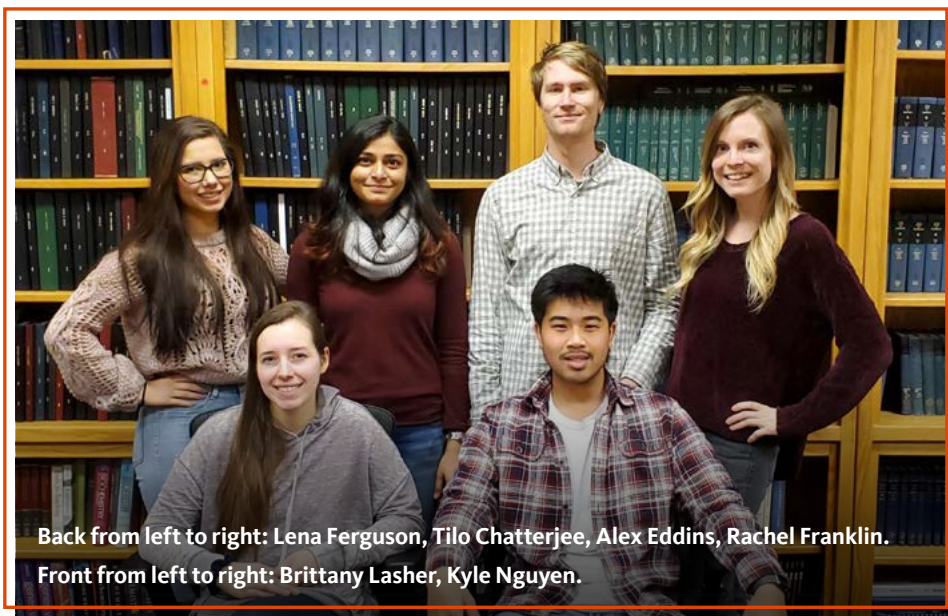
### Janet Helena (Lena) Ferguson

received a B.S. in chemistry at OSU in 2017. Since graduation, she has worked at Gene Tools, LLC on multi-drug resistance to established chemotherapies, and she hopes to develop drugs that may eliminate resistance and thus improve outcomes of cancer treatment. Her primary research interest is developing innovative cancer therapeutics.



Mikayla Pivec

**Mikayla Pivec**, a native of Lynnwood, Washington and Oregon State Beavers basketball star, recently graduated from the OSU Honors College with a major in BioHealth Sciences and a minor in chemistry. As an Accelerated Masters Platform student, she plans to investigate whether cancer patients are receiving adequate nutritional guidance and produce distribution materials to help healthcare professionals communicate important dietary guidelines to improve patient health outcomes.



Back from left to right: Lena Ferguson, Tilo Chatterjee, Alex Eddins, Rachel Franklin.  
Front from left to right: Brittany Lasher, Kyle Nguyen.

**Delaney Smith** graduated from OSU in 2019 with a double major in biochemistry and biophysics and education as well as a minor in chemistry. An Accelerated Master's Platform student, Smith began working in Elisar Barbar's lab. Currently, she is completing a Fulbright fellowship in Ghent, Belgium, where she is studying the structure of cytokines in Savvas Savvides' lab (see p. 16).

### Graduate student awards and honors

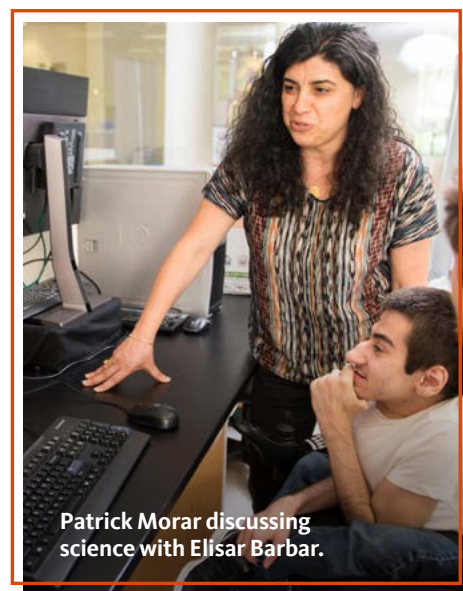
**Patrick Morar**, a second-year doctoral student, was awarded the department's 2019-20 Christopher and Catherine Mathews Graduate Fellowship, in recognition of his academic merit, teaching acumen and research potential. Working in the Hendrix Lab, Morar researches the mutations that cause osteogenesis imperfecta, or brittle bone disease, a rare genetic disorder that he suffers from himself, in order to develop more effective treatments.

**Miranda Leek** won a \$500 travel award from the Society for Redox Biology and Medicine to attend the 26th Annual Conference last November in Las Vegas, Nevada. She also won the Graduate Student Poster

Award at OSU's Center for Genome Research and Biocomputing Fall Conference last September.

**Allyson Erlendson** completed OSU's Graduate Certificate in College and University Teaching. This program provides advanced course work and experiential learning opportunities to students who plan to pursue careers in teaching in higher education settings.

**Kayla Jara** received a donor-supported Graduate Travel Award to support her Oregon Museum of Science and Industry Communication Fellowship for Spring 2020 in Portland, Oregon.



Patrick Morar discussing science with Elisar Barbar.



# Research

DRIVING INNOVATION





## WHEN BASIC RESEARCH UNLOCKS NEW CURES ► MARIA CLARA FRANCO LAB

The Franco Lab is on a roll. In the last year, the lab's fundamental research into what happens when heat shock protein 90 (Hsp90), a chaperone protein expressed in all tissues, becomes oxidized under certain pathological conditions has opened up exciting new drug targets for two unrelated diseases, Neurofibromatosis type 2 (NF2) and ALS (amyotrophic lateral sclerosis), as well as other neurodegenerative diseases and cancer.

Franco's team made the breakthrough discovery while studying NF2, which is characterized by the development of tumors of the nervous system called schwannomas. Due to the lack of the tumor-suppressor Merlin, schwannoma cells increase production of the powerful oxidant peroxynitrite, which in turn oxidizes proteins. One or more of these oxidized proteins supports tumor growth, including oxidized Hsp90 in the form of tyrosine nitration. Because the nitrated form of Hsp90 is generally present in tumor cells but not in normal tissues, targeted therapies could be developed that spare healthy cells, resulting in minimal to no side effects for patients. **Jeanine Pestoni**, a biochemistry and molecular biology undergraduate, is the first author on the study, published in the *Journal of Biological Chemistry* last year, and undergraduate **Oliver Valdivia-Camacho**, a co-author.

The second major discovery in the Franco Lab, published in *Experimental Biology and Medicine* in collaboration with **Alvaro Estevez**, is understanding why certain cells in the nervous system are prone to dying, as in

patients with ALS. Once again, nitrated Hsp90 plays a pivotal role.

Motor neurons, whose long axons extend from the spine and brain stem to control muscles, are regulated by many external stimuli that activate receptors located on the motor neuron surface. Hsp90 typically blocks the P2X7 receptor, which when activated stimulates motor neuron death. Franco and Estevez discovered that the P2X7 receptor complex is highly sensitive to Hsp90 inhibition. Moreover, when Hsp90 is nitrated, it activates the receptor instead of blocking it, and induces motor neuron death. These findings may have broad implications in terms of understanding why motor neurons are vastly more susceptible to degeneration than other cell types in neurodegenerative disorders like ALS.

The findings also suggest that certain chemotherapies may have the unintended consequence of putting nerve cells at risk. "Developing inhibitors specific to the nitrated form of Hsp90 would target cancer cells and preserve healthy tissue, as well as treat neurodegenerative disorders involving nitration of Hsp90," said Franco. "We are working towards understanding how the structure of Hsp90 changes at the atomic level after nitration, to pave the way for the discovery or development of such inhibitors."

It's exactly this sort of flow from basic to applied research that Franco hoped to achieve two-and-a-half years ago when she opened up her lab at OSU and assembled a diverse team of students and interdisciplinary

collaborators. "I envisioned a pipeline in which we, as a team, identify new pro-oncogenic proteins, uncover their mechanism of action, and develop new therapeutic strategies for patients with solid tumors."

Franco's enthusiasm for her team is infectious. "Currently I have a fantastic lab manager, **Carrie Marean-Reardon**, two exceptional graduate students, **Miranda Leek** and **Kyle Nguyen**, and a crew of seven amazing undergraduate students. Without them and our many diverse collaborators both inside and outside of OSU, our research would not be possible."

Franco is grateful for OSU's unique Genetic Code Expansion facility, collaborating with them even before she moved her lab here. "We produce recombinant Hsp90 that is nitrated only in very specific locations, which is key to understanding what parts of nitrated Hsp90 are pro-oncogenic."

**"Many exciting things are happening in the fields of tumor and redox biology, and our lab is poised to play a key part."**

- Maria Clara Franco

Does Franco foresee more discoveries ahead? Most certainly. "Many exciting things are happening in the fields of tumor and redox biology, and our lab is poised to play a key part."

Franco Lab graduate students Kyle Nguyen and Miranda Leek discussing results.



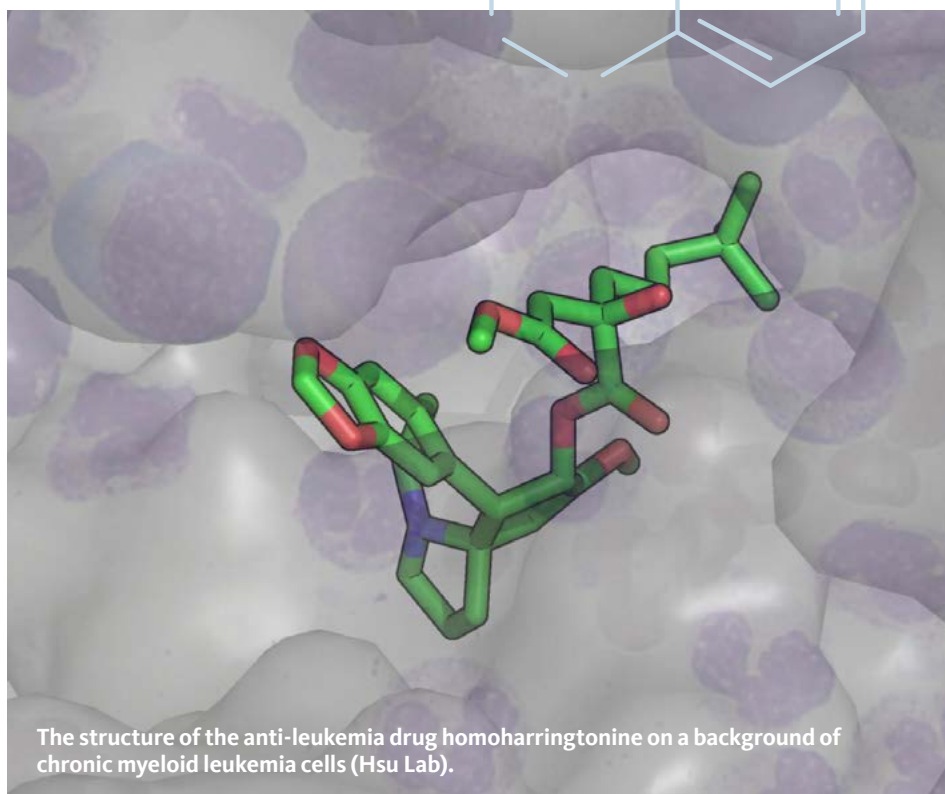
Undergraduate Mihir Palan



Undergraduate Dorice Goune Goufack and Maria Franco.



Victor Hsu



The structure of the anti-leukemia drug homoharringtonine on a background of chronic myeloid leukemia cells (Hsu Lab).

## BUILDING A BETTER CANCER DRUG ► VICTOR HSU LAB

Homoharringtonine (HHT), a plant alkaloid isolated from the plum yew *Cephalotaxus harringtonii*, shows great promise as a starting point for the development of new medicines for multiple forms of cancer. Unfortunately, HHT is highly expensive and difficult to acquire. **Victor Hsu**, working across disciplines with Chris Beaudry (Chemistry) and Siva Kolluri (Environmental and Molecular Toxicology), seeks to overcome this limitation by synthesizing analogs of HHT with improved pharmaceutical properties. The group received a College of Science Research and Innovation Seed (SciRIS) Stage II award for their project.

None of the more than 600 previously synthesized structural analogs of HHT involved any modifications of the cephalotaxine moiety. Chris Beaudry's group, however, recently developed an efficient synthetic route to cephalotaxine,

paving the way to explore a whole new class of HHT analogs.

Hypothesizing that the mechanism of HHT binding to the peptidyl transferase center of the human ribosome involves stacking interactions between the electron-rich benzodioxole group of HHT and the bases of rRNA, Hsu's Lab is simulating and evaluating the geometry and energetics of drug binding by systematically varying synthetically-tractable substitutions on the benzodioxole portion. Hsu is also developing machine learning techniques to further inform the molecular docking simulations.

All new HHT compounds will then be screened in the Kolluri Lab against cancer cell lines. An exciting context for the project are recent demonstrations in human trials that HHT is also active against other cancers. A viable HHT analog could therefore have an enormous impact on human health.



## TARGETING MITOCHONDRIA TO IMPROVE HEALTHSPAN ► TORY HAGEN LAB

**Tory Hagen's** lab is delving into the role that mitochondria, the powerhouses of the cell, play in both cellular aging and age-associated diseases. Scientists now consider mitochondrial decay an integral part of the aging process and of age-associated diseases. This is because dysfunction of mitochondria affects metabolic energy production, promotes programmed cell death and enhances chronic inflammation. The Hagen Lab strengthened this idea by showing that mitochondrial reactive oxygen species (ROS), by-products of metabolic energy production, lead to protein and DNA damage. In turn, as mitochondrial damage increases, cells produce more ROS, which ultimately creates a vicious spiral of mitochondrial damage and further decay with age.

The lab has also identified that an intrinsic aspect of age-related mitochondrial dysfunction revolves around redox perturbations. As a result, the lab seeks to identify metabolites that may preserve mitochondrial redox homeostasis and thereby protect mitochondria even into advanced age. The goal

is to determine if preserving the mitochondrial redox environment also slows or prevents the loss of “healthspan,” or the time of one’s life that is free from chronic disease and disuse syndromes. To this end, the lab utilizes (R)-alpha-lipoic acid (LA), a natural vitamin-like metabolite that serves as a cofactor for certain mitochondrial enzymes associated with metabolic energy production. They showed that LA prevents the age-related decline in mitochondrial redox status in rodents, which maintains their metabolic energy levels. Moreover, they just concluded a National Institutes of Health-sponsored double-blind, placebo-controlled clinical trial at Oregon Health Sciences University that showed LA supplementation significantly lowers adiposity and promotes weight loss in clinically obese subjects. Thus, LA improves energy catabolism and mitochondrial function.

A new research focus, in collaboration with **Joseph Beckman, Pam Bielby,** and Kathy Magnusson (College of Veterinary Medicine) relates to the role that mitochondria play in neurodegenerative diseases of aging. Using transgenic rodent models that

mimic the aberrant expression of amyloid seen in Alzheimer’s disease, the lab discovered that significant mitochondrial decay occurs very early in the disease process in the hippocampus (where learning and memory are centered) before any noticeable learning and memory deficits appear in these animals. The mitochondrial damage is similar to that which occurs during low oxygen events, and suggests that a novel “pseudo-hypoxia” window may occur just as amyloid expression begins. This window presents a unique opportunity to not only understand the importance of mitochondrial dysfunction in initiating neurodegenerative diseases, but also to direct therapies by which cognitive decline could be either slowed or prevented. To this end, the lab has shown that a novel compound they developed, triphenylphosphonium-glutathione (“MitoG”) can target mitochondria and significantly diminish amyloid-related mitochondrial damage. MitoG and other derivatives may be part of a new arsenal of compounds to prevent mitochondrial dysfunction during aging or in age-associated diseases.



Franco lab manager Carrie Marean-Reardon (L) and undergraduate Rina Mullendore.



Tory Hagen

# News



Elisar Barbar with grad students Heather Forsythe and Kayla Jara.

## At the helm

A warm welcome to **Elisar Barbar** the new head of our department, effective January 1, 2020. Barbar brings deep research experience, a passion for student success and a conviction that science is not confined by international borders.

“I am eager to lead this strong department,” says Barbar. “My vision is to move the department forward in pursuing impactful research, and facilitating and promoting accessible, innovative education and outreach. I look forward to working with

extraordinary colleagues to address the needs of a changing world.”

Barbar joined the department in 2004 and was promoted to full professor in 2011. Her lab’s work on intrinsically disordered proteins has strengthened OSU’s growing international reputation in a vital frontier of biochemical and medical research.

As the director of Oregon State’s Nuclear Magnetic Resonance (NMR) Facility, Barbar has established OSU as a center of excellence for biological NMR research by leading efforts to secure over \$2M in funding for its high-powered 800 MHz spectrometer, one of only 50 nationwide.

Former head **Andy Karplus** announced in summer that he would step down from his post, which he has held since 2015 and from 2007-11. We have been enriched by his effective leadership and are deeply grateful for his many contributions. He returns to his teaching and research, as well as serving part-time as associate department head.

Barbar’s desire to prepare the next generation of science leaders goes back to her roots in Beirut, Lebanon. Growing up in a family of teachers, she developed an early love of learning and education that defied expectations of what was possible in a war-torn country.

She earned her bachelor’s degree in chemistry at the American University of Beirut. After teaching high school for few years, she earned a Ph.D. in chemistry at Portland State University and performed postdoctoral research in biophysics at the University of Minnesota.



**Nathan Waugh** and graduate students put on an amazing weeklong Biochemistry and Biophysics Summer Camp for middle schoolers!



Through games and hands-on projects, the 2019 Computational Biology Camp led by **David Hendrix** and graduate students introduced middle school students to basic computer programming and concepts.







IN MEMORIAM

## KENSAL E. VAN HOLDE 1928–2019

By *Chris Mathews*

**Kensal van Holde**, one of the world's premier physical biochemists and a longtime Distinguished Professor in our department, died peacefully at home on November 11, following a brief illness. He was 91.

Ken's scientific odyssey began in the 1950s with a focus on the ultracentrifuge. At the University of Wisconsin, he developed a method for rapid approach to sedimentation equilibrium and its use to analyze the size and shape of protein molecules. This led to a chemistry faculty position at the University of Illinois, where he designed improvements in light scattering and circular dichroism, as well as ultracentrifugation.

Over time, Ken sought an environment where he could focus his biophysical strengths on problems in biology. So in 1967, he moved his laboratory to OSU's newly formed Department of Biochemistry and Biophysics. There, Irvin Isenberg introduced him to chromatin. Using a centrifuge, Irv and Ken described the nucleosome

core particle in disagreement with the prevailing model. Others took notice, and Ken's group was then in a race to define chromatin, a process that continued until 1997, when X-ray crystallography confirmed the van Holde model.

I met Ken in 1977, when I was a candidate for department chair. Thanks to a recent American Cancer Society research professorship, Ken was relieved of all departmental duties. I asked how he wanted to contribute, and he said he would maintain a full teaching load so long as I promised not to put him on any committees. To say that I was delighted would be an understatement.

A spellbinding lecturer, Ken was as devoted to teaching as to research. In the summers he regularly decamped to Massachusetts, where he taught in the Marine Biological Laboratory at Woods Hole.

Ken's research group was devoted to him—to a greater extent than I have seen with other professors. Their



**Ken van Holde with colleagues and former students as he received the 2012 Sigma Xi Monie Ferst Award given to inspiring research mentors.**

striking esprit de corps was evident on Friday afternoons in the "Cave," a small room off the back of Ken's laboratory in Weniger Hall, where biochemists gathered to drink beer and talk science. As liquor was forbidden on campus, the Cave was eventually shut down, even though it was the locus of some excellent science.

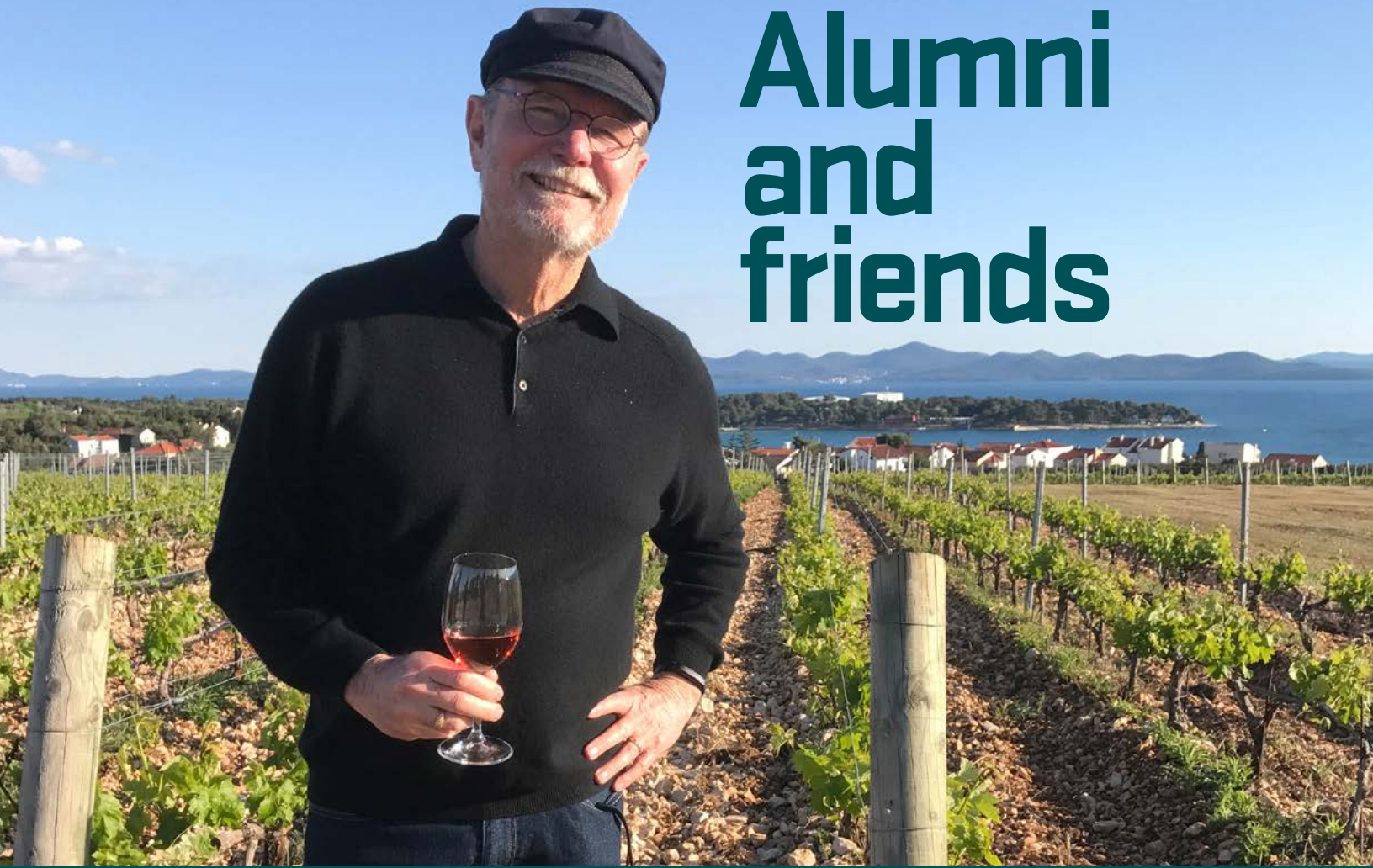
Many of Ken's former students hold faculty positions in leading universities and have made striking contributions to the field. His success as a mentor was acknowledged in 2012, with a major award by Sigma Xi.

Ken was a gifted writer, as was shown in his research monographs and the co-authorship of several textbooks, *Principles of Physical Biochemistry*; *Biochemistry*; *Molecular Biology*, and in 2018, barely a year before his death, *The Evolution of Molecular Biology*, a historical account.

Ken enjoyed a rich family life. With his wife Barbara and their four children, he shuttled between Corvallis, Woods Hole, and their mountain retreat in the Oregon Cascades. Some years after Barb's death in 2010, Ken reconnected with a widowed OSU faculty wife, Myrna Shepper, and they were married in 2015.

Ken was elected to the National Academy of Science in 1989 and to the American Academy of Arts and Sciences in 1996.

# Alumni and friends



## Finding his true north

Before he founded world-famous Ravenswood Winery, **Joel Peterson** (Microbiology '69) was a pre-med student, ambulance driver, backpack traveler and research immunologist. Given these twists and turns, he well understands the vital role that exposure to a diverse range of professional experiences can play for undergraduates searching for their true passion.

To help undergraduates find their calling, Peterson funds discipline-related travel grants for biochemistry and biophysics and microbiology majors to participate in professional conferences, present their research or pursue a distant internship.

“Science is as much about the people as anything,” says Peterson, who only understood the breadth of career options after traveling to professional microbiology conferences. “I wanted students to have access to the same insights I had so that they could make more strategic decisions about their own future.”

**“I wanted students to have access to the same insights I had so that they could make more strategic decisions about their own future.”**

**- Joel Peterson**

Serving on the College of Science Board of Advisors since 2015, Peterson has enjoyed bringing an entrepreneurial background to help the College monetize more of its activity in a belt-tightening era. He is a strong proponent of diversity and ensuring that all science students have an equal chance at success.

Peterson says seeing students' enthusiasm and idealism “makes me feel like I'm doing something worthwhile.” He advises students to “work your a## off, learn as much as you can and understand that you're in a world that doesn't necessarily believe in science, but you're one of the few people who can make a huge difference.”





## A honking celebration

At a wonderful dessert gathering last spring to celebrate the achievements of our nearly 40 graduates of the class of 2019, **Victor Hsu** created bumper stickers for each student “Honk if you passed biophysics!” These were a big hit! Some graduates were looking to move straight into the workforce, but most were targeting graduate, medical or pharmacy school. Along with recognizing each graduate, we gave “Outstanding Senior Awards” to four of our graduates – **Savanna Avila-Crump, Jenna Beyer, Cooper Stateler** and **Hannah Stuwe** – in recognition of their leadership, service and community-building, and passion for all things biochemistry and biophysics. The evening ended with lots of energy and laughter as the graduates joined in a longstanding tradition, the singing of a couple of **Kevin Ahern's** rousing metabolic melodies. This spring we look forward to celebrating our 2020 graduation cohort, our biggest yet, with close to 80 total graduates.

## 2019 Distinguished Alumni Award

**Janet Leeds** (Ph.D. '86) won our 2019 Distinguished Alumni Award, which recognizes biochemistry and biophysics alumni who have achieved distinction and brought

honor to the University through exemplary contributions to society and the world. Pictured here with graduate student hosts Amber Vogel and Lillian Padgitt-Cobb, Janet is currently Executive Director of Drug Metabolism and Pharmacokinetics at Portola Pharmaceuticals. She served in the Peace Corps and worked with Chris Mathews on her doctoral research at OSU before launching a 30-year impactful career in the pharmaceutical industry that continues today.



Janet's professional achievements are exemplary. Over eight years at Isis Pharmaceuticals, she built and managed the bioanalytical group, in the process developing several novel patented analytical methods. In the Toxicology and Pharmacokinetics Department, her investigation of dose-limiting toxicities of systemically administered

phosphorothioate oligonucleotides was critical in the elucidation of plasma concentrations associated with complement activation in non-human primates and allowed oligonucleotides to be safely administered by IV infusions in early clinical development. Janet also worked on studies and reports used in the preparation of seven investigational new drugs (INDs), as well as the new drug application (NDA) for Vitravene™, which was the first approved antisense drug. At Biota, Inc., an anti-viral start-up company, Janet worked on the team that discovered a novel chemistry that, when conjugated to known HIV-reverse transcriptase inhibitors, were 1,000-fold more active against resistant clinical isolates of HIV than the parent nucleoside analogues themselves. She has worked on therapeutics for a broad range of indications, from anti-infectives to central nervous system disorders, cancer and inflammation. While working at SIGA Technologies, Janet oversaw all toxicology, pharmacokinetics, and bioanalytical work for the anti-poxvirus therapeutic as well as discovery projects, including the dengue fever and Arena virus programs. For the last five-and-a-half years Janet has worked at Portola Pharmaceuticals in South San Francisco. Portola focuses on diseases of the blood and Janet has overseen successful submissions of all pharmacokinetic, clinical

pharmacology and toxicology sections of NDAs for two compounds approved by the Food and Drug Administration.

While on campus last spring to receive her award, in addition to her research seminar Janet met with about 25 undergraduates to talk about career paths. Congratulations, Janet, and thank you for sharing your insights and experience with our students!

## Recognized for research

**Delaney Smith** (Biochemistry and Biophysics '19) was selected for a 2019-20 Fulbright scholarship, one of the most prestigious national awards a student or alumnus can receive. Delaney is conducting research as a Fulbright Fellow at Ghent University in Ghent, Belgium in the laboratory of professor of structural biology Savvas Savvides, which focuses on the structures and mechanisms of proteins and their role in inflammation, autoimmune disorders and cancer.

Delaney, who is a member of our Accelerated Master's Platform, will also be taking specialized courses in proteomics, bioethics, biostatistics and experimental structural biology.



Delaney Smith

She plans to enroll in a joint M.D.-Ph.D. program and pursue a career with one foot in research and the other foot in medicine.

## Three biochemistry and biophysics alumnae received prestigious National Science Foundation (NSF) Graduate Research Fellowship Program (GRFP) awards in 2019:

**Delaney Smith** ('19) was awarded the NSF graduate fellowship based in part on her undergraduate research project in Elisar Barbar's lab on the characterization of how phosphorylation of disordered regions of certain cellular units modulates the activity of the motor protein dynein. The latter is responsible for moving cargo around a cell. Dynein also interacts with thousands of other proteins and is implicated in a vast number of vital cellular functions.



Jenna Beyer

**Jenna Beyer** ('19) won an NSF graduate fellowship based in part on her research in one of the most innovative areas of biochemistry at OSU — genetic code expansion, or the incorporation of non-standard amino acids into proteins to create new chemical functionality and engineer living systems. As an undergraduate in the lab of biochemists Ryan Mehl and Richard Cooley, Jenna characterized



Nathan Jespersen with mentor Elisar Barbar.

the function and solved the crystal structures of computationally-designed, improved synthetases specific for the non-standard amino acid 3-nitro-tyrosine (nitroTyr). The advances overcame some long-term challenges faced by the Mehl Lab and also guided a deeper understanding of synthetase catalysis.

Jenna is currently pursuing a Ph.D. in biochemistry and molecular biophysics at the University of Pennsylvania in Philadelphia.

**Lynda Bradley** ('15) is now pursuing a Ph.D. in the Department of Biology at Emory University. She conducted research on infectious diseases at the KwaZulu-Natal Research Institute for Tuberculosis and HIV in South Africa as a Fulbright Scholar during 2017-18.

## Newly Minted Ph.D.s and Masters graduates

**Nathan Jespersen** completed his Ph.D. in the Barbar Lab in September





virology work at the University of Paris for nine months.

Nathan published three first-author papers, in *Life Science Alliance* (2019), *Journal of Molecular Biology* (2019, with cover art), and *Trends in Biochemical Sciences* (2020). In addition, he was a middle author of two articles, one in *FEBS Letters* (2015) and *Journal of Biological Chemistry* (2020). He presented his work at the Gibbs Biothermodynamics and the Protein Society conferences. He also gave talks at the dedication ceremony of OSU's new 800 MHz spectrometer, which was attended by the OSU president and provost, and at the inaugural Nuclear Magnetic Resonance Symposium in summer of 2017.



Dan Breyse

Nathan is currently a postdoc in Sweden at the Laboratory for Molecular Infection Medicine Sweden at Umeå University, working with Jonas Barandun. Nathan is fondly remembered by our department for his congenial nature, his willingness to help everyone, and his tendency to always ask the most questions in a group.

**Dan Breyse** completed his M.S. degree in June 2019. His thesis research with Gary Merrill focused on identifying the enzymes that convert the widely used chemotherapeutic drug doxorubicin to a highly cardiotoxic metabolite, doxorubicinol. The research, done in collaboration with others at OSU, the University of Washington and Montana State University, is published in the March 2020 issue of *Drug Metabolism and Disposition*. Currently, Dan is working at the Corvallis Clinic. He plans to attend medical school in the fall.

2019. As a doctoral candidate, he distinguished himself by competing and receiving prestigious international and university-wide awards, including the 2017 Chateaubriand Fellowship from the Embassy of France in the U.S. and the Robert and Clarice MacVicar Animal Health Scholarship from OSU in 2018. Both allowed him to conduct



## Honor Roll

We are proud to recognize the department's annual supporters who have made outright gifts or pledge payments totaling \$250 or more between January 1, 2019, and December 31, 2019.

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## Thank you!

Every attempt has been made to ensure the accuracy of these lists. However, if you notice an error, please contact Pam Powell, Associate Director of Stewardship, OSU Foundation, **541-737-5820** or **Pam.Powell@osufoundation.org**.



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